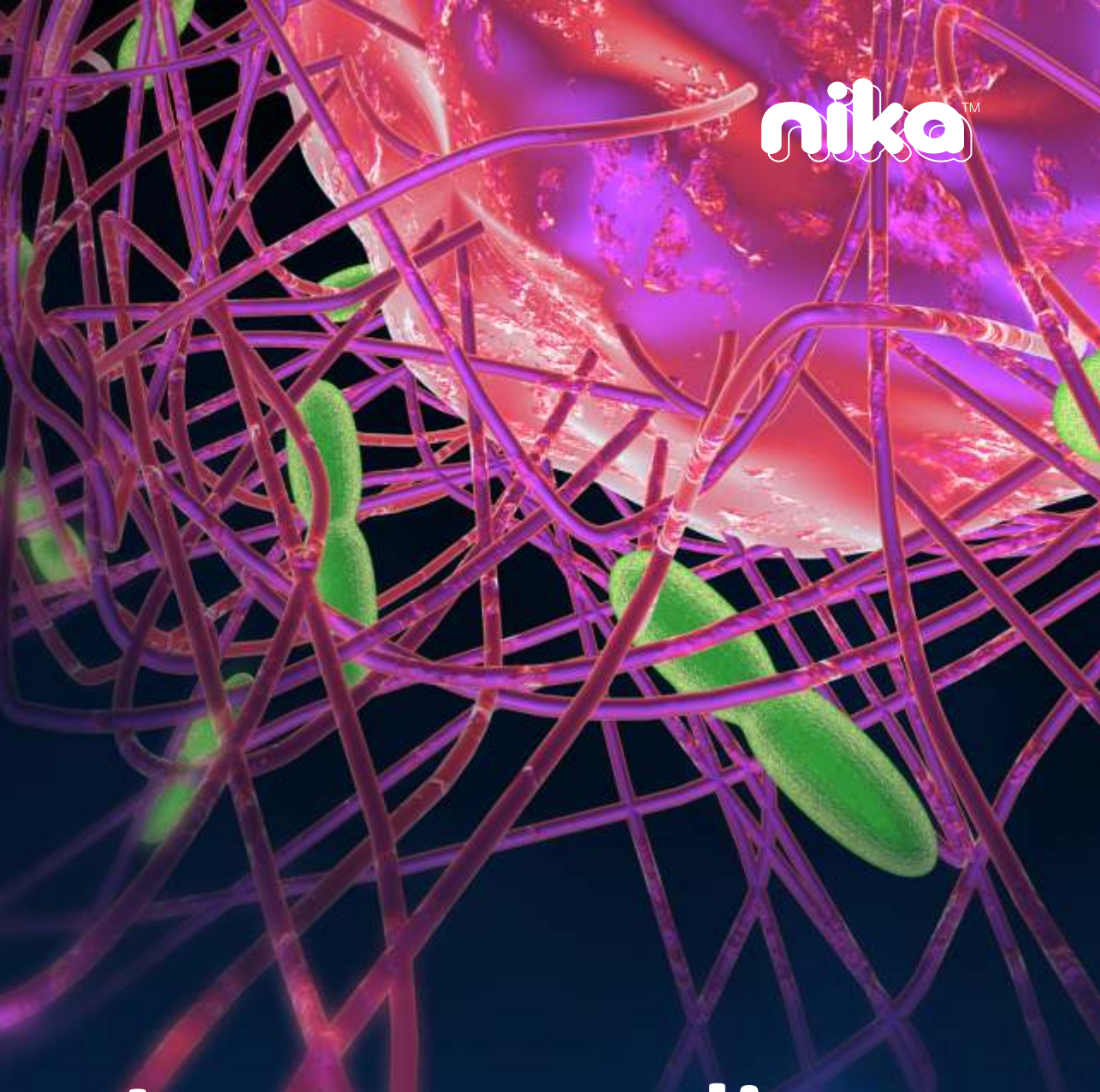

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Lysozyme dimer

in therapy and prophylaxis of animal diseases

QUARTA - Wydawnictwo i Realizacje Multimedialne

Edward Malinowski

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NIKA Health Products Sp. z o.o.
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Lydium-KLP™

We shall hear more about lysozyme.

Alexander Fleming

CONTENTS

PROFESSOR WITOLD KICZKA

Prof. Witold Kiczka M.D., Ph.D (1924-2006) has been conducting research on lysozyme and on the lysozyme dimer for many years. His work has led to complete success.

The lysozyme dimer was synthesized, an in vitro evaluation method was developed, preclinical trials have been conducted on laboratory animals, and clinical trials have been conducted on both healthy and sick animals.

As a result, the lysozyme dimer became a medication called Lydium-KLP. Neither the therapeutic dose nor the concentrations up to 1000 times higher than the therapeutic dose show any toxic, cytotoxic or mutagenic effects.

When compared to the substrate (chicken egg lysozyme), the dimer is about 500 times less toxic (32,33,44).

PROPERTIES AND ACTIVITY

The lysozyme dimer modulates the synthesis of TNF& and stimulates the production and release INF& (Table 1) as well as Il-2 and Il-6 in high concentrations by human lymphocytes stimulated with concanavalin A (32,42). This dimer activates the proliferion of T and B lymphocytes, stimulates the production of Il-1, Il-2, INFγ, and modulates secretion of TNFα in healthy piglets (137). The increase of production of Il-1, Il-2,Il-6, and INF was noted as effect of lysozyme dimer activity in the fish model of experiments (134,135).

It was shown on laboratory animals that the dimmer increases the response to nonspecific antigen and immunoglobulin production (116,120), stimulates enzymatic activity of pulmonary macrophages (59), protects against antibiotic immunosuppression (143,145,148), eliminates the immunosuppression effects of cyclophosphamide (118), and lowers the level of free oxygen radicals in blood and inflamed udder secretions (91,102). The lysozyme dimer activates in vitro and in vivo phago-

cytosis, which is reflected in a higher percentage of granulocytes and macrophages capable of ingestion of bacteria and NBT reduction than in the control group, and a higher phagocytic index (10, 20, 35, 37, 38, 39, 55,107,143,153).

Table 1.
The effect of the lysozyme dimmer on the production of TNFα and INFα by human lymphocytes stimulated with concanavalin A (32).

Concentration of lysozyme dimer	TNFα pg/ml	INFα unit/ml
control	205.11	4.97
1 mg/ml	38.07	8.81
0.3 mg/ml	17.19	9.44
0.1 mg/ml	13.75	17.96
33 µg/ml	36.11	3.67
10 µg/ml	22.22	7.56
3.3 µg/ml	54.91	6.26
1.0 µg/ml	18.47	33.91
0.3 µg/ml	14.47	10.07
0.1 µg/ml	94.16	4.97
33 ng/ml	172.46	10.07

In vitro studies show that lysozyme dimer influences the oxygen metabolism of phagocytic cells in blood, milk and secretions from the inflamed udders of cows. Stimulation or inhibition of the production of reactive oxygen radicals depends on concentrations of lysozyme dimer (Table 2, Figure 1). Lysozyme dimer in concentrations of 0,25 µg/ml or even 0,1 µg/ml activates chemiluminescence inducted by zymosan in blood samples. It decreases the spontaneous chemiluminescence in secretions from inflamed udders in concentrations of 0,5 µg/ml and 5,0 µg/ml.
The recorded influence on spontaneous chemiluminescence was determined after a 20 min. preincubation. It seems probable that longer incubations of blood or milk (inflamed secretion) with lysozyme can bring more precise results. Stimulation of zymosan-induced chemiluminescence and the inhibition of spontaneous chemiluminescence seem to be the most significant treatment factors.

Table 2.
The effect of the lysozyme dimer on the spontaneous and zymosan stimulated chemiluminescence levels in blood samples from healthy calves (mV/0.1ml) (102).

Concentration	Level	Timing of measurements (minutes)						
		0	05	10	15	20	25	30
Control n=10	$\bar{X}$ SD	719 80	1 099 253	1 146 257	986 171	836 86	760 59	727 50
0.05 µg/ml n=10	$\bar{X}$ SD	711 64	1 099 234	1 138 243	972 158	831 96	758 57	720 44
0.1 µg/ml n=10	$\bar{X}$ SD	695 27	1 090 212	1 152 277	982 171	826 100	757 57	725 41
0.25 µg/ml n=10	$\bar{X}$ SD	700 53	1 112 206	1 185• 259	997 156	841 92	763 56	719 40
0.5 µg/ml n=10	$\bar{X}$ SD	702 50	1 080 221	1 113 220	952* 148	830 90	753 56	727 40

Explanation: “0” spontaneous chemiluminescence before stimulation by zymosan,
*P<0.05; •P<0.0001.

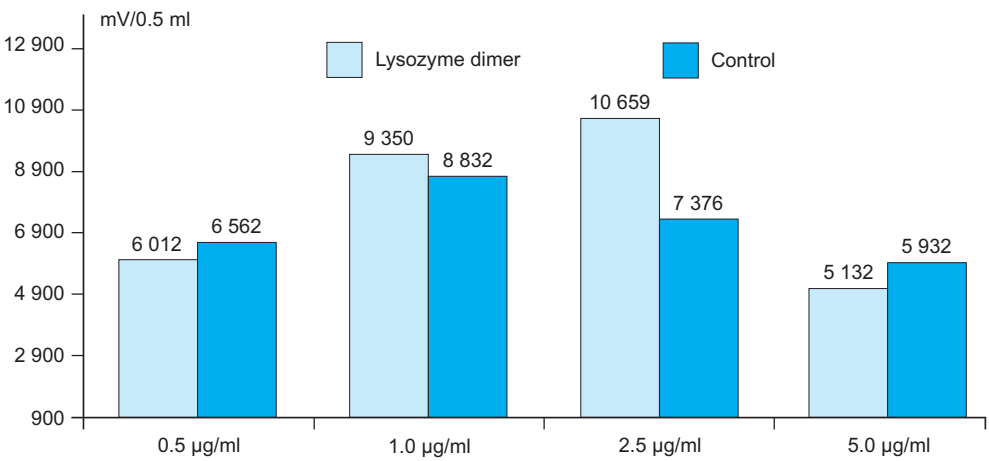

Figure 1.
The effect of different concentrations of lysozyme dimer (KLP-602) on peak values of chemiluminescence in secretion from clinically inflamed udders (91).

Comparison of the influence of the lysozyme dimmer in concentrations of 0.5 µg/ml and 5.0 µg/ml and the also slightly different reaction in the whole blood of cows, depending on the health condition, seems to point out that lysozyme dimer can stimulate or inhibit the NADPH oxidase and superoxide dismutase as well as catalase and glutathione dehydrogenase.

The injection of Lydium-KLP can accelerate phagocytosis and at the same time prevent tissue and organ injury by reactive forms of oxygen (free oxygen radicals).

Lysozyme dimer is also capable of inhibiting virus replication in chicken embryos and in tissue culture. The antiviral activity of lysozyme dimer against Influenza virus A/Shanghai is 100 times higher in embrionated hen eggs than in the standard substance ematadine. In vitro tests of VERO cells infected with the Measles virus and the Mumps virus showed a virus titer reduction of more than 60% or 75% respectively at a dosage of 0.5mg/ml of medium. A dosage of 0.1mg/ml of medium resulted in the inhibition of more than 95% in VERO cells infected with the Herpes simplex virus. The results indicate the mode of action to be an inhibition of the virus penetration into the cells. Antiviral acticity of lysozyme dimer was also confirmed for Vaccinia and Polio virus.

In vivo challenge-experiments showed antibacterial activity of lysozyme dimer against Pasteurella haemolytica in calves and Actinobacillus pleuropneumoniae in pigs (45). Lydium-KLP also inhibits the development of lymphatic leukemia in AKR mice, and limits the extent and intensity of interstitial pneumonia experimentally inducet by the influenza virus (58,59).

Table 3.
Effect of lysozyme dimer (KLP-602) on the survival of the chick embryo fibroblasts and the CC81, TBTR and MDBK cell lines maintained in Parker's medium without serum (152).

Concentration of lysozyme dimer	Chick embryo fibroblasts	Cell line CC81	Cell line TBTR	Cell line MDBK
1.0	6*	0*	3*	2*
2.5	6*	1*	3*	2*
5.0	6*	4*	6*	2*
10.0	6*	3*	8*	0*
25.0	NT	3*	NT	NT
50.0	NT	T	NT	NT
100.0	NT	T	NT	NT

Explanation: * - prolongation of survival time of cells expressed in days in relation to the control, NT - not tested, T - toxic action.

In the different systems used in vitro it was found that lysozyme dimer (KLP-602) shows multiple indirect and direct effects on the process of bovine oocyte fertilization which depends on the concentration of the substance. Lysozyme dimer at a concentration of 10 mg/ml, favorably affected the oocyte maturation, showing the highest rate of oocyte which reached stage II metaphase after 36h of culture. Furthermore, a significant increase in the fertilization rate was observed at concentrations of 0.1 to 10 mg/ml of this drug. The percentage of fertilized oocytes that reached the morulae and blastocyst stages was significantly higher in the case of oocytes fertilized in the presence of 10 mg/ml of lysozyme dimer (47).

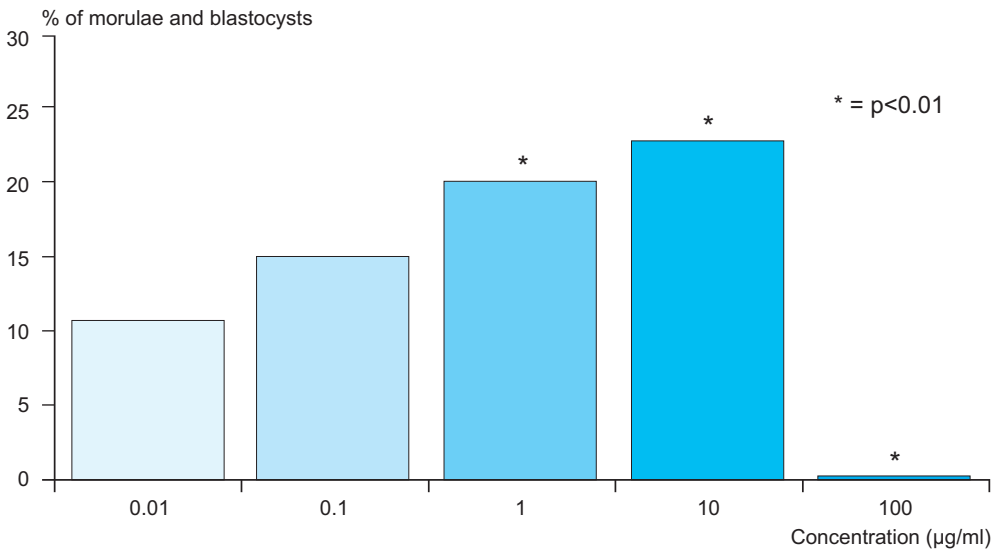

Figure 2.
Development of oocytes fertilized in the presence of different concentrations of lysozyme dimer (47).

In cases of simultaneous irradiation of rat chests, Lydium-KLP decreased vascular endothelium damage and reduced interstitial inflammatory reaction in the alveolar septa. A decrease in epithelium damage and its intensified regeneration was observed in bronchi. In the trachea, the inflammation of respiratory epithelium was also reduced. The results point to the protective effects of Lydium-KLP upon early postirradiation damage (141). It seems that the mild effects of lysozyme dimer upon the inflammation associated with early postirradiation reaction results likely from its antiinflammatory influence via decreased levels of free radicals in the blood serum (58, 141).

It was determined (Table 3) that the lysozyme dimer at the level of 1-50 mg/ml of the medium was not only nontoxic for the cells under investigation, but it also benefi-

ficially influenced the duration of their survival: they remained in the form of unchanged monolayers for 3-6 days longer than the controls (152).

In concentration of 10 µg/ml and 15 µg/ml, lysozyme dimer beneficially affect the motility and acrosome integrity of dog and boar spermatozoa in vitro (2, 112). Adding from 4-10 µg of lysozyme dimer to 1 ml of fresh stallion sperm resulted in a significant increase in the percentage of normally mobile spermatozoa in vitro (2, 112). Adding from 4-10 *m*g of lysozyme dimer to 1 ml of fresh stallion sperm resulted in a significant increase in the percentage of normally mobile spermatozoa after defrosting the sperm. It also revealed an improvement of the mean values of mobility and AspAt activities in experimental sample compared to the control of boar spermatozoa both after equilibration and following defrosting. Based on the results of laboratory examinations, it can be surmised that lysozyme dimer may stabilize the cell membranes of spermatozoa during their preservation at low temperatures (26, 27).

In vitro studies demonstrate that lysozyme dimer restores the susceptibility of MRSA and MSSA to gentamicin, clindamycin and trimethoprim-sulfamethoxazole (41,43). This phenomenon was also observed in animals with wounds infected with antibiotic resistant strains of Staphylococcus aureus (MRSA).

It should also be emphasized that lysozyme dimer is effective in the treatment of human alopecia androgenetica and alopecia areata (1).

Lysozyme dimer used as injections of Lydium-KLP is active and effective in the treatment of many diseases in various animal species (7). Lydium-KLP was administered to cows as treatment of acute, chronic and sub-clinical mastitis, placenta retention, ichoroid metritis, chronic endometritis, and wounds and purulent fistulas of the udder. It was shown that intrauterine infusions of Lydium-KLPare useful in treating cystic ovary disease. This drug was administered to calves affected with gastroenteritis or bronchopneumonia. The preparation was given to horses as treatment of enteritis, influenza, bronchopneumonia and phlegmon, and mares as treatment of metritis. It was also administered to sows in cases of mastitis-metritis-agalactia syndrome, to pigs in cases of pneumonia and edema disease, and piglets in cases of gastroenteritis. The preparation was effective in treating dogs for inflammations of the alimentary tract, the respiratory system, the skin, and the ear as well as in treating panleukopemia in kittens and paratyphus in fox cubs. The drug also had favorable effects on bacterial and viral diseases of poultry.

Lysozyme dimer demonstrates prophylactic activity against selected diseases of cows, calves, piglets, sows, foals and fowl.

Lydium-KLP was administered intravenously, intramuscularly, subscutaneously, intramammarily, and intrauterinealy in doses of 0.1 to 0.01 mg/kg of body weight once or every 12 or 24 hours for several days. There were single and multiple intramammary administrations and medication was administered intrauterinealy once or twice at 14-day intervals.

In all these cases, the following therapeutic effects of the preparation wereobserved: complete recovery, periods of improvement, increased antibiotic efficacy, and faster impregnation among cows and sows.

Based on the studies and observations, it was ascertained that 0.02 mg of lysozyme dimmer per 1 kg of body weight is the therapeutic dose, and the improvements observed in bacterial and viral diseases are clearly tied to the first injec-

tion of the preparation. When administered in combination with antibiotics, a 0.01 -mg/kg injection of Lydium-KLP was shown to be sufficient.

Summary

Lysozyme dimer stimulates the synthesis of some interleukins and interferon alpha and gamma. It also modulates the generation of TNF alpha, precluding all the negative effects associated with the excess level. Lysozyme dimer induces the activity of phagocytizing cells and at the same time prevents the excess generation of free radicals. It also demonstrates considerable antiviral activity against several viral strains. Lysozyme dimer is less active against bacteria in vitro, but in vivo its antibacterial properties are similar to the antibacterial activity of some antibiotics. Lastly, lysozyme dimer causes a reversal of antibiotic resistance in drug resistant strains of Staphylococcus aureus (MSSA and MRSA).

Lysozyme dimmer is currently approved for use in veterinary medicine. It is very useful in treatment of some animal's diseases as the only drug. However, lysozyme dimer also significantly increases the efficacy of antibiotics.

Profitability of dairy cattle farming is largely dependent on the ability to control two groups of diseases commonly affecting dairy cows, i.e. inflammations of the mammary gland and fertility disorders. Antibiotics are widely used in treatment and prophylaxis of mastitis, and hormones combined with antibiotics are often considered good remedies in controlling infertility. However, antibiotic and hormone residue in milk and meat can be harmful to human health. Therefore, a search continues for new methods of treatment and prophylaxis that would allow to reduce their use.

Lydium-KLP has several very interesting and promising properties with possible applications in this area of study.

LYDIUM-KLP IN TREATMENT AND PROPHYLAXIS OF MASTITIS

Each year, 20-50% of cows are affected by mammary gland inflammation with local and systemic clinical symptoms. In some herds, up to 150-200 cases of clinical mastitis were observed per 100 cows during one year. Susceptibility to the diseases increases proportionately to high milk productivity. Pathological changes last for 6-14 days depending on etiological factors, the clinical course of the disease, and the time when treatment began. Large percent (20-40%) of cases do not respond to the first therapy and the treatment must be repeated.

The etiological agents of bovine mastitis are: bacteria, yeast-like fungi, mycoplasmas, viruses, and even algae. Some of these microorganisms are pathogenic for humans. About 80-90% of mammary gland infections in cows are caused by tree genes of bacteria, i.e. streptococci (Str. agalactiae, Str. dysgalactiae, Str. uberis), staphylococci (Staph. aureus, CNS - coagulase negative staphylococci), and colibacillus (mainly E. coli). Streptococcus- and Staphylococcus-genes of microorganisms cause all forms of mastitis, and Escherichia coli frequently causes the per-acute and acute form. During the last few years an increase in yeast mastitis has been observed as a result of the unreasonable use of antibiotics.

Clinical mastitis is treated with intramammary applications of antibiotic products (solutions) for 2-5 days. Severe cases also involve systemic treatment (antibiotics, electrolyte fluids, glucose, calcium preparations, cardiac drugs, vitamins, and hormones). Efficacy of treatment of acute cases with the use of intramammary antibiotic products is 50-80%. The success rate of repeat treatment is only 25%. Inflammations caused by Staphylococcus aureus and Arcanobacterium pyogenes are especially difficulte to treat. Low efficacy of the initial and follow-up treatments is caused by antibiotic resistance of the bacteria strains and by the inefficiency of the udder's immune system. The system is further suppressed during treatment by high doses of antibiotics and by the media components of intramammary preparations.

About 30-70% of cows are permanently affected with subclinical mastitis, which is the maim reason for quantitative milk losses and significantly affects changes in the microbiological and biochemical compositions of milk. Streptococci and staphylococci are the main etiological factors of subclinical mastitis. Other microorganisms cause the disorder less frequently. In many cases, despite of an increased somatic cell count, the results of a routine microbiological test are negative. Such a condition is called non-bacterial irritation or aseptic subclinical inflammation. Subclinical inflammations last for 3-6 month or more and spontaneous recoveries occur in only 10-20% of cases.

Subclinical mastitis is usually treated when the udder is dry. Intramammary administration of extended-action DC preparations has proven to be the most effective. These preparations usually contain penicillin and streptomycin or other antibiotics (cloxacillin, nafcillin, neomycin, erythromycin, tetracycline, cephalosporins). Intramammary administration of drugs during lactation is expensive, not always effective, and less valuable due to disease recurrence and the possibility that milk designated for human consumption will become contaminated with antibiotics if the hiatus periods are not observed. These are the reasons why administering antibiotics to entire herds of lactating cows has not been widely accepted. However, due to the losses caused by subclinical mastitis, suggestions are being raised to approach it just like clinical mastitis and to begin treatment immediately after the disease has been detected.

TREATMENT EFFICACY AND THE COURSE OF REGRESSION OF SUBCLINICAL MASTITIS FOLLOWING INJECTION OF LYDIUM-KLP

Material and methods

The study was conducted on 218 cows from 10 herds. The cows were 3-10 years of age, had a daily milk output of 6-30 kg, were in various stages of lactation, and were kept under different conditions of cleanliness. The cows selected for treatment had increased cell counts (CMT ++, +++) 2-4 weeks prior to treatment in at least one udder quarter. The changes were confirmed one week later and on the day the treatment began. The diagnosis was based on clinical examination, CMT and results of laboratory tests of samples collected aseptically from each quarter. Bacteriological examinations were performed according to generally accepted principles (Diagnostyka Laboratoryjna Mastitis, Puławy 1978). Somatic cell count (s.c.c.) was determined by the Fossomatic 90 (Foss-Electric Denmark).

The experimenthal treatment covered the following disorders: subclinical bacterial inflammations where Streptococcus agalactiae or Staphylococcus aureus were fond with an s.c.c. higher than 400,000/ml; Strptococcus uberis, Streptococcus dysgalactiae, coagulase negative Staphylococci, and yeast with an s.c.c. higher than 500,000/ml, and Corynebacterium bovis, Escherichia coli, Micrococcus species or Streptococcus species with an s.c.c. higher then 800,000/ml. When bacteriological test results were negative and the somatic cell count was higher than 800,000/ml, subclinical aseptic inflammation was diagnosed. Latent udder inflammations (s.c.c. below 400,000/ml) caused by Streptococcus agalactiae or Staphylococcus aureus were also considered pathological.

Nine to 31 cows were treated per individual herd. One hundred nineteen of them had recently calved or were less than 5 month pregnant. Eighty-five cows had one affected quarter and 133 had subclinical inflammations in 2-4 quarters. The s.c.c. was below 3,000,000/ml in 304 quarters and it was higher (3,000,000-8,000,000/ml) in the remaining 133 quarters.

Treatment consisted of a single intravenous injection of 0.02 mg/1 kg of body weight of Lydium-KLP. The drug was not administered during the first week after calving or two weeks prior to anticipated drying. Clinical and bacteriological control tests and the somatic cell count were done 7, 14, 21, and 28 days following the injection. In cases of aggravation made visible through clinical changes, antibiotics were administered intramammarily. If the bacteriological test results were negative and the quarter milk s.c.c. was below 400,000/ml, the treatment of this quarter was considered effective.

Results

Figure 3 illustrates the regression dynamics of subclinical mastitis following injection of Lydium-KLP. On day “zero”, 417 quarters were affected, 71,5% of which were subclinical bacterial inflammations, 23% were non-bacterial inflammations, and 5,5% were latent infections that had been usually found in quarters adjacent to the ones affected with bacterial or aseptic inflammations in the same cow. Control tests performed on day 7 showed that the bacterial inflammations had decreased by one half, the percentage of aseptic inflammations had increased, and the milk from some quarters showed macroscopic changes that were sometimes accompanied by clinical changes in the udder. Further tests showed that the number of healthy quarters continued to grow with an s.c.c. below 400,000/ml and a negative bacteriological test result.

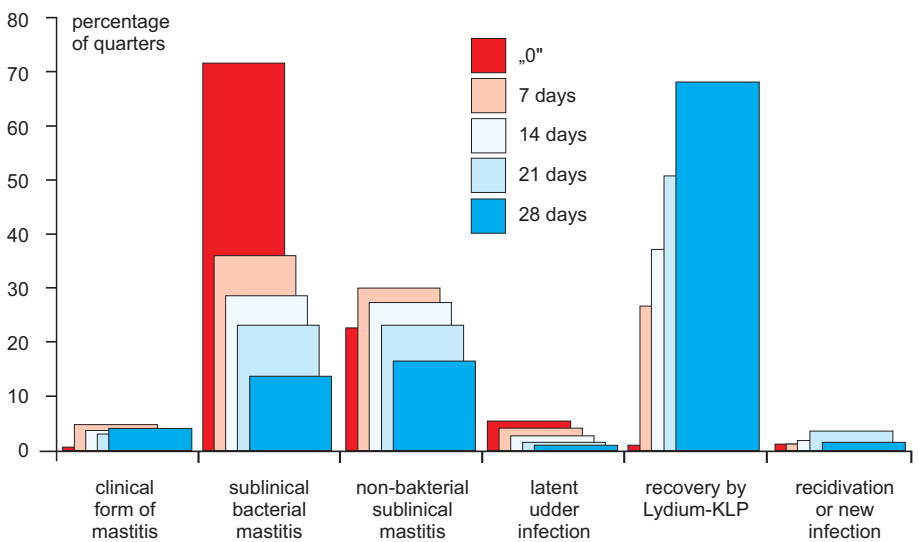

Figure 3.
Regression of subclinical mastitis after an injection of Lydium-KLP (67, 70).

On day 28, 62,6% quarters were found to have recovered as a result of Lydium-KLP injection. When evaluating the drug's efficacy, it is also important to consider 30 quarters (7,2%) that were re-infected and showed subclinical inflammation after the original changes disappeared. The overall recovery rate following Lydium-KLP injection was 69,8%.

Subclinical bacterial inflammation remained in 12.5% of the quarters. Certain portions of them were recurrences or infections with a bacterium different than the original. Following are the recovery rates of quarters infected with different types of bacteria: Staphylococcus aureus: 50%, Str. agalactiae: 59.7%, Streptococcus dysgalactiae: 66.7%, Streptococcus uberis: 78.3%, and coagulase negative Staphylococci or other microorganisms: 86.2%. Among others, two cases of mastitis caused by yeast turned out to be unsusceptible.

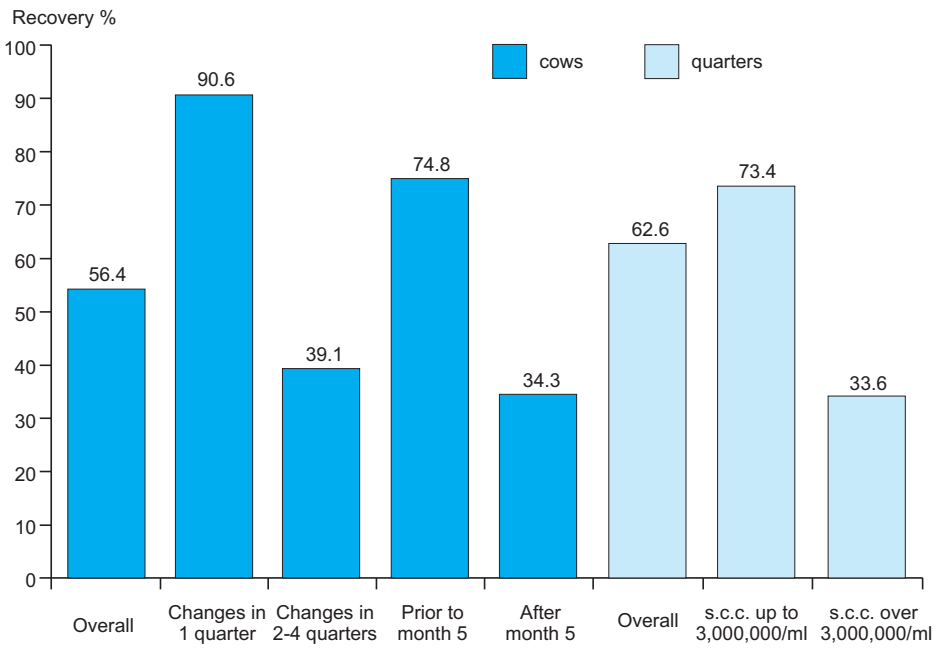

Figure 4.
Efficacy of Lydium-KLP depending on the number of affected quarters, the lactation phase, and the somatic cell count (recovery rates in individual herds) (70, 73).

As shown in Figure 4, cows with one affected quarter and whose treatment began relatively early, i.e. after calving or during the first half of pregnancy, had a high recovery rate (90%). The rate cleary decreased when 2-4 quarters were affected in cows near calving. Overall, 123 cows (56,4%) fully recovered and the individual quarters recovered in some of the remaining cows. There were marked differences in the recovery rates between herds. The efficacy was over 73% in the quarters with an s.c.c. lower than 3,000,000/ml in “zero” test, and it was as low as 34% when the s.c.c. was higher, which primarily occurred during the last month before drying.

Table 4.
Efficacy of treatment of subclinical mastitis depending on etiological agents and somatic cell count (84, 86).

Itemisation	Quartes (n)	Percentage recoveries
Total	94	72.3
Decrease s.c.c. to ≤14 days	35	37.3
≤ 21 days	10	10.6
≥ 21 days	23	24.5
Exacerbation	5	5.3
No effect	21	22.3
S. aureus	5	40.0
CNS	33	81.8
St. agalactiae	6	33.3
CAMP - Str.	0	70.0
Other bacteria	6	50.0
Non specific mastitis	24	83.3
s.c.c.<1 mln/ml	14	89.7
s.c.c.>1 mln/ml	66	60.6

The study shows that in cows with high milk production that were kept under good hygienic conditions and only one udder quarter affected by the disease, the recovery rate was high and either did not differ from the recovery rate achieved with antibiotics, or was even higher. However, when Lydium-KLP is used, there is no need for the withholding period, which makes is significantly more cost effective. Recoveries were observed in cases of infections with major and minor pathogens for the udder. The number of quarters affected and the timing of treatment onset were more significant for the efficacy than the etiological factors. Low efficacy during the second half of pregnancy may be caused by an increased number of affected quarters in the

same cow and the stable, long-lasting subclinical inflammatory process. Similarly, chronic cases with increased cell count are less susceptible to antibiotics. When assessing the effects of Lydium-KLP injections near the end of lactation, one needs to consider that there is a lower blood supply to the udder due to the developing pregnancy, and a decreased milk secretion, which causes a lower supply of neutrophils - effector cells in resisting infection. Another factor to consider may be the granulocytes' decreased capability to generate oxygen radicals that occurs in the final pregnancy stages as a result of extended progesterone activity with immunosuppressing effects of the mammary gland secretion. Results of this work were later confirmed and recovery rates were even higher. Following a single injection of Lydium-KLP, 72.4% of quarters (68% of cows) recovered from subclinical mastitis (53).

Conclusion

In conclusion, it must be stated that treatment of subclinical mastitis in lactating cows with a single injection of 0.02 mg/kg of Lydium-KLP is safe and effective. Recovery from subclinical mastitis during the first half of lactation is highly advantageous (even if antibiotics are used) because milk losses are lower and there are fewer cases of clinical mastitis. Lydium-KLP is significantly less costly than antibiotics and the chance of transferring antibiotics into the food chain is eliminated.

EFFICASY OF LYDIUM-KLP IN THE TREATMENT OF CLINICAL BOVINE MASTITIS

Material and methods

Thirty-seven cows were affected with subacute or acute mastitis for a total of 51 quarters. They were treated with single intravenous injections of 0.02 mg Lydium-KLP per 1 kg of body weight. Clinical, bacteriological and s.c.c. tests were done every day for 5 days and again on Days 7, 14 and 21 following the injection. If there was no clear improvement, antibiotics were administered.

Results

Table 5 shows that 19 (37.3%) of the 51 quarters affected with clinical mastitis recovered. Changes in the udder and in milk regressed within 4-6 days. Bacteria disappeared altogether or their number decreased (usually within 24-48 hours) and pain and swelling, the typical acute symptoms, regressed. The number of micro-organisms decreased in 10 quarters. This was accompanied by a 2-4 day period of normal appearance of the secretion, which then showed other changes, most frequently suppurative and more pronounced than before. The only favorable changes observed in the remaining 22 quarters were decreased pain and swelling. The quarters that were not susceptible to intravenous Lydium-KLP treatment (no improvement or transient improvement) usually reacted well to antibiotics.

Table 5.
Efficacy of Lydium-KLP depending on the somatic cell count and the etiological agents (60, 61).

Dependence on somatic cell count			Zależność od czynników etiologicznych		
s.c.c. 10^6/ml	number of quarters	recovery rate (%)	micro-organisms	number of quarters	recovery rate (%)
up 5	15	76.5	*S. agalactiae*	26	26.9
5-10	5	60.0	*S. uberis*	7	57.1
10-20	9	33.3	*S. epidermis*	6	66.7
over 20	20	0	*E. coli*	6	33.3
Total	51	37.3	Other	6	33.3

Lydium-KLP injections were highly efficient in new acute cases when the somatic cell count did not exceed 5,000,000/ml (76.5%). The efficacy decreased as the changes in the secretion intensified. When the number of cells exceeded 10,000,000/ml, efficacy was 33.3%. None of the suppurative quarters with a cell count above 20,000,000/ml recovered. The inflammations caused by Staph. epidermidis and Str. uberis were most susceptible to treatment. Recovery rate was low in infections caused by Str. agalactiae, Staph. aureus, and E. coli.

The study proved that the lysozyme dimmer is an active therapeutic agent with regard to clinical forms of bovine mastitis. A single intravenous injection of 0.02 mg/kg of Lydium-KLP resulted in a 37.3% recovery rate of the diseased quarters, and two intravenous injections (0.02 mg/kg) in combination with intramammary infusions (0.2 mg) resulted in a 41.1% quarter recovery rate.

Recovery was only observed in relatively new cases when the somatic cell count did not exceed 10,000,000/ml. Of significant importance was the phagocytic activity of granulocytes found in the inflamed mammary gland secretion.

Conclusion

Single intravenous or intramuscular injection of Lydium-KLP in the dose 0.02 mg/kg of body weight shows satisfactory therapeutic efficacy regard to the clinical forms of mastitis when the somatic cell count does not exceed 5,000,000/ml.

THE EFFECT OF LYDIUM-KLP INJECTION ON EFFICACY OF INTRAMAMMARY ANTIBIOTIC PREPARATIONS

Introduction

The efficacy of mastitis treatment is not satisfactory. One of the reasons seems to be the adder's weak immune system. Phagocytosis is the basic antibacterial mechanism of the cow's mammary gland. The oxygen dependent route plays a principal role in intracellular killing of absorbed bacteria. Reactive oxygen metabolites (ROM) are highly toxic to microorganism and they cause damage of tissues and organs during inflammation. Lysozyme dimer (Lydium-KLP) and some intramammary preparations on the production of reactive oxygen matabolites by phagocyting cells in vitro, and to evaluate the effect of a Lydium-KLP injection on the efficacy of mastitis treatment with intramammary antibiotic products which contain corticosteroid or acetylsalicylic acid.

Material and methods

Laboratory tests were conducted on blood and milk samples from healthy and mastitis cows. Assays of the spontaneous and zymosan-induced chemiluminescence were performed after lysozyme dimer or diluted intramammary preparations were performed after lysozyme dimer or udder secretion. The field trials were conducted on 200 cows with clinical forms of mastitis (254 quarters). The control cows were treated with antibiotics containing corticosteroid (Synulox, Tetradelta, Lincocin forte) or ASA (a new experimental preparation) and with a preparation containing no anti-inflammatory component (Pathozone). In the experimental groups, single-dose i.v. injection of 0.01 mg/kg b.w. of Lydium-KLP (NIKA Health Products) was administered in conjunction with intramammary preparations.

Results

It was indicated that Lydium-KLP at a concentration of 0.1µg/ml increases zymosan-induced chemiluminescence in blood samples from healthy and mastitis cows. High concentrations of tested intramammary preparations decrease the ROM production in mastitic samples. They also affect reactive oxygen matabolites in blood samples depending on the kind of preparation and the status of animal health. A single i.v. injection of Lydium-KLP causes a temporary increase of zymosan-induced chemiluminescence in the blood and milk of mastitic cows. The efficacy of intramammary antibiotic therapy was 51.4-71.9%. One i.v. injection of Lydium-KLP in a dose of 0.01mg/kg b.w. increases the recovery rate by 12-15%. It also accelerates the disappearance of clinical symptoms and the normalization of the s.c.c. level.

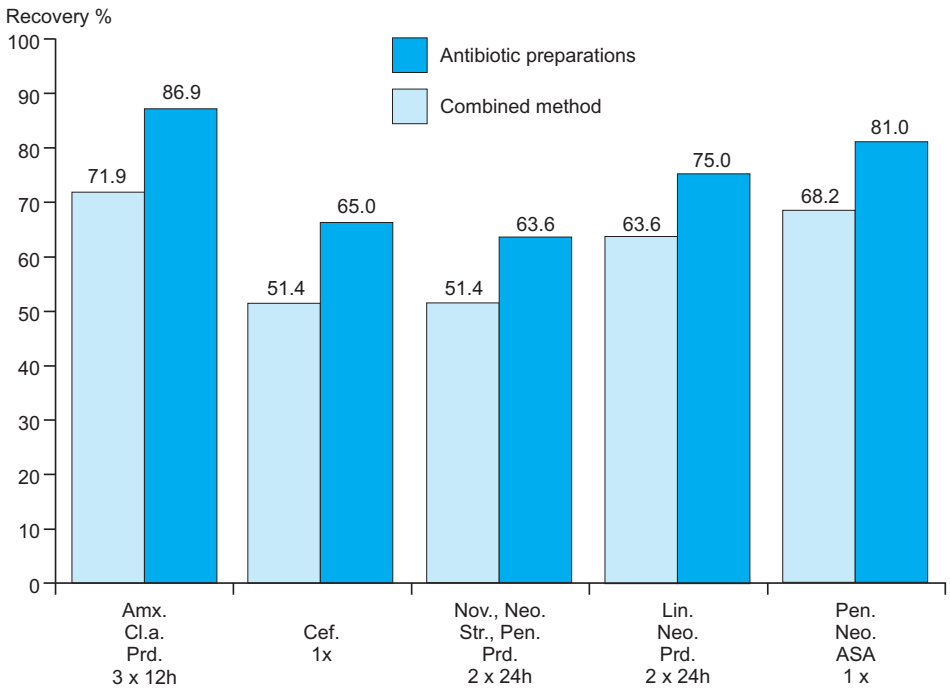

Figure 5.
The effect of treatment of acute forms of mastitis with intramammary antibiotic products versus the combined method (explanation: Amx. - Amoxicillin, Cl.a. - Clavulanic acid, Prd. - Prednisolone, Cef. - Cefoperazone, Nov. - Novobiocin, Neo. - Neomycin, Str. - Streptomycin, Pen. - Penicillin, Lin. - Lincomycin, ASA - acetylsalicylicacid) (71, 75, 78).

THE EFFECT OF THE LYSOZYME DIMER INJECTION ON THE EFFICACY OF SYSTEMIC ANTIBIOTIC TREATMENT OF MASTITIS IN COWS

Introduction

The efficacy of antibiotics in the treatment and prophylaxis of mastitis continues to decrease despite the introduction of new generations of antibiotics and new compounds. Chronic, purulent cases, which are caused by Arcanobacterium pyogenes or Staphylococcus aureus, are especially resistant to treatment. This is due to the resistance to treatment. This is due to resistance of bacteria to antibiotics and the weak immune system of the udder. The active ingredient of Lydium-KLP is lysozyme dimer. Lysozyme dimer affects various immunological machanisms, such as cytokine production and phagocytosis.

The purpose of the study was to determine the effect of a lysozyme dimer injection (Lydium-KLP NIKA) on the efficacy of systemic injections of antibiotics in the treatment of chronic mastitis.

Material and methods

The field trial was conducted on 99 cows that suffered from the chronic purulent from of mastitis (a total of 162 quarters). Most of the animals were owned by small farmers and all were ineffectively treated with intramammary antibiotic preparations at least twice. Thirty cows (45 quarters) that were treated with systemic injections of antibiotics (four days) constituted the control group. Sixty-nine cows (117 quarters) that were treated with the same antibiotics that were used in conjunction with Lydium-KLP was injected once i.m. or i.v. in a dose of 0.02 mg/kg b.w. Clinical, bacteriological and somatic cell count (s.c.c.) tests were conducted at the start of the treatment (day "zero") and then on days 7 and 14 after treatment. The recovery criteria were: regression of clinical symptoms, normal milk appearance, negative bacteriological tests results, and a decrease of s.c.c.

Results

The recovery rates were 42.2% of quarters (43.3% of cows) in the control group (Table 6) and 70.1% of quarters (66.7% of cows) in the experimental group (Table 7).

Table 6.
Efficacy of chronic mastitis treatment with the use of systemic injections of antibiotics (77,84).

Ethiological agent (n)	Penicillin		P. + S.		Tylosin		Oxytetr.		Total	
	+	-	+	-	+	-	+	-	+	-
A. pyogenes	1	2	0	3	0	0	2**	2	3	7
S. aureus	x	x	1	2	0	2	x	x	1	4
CNS	x	x	3	0	1	0	0	1	4	1
Str. agalactiae	2	1	2	4	2	4	x	x	6	9
Other Strept.	2	1	3	3	0	1	x	x	5	5
Average (n)	5	4	9	12	3	7	2	3	19	16
%	55.6	44.4	42.9	57.1	31.0	70.0	40.0	60.0	42.2	57.8

Explanation: +/- effective; - ineffective; ** - one asterisk means on dry quarter; x - not use; P.+S. - penicillin with streptomycine.

Table 7.
Efficacy of chronic mastitis treatment with systemic injections of antibiotics in combination with one injection of Lydium-KLP (77, 84).

Ethiological agent (n)	Penicillin		P. + S.		Tylosin		Oxytetr.		Total	
	+	-	+	-	+	-	+	-	+	-
A. pyogenes	5*	2	6*	3	3	4	1	0	16	9
S. aureus	x	x	4	1	x	x	x	x	4	1
CNS	6	3	9	4	3	1	9	2	27	10
Str. agalactiae	3	x	11	4	0	0	5	0	19	7
Other Strept.	10	3	3	4	0	0	2	2	16	8
Average (n)	24	11	32	15	6	5	17	4	82	35
%	68.6	31.4	68.1	31.9	54.5	45.5	80.9	19.1	70.1	29.9

Explanation: +; -; P.+S. as in Table 6; * - 3 quarters were dry in each subgroup.

With the combined method, the recovery rates were 64% for cases caused by A. pyogenes, 80% for cases caused by S. aureus and 73% for cases caused by Str. agalactiae, and with antibiotics used alone they were 30%, 20% and 40% respectively (Figure 6).

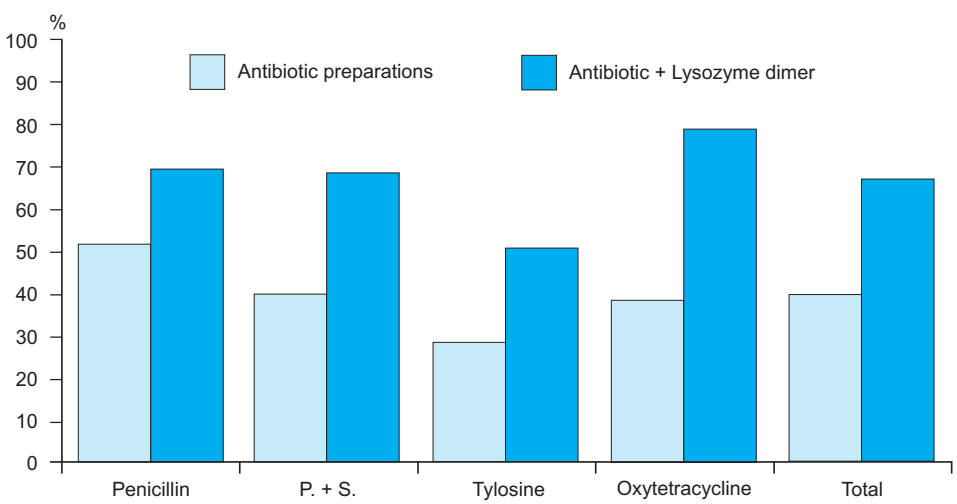

Figure 6.
The effect of the Lydium-KLP injection on effectiveness of antibiotics in treatment of chronic, purulent forms of mastitis (77, 84).

Conclusion

The single injection of lysozyme dimer in a dose of 0.01 mg/kg b.w. increases the efficacy of antibiotics in mastitis treatment regardless of the presence of anti-inflammatory agents.

THE USE OF LYDIUM-KLP IN TREATMENT OF PLACENTA RETAINED AND PUERPERAL METRITIS

Introduction

The retained placenta and puerperal metritis occur in 10-30% of cows, or even more. These diseases often cause chronic endometritis and ovarian cysts, and increase the insemination and pregnancy indices. Manual operations performed during therapy of retained placenta and puerperal metritis can be the cause of intrauterinary septic status. Inlocation of antibacterial drugs is the cause of residue in milk and meat.

The goal of the study was to evaluate the efficacy of the treatment of these diseases with the use of lysozyme dimer with or without antibiotics.

Material and methods

Field study was conducted on 70 cows with retained placenta and 75 with puerperal metritis, which were randomly assigned to one of the four groups. In group I (20 cows with retained placenta and 20 with puerperal metritis) only lysozyme dimer (Lydium-KLP) was given once i.m. in a dose of 0.02 mg/kg. In group II (30 cows with retained placenta and 20 with puerperal metritis), the antibiotic product (Metrisan) was intrauterinally introduced in connection with an i.m. injection of lysozyme dimer in a dose of 0.02 mg/kg. The remaining animals constituted control groups III (15 cows with retained placenta and 10 with puerperal metritis) received Metrisan in combination with alphaprostanol (Gabbrostim) i.m. in a dose of 1.5 mg/100 kg. Cows were clinically examined on days 0, 3, 7, 14 and 28 after the start of the therapy. Fertility indicators (the time to first estrus, service period, pregnancy index, insemination index, interpregnancy period and the culling rate) were calculated.

Results

The best results with regard to the time of recovery were achieved through the combined method (Metrisan + lysozyme dimer). The spontaneous excretion of placenta was observed within 4 days after calving in 40% of the cows (Table 8).

Symptoms of metritis disappeared in 76.7% of the cows up to 7 days after the first inlocation of Metrisan. In the first group spontaneous excretion of placenta was noted in 25% of cows, and 65% recovered from puerperal metritis due to the effect of the lysozyme dimer injection. No spontaneous retained placenta excretions were noted in the control groups. The cure rate of metritis was 60% in the third and 73.3% in the fourth group. It was also noted that reproduction indices were the best in the second group, but the differences were not statistically significant.

Table 8.
The efficacy of some therapy methods in cows with retained placenta and puerperal metritis (31).

Therapy method	G	Disease	n	Results of treatment			
				effective		ineffective	
				n	%	n	%
Lysozyme dimer i.m. once	I	RP	20	5*	25	15	75
		PM	20	13**	65	7	35
Antibiotics i.u. + Lysozyme dimer i.m.	II	RP	20	8*	40	12	60
		PM	30	23**	76.6	7	23.3
Antibiotics i.u. + propranolol i.m.	III	RP	15	-	-	15	100
		PM	10	6**	60	4	40
Antibiotics i.u. + PGF-2α i.m.	IV	RP	15	-	-	15	100
		PM	15	11**	73.3	4	26.7

Explanations:
RP - retained placenta, PM - puerperal metritis, i.u. - intrauterinealy, G - group, * - spontaneous excretion within 4 days after calving, ** - dissapearance of symptoms within 7 days after the start of therapy.

Conclusions

The intrauterine introduction of an antibiotic preparation (Metrisan) in connection with an i. m. injection of lysozyme dimmer in dose of 0.02 mg/kg or even a lysozyme dimer injection alone can cause the spontaneous excretion of retained placenta in some cows.

Using antibiotics in combination with a lysozyme dimer injection is a useful method to treat puerperal metritis.

USE OF LYDIUM-KLP IN TREATMENT OF ACUTE AND CHRONIC ENDOMETRITIS

Introduction

Metritis affects 10-40% of puerperal cows as a result of uterine atony or retained placenta, and the clinical symptoms are frequently severe (ichorous metritis, pyometra). Later, the mucous membrane becomes inflamed and the secretion is mucous and sometimes suppurative. Depending on the intensity, endometritis of the first, second, and third degree can be distinguished (E-1, E-2, E-3). This disease has been recognized as one of the main causes of bovine infertility. Various authors estimate that it causes 20-70% of repeat estrus cycles. Metritis is also one of the factors leading to cystic degeneration of the ovaries.

The etiological or complicating factors of bovine metritis are bacteria, fungi, mycoplasmas, viruses, and protozoans. The following types of bacteria have been isolated most frequently: Actinomyces, Staphylococcus, Streptococcus, Enterococcus, Escherichia, Protus, Brrucella, Pasteurella, Pseudomonas, Fusobacterium, Leptospira, and others.

Puerperal metritis is treated ith various agents administered systemically and intrauterinely. The less severe conditions are treated mainly with intrauterine inlocations. The following drugs were administered systemically: antibiotics, sulfonamides, hormones, anesthetics, glucose, and electrolyte solutions. The following agents were used intrauterinely: antibiotics, acridine dyes, sulfonamides, hormones, vitamins, herb extracts, iodine solutions, chlorine solutions, organic acid solutions, salt solutions, and many others. Efficacy depended on when treatment began and how advanced the disease was.

Nowadays, it is increasingly emphasized that further developments in treating bovine mastitis and fertility disorders will depend on boosting the immune activity of the body, which reinforces the necessity of restricting antibiotic residue in milk and in meat.

Material and methods

The study was conducted on 140 puerperal cows diagnosed with the second and third degree of endometritis (E2 - E3). Ninety cows were in the experimenthal group (I) and 50 were in the control group (II). The experimental cows received Lydium-KLP intrauterinealy in the form of 2 mg of the active component in PBS once or twice. The control cows received antibiotic solutions intrauterinealy. The following factors were monitored in both groups: the condition of the uterus and cervix, uterus involution, filling of the uterine cavity, the amount, nature and smell of the discharge, the ovary function, and the return of the uterus to its physiological condition. The following indicators were analyzed: lengths of the involution process, number of cows that recovered and were fertilized, average interpregnancy period, and the insemination index.

Results

Twenty four to 36 hours after intrauterine infusion of Lydium-KLP, obvious changes were observed in the nature, amount, and smell of the reproductive organ discharge. On days 3 and 7, per rectum examinations revealed a clear progress of uterus involution, increased tone, and decreased content inside the uterus. During the same time period, the control group only showed insignificant changes in the nature, amount, and smell of the discharge. The uterus involution was considerably slower and its tone also increased much more slowly. The smears collected prior to treatment from both groups contained the following: Staphylococcus sp., Streptococcus sp., Enterococcus sp., Clostridium perfringens, and E. coli. Following the administration of Lydium-KLP, a statistically significant ($p<0.01$) decrease of the overall number of microorganisms was observed as opposed to the control group, despite the microorganisms'sensitivity to the antibiotics used. Milk from the cows receiving Lydium-KLP contained no inhibitors that were found 2 and 5 days after intrauterine antibiotic infusions.

Table 9.
Selected fertility indices in cows treated with Lydium-KLP or antibiotics (12).

Indices	Groups	
	Experimental (Lydium-KLP)	Control (antibiotics)
Number of cows tested	90	50
Number of fertilized cows	82 (91.1%)	36 (72.0%)
Uterus involution (days)	39.8±4	48.4±5
Insemination index	1.36-1.42	1.9-2.4
Interpregnancy period (days)	86.0±6.0	112.0±9.0

Lydium-KLP proved highly effective in the treatment of endometritis. The type of treatment used had a particular effect on the number of cows that became fertilized. In group I, 91.1% of cows entered the next reproductive cycle, as opposed to 72.0% of cows from group II. In cows that received Lydium-KLP, the average uterus involution was 9,5 days shorter and ovary secretion resumed sooner. The treatment clearly shortened the inter-pregnancy period in group I by 26.0± 9 days on average.

Conclusion

Intrauterine infusion of 2 mg of Lydium-KLP is effective in the treatment of bovine endometritis.

USE OF LYDIUM-KLP IN THERAPY OF OVARIAN CYSTS

Introduction

Cystic ovarian didease (COD) can affect 10-40%, or more, of high-yielding dairy cows. The most frequent symptom is lack of sexual activity, but the disease also shortens the sexual cycle or intensifies the estrus symptoms. At present, the main symptom of COD is the disappearance of the ovarian cycle. Cows remain infertile as long as the cystic structures are in place and the intervals between calvings are longer than normal. The mean interval between the cyst diagnosis and conception is 50 days. Clearly, ovarian cysts are a significant sourse of economic losses for dairy farms.

Cysts are generally defind as single or multiple structures filled with fluid, at least 20-25 mm in size that are present for ten or more days in the absence of corpus luteum, although in some cases corpus was found alongside the cysts. The cysts are classified as follicular or luteal. The follicular cysts are usually thin- walled and secrete small amounts of progesterone. The luteal cysts have thicker walls and secrete varying amounts of progesterone. They are dynamic structures and their development and life span are likely associated with altered hypothalamic-hypophysial-ovarian function. The etiology and pathogenesis of COD are not fully known because there are several causes of the disease. A mojority of cysts develop during the 30-60 day period following calving. Their development has been associated with a number of clinical, environmental, and hereditary factors. Insufficient amount and quality of feed, endocrinological and immunological disorders, endometritis, and stress may cause cystic ovarian disease. Energy levels during the early postpartum period influences ovarian activity, and spontaneous caloric deficit reduces secretions of progesterone. Significant predictors of ovarian cysts are dystocia, early metritis, silent heat, and ketosis.

The current treatment of COD mainly consists of injections of gonadotropin-releasing hormone (GnRH) analogues. If luteal cysts are diagnosed, they can be treated with prostaglandin F2 alpha. Human chorionic gonadotropin (hCG) by itself or in combination with progesterone is also used. Some practitioners prefer intrauterinare infusions of Lugol's solution or manual rupture of cysts. Sometimes this method leads to ovarian-bursal adhesions is made, the biochemical condition of the animal's body and the timing of therapy. The results vary from 30 to 80 percent, regardless of what drugs and therapy are used. In addition, some cysts disappear spontaneously, particulary those that develop during the postpartum period.

The purpose of the study was to determine the efficacy of COD treatment with the lysozyme dimer versus GnRH.

Material and Methods

The field trials were carrid out on 140 cows over a two-year period at four farms where the animals were tide up at their stations. The first farm (MG) had 180 cows

with an average milk yield of 5.800 kg per year. On the second farm (MD) there were 200 cows with an average milk yield of approximately 5,500 kg. The trhird farm (LU) had 150 cows (6.500 kg), and the fourth farm (BZ) had 240 cows with an average milk yield of about 5,400 kg per year. The diet of all the cows was the same (grain mix, corn silage, hay, haylage, and mineralized salt).

The animals included in the study showed no symptoms of estrus at least 60 days after calving and they received no treatment before the experiments. The cysts were diagnosed during bi-weekly rectal examinations of the uterus and ovaries. The cystic animals were divided into four groups: two experimental groups and two control groups. Blood samples were collected before treatment from 30% of the experimental animals. The cows from the positive control group were treated with one intramuscular injection of GnRH. A Receptal (MSD) containing 20 mg of busereline was applied. The animals from the experimental group received an intrauterine infusion of 2 mg of lysozyme dimer. One vial of Lydium-KLP containing 2 mg of lysozyme dimer was dissolved in 40 ml of 5% glucose solution and an intrauterine inlocation was made with a sterile catheter. The first (I) negative control group (20 animals) received no drugs.

The experimental and control cows were clinically examined 14, 28, 42, and 90 days after treatment. The times of the first estrus, the cysts regression, and artificial inseminations were noted. The inseminated cows were examined per rectum for pregnancy. Authors performed the diagnosis, treatment and foloow-up.
Chi-square test was applied to evaluate significance of differences.

Results

The cows treated with GnRH and Lydium-KLP and thr control animals were the same age ad their treatment started at the same time after calving (Table 10).

Table 10.
Efficacy of COD treatment with GnRH and lysozyme dimer (74, 100).

Group	n	Age of cows (years)	From calving to treatment (days)	Estrus within 30 days (%)	Estrus within 60 days (%)	Time from treatment to estrus (days)
GnRH i.m.	50	4.0±1.5	88.3±25.3	66[ab]	86[ab]	19.8±10.4
Lysozyme dimer i.ut.	50	4,3±1.6	85.5±27.3	72[ab]	90[ab]	21.8±17.7
Control I (glucose sol.) i.ut.	20	4.7±1.5	84.4±26.3	25	40	19.4±12.8
Control II (no drugs)	20	4.2±1.6	81.0±24.8	35	50	23.5±18.5

Explanation:
i.m. - intramuscularly; i.ut. - intrauterinealy; [ab] - significant difference ($P<0.05$); [a] - as compared with control I and [b] - with control II.

The symptoms of estrus appered in 68% of cows from the GnRH group, 72% of cows from the lysozyme dimer group, and 25-35% from the control groups. The average time between treatment and heat was 20 days (for the GnRH group) and 21,8 days (for the Lydium-KLP group).

The cows in heat were inseminated and some from each group became pregnant (Table 11). The best pregnancy rate during 30 days following treatment was observed in the GnRH group. The pregnancy rates during 60 days were almost the same in the GnRH group (68%) and the Lydium-KLP group (66%), and only 35-40% for the control group cows. However, fertility indices like the interpregnancy period and the artificial insemination index were slightly better in the GnRH group than in the other groups.

Table 11.
Fertility indices after COD treatment with GnRH and lysozyme dimer (74, 100).

Group	Pregnancy within 30 days		Pregnancy within 60 days (together)		Days from treatment to pregnancy	Inter-pregnancy period	Artificial insemination
(n)	n	%	n	%	n	days	index
GnRH (50)	24[a]	48	34[a,b]	68	24.7±16.3	110.7±30.9	1.2±0.5
Lysozyme dimer (50)	19	38	33[a,b]	66	34.5±28.4	121.2±32.3	1.5±0.7
Control I (glucose sol.) (20)	4	20	7	35	37.5±31.5	134.8±34.8	1.9±0.9
Control II (no drugs) (20)	6	30	8	40	35.6±29.8	135.2±33.7	1.9±0.9

Explanation:
[a,b] - significant difference (P<0.05); [a] - as compared with control I and [b] - with control II.

Conclusion

The study shows that the efficacy of Lydium-KLP in a dose of 2 mg in the form of intrauterine infusion is equal to that of standard GnRH therapy of COD in cows and it can be used as an alternative treatment.

LYDIUM-KLP IN THE PROPHYLAXIS OF POSTPARTURIENT DISEASES IN COWS

It is well known that some diseases such as retained placenta, ichoroid or purulent puerpal metritis and acute forms of mastitis are due to insufficient immunity and matabolic disorders. The purpose of the investigation was to evaluate the prophylactic effect of Lydium-KLP application before parturition.

Material and methods

The experiment was carried out on 120 clinically healthy pregnant cows. The cows from the experimental group (60 heads) were injected with Lydium-KLP in a single dose of 0.02 mg/kg 10-7 days before parturition. Control cows received no medicine. All cows were observed for 4 month after calving. Incidences of disease were noted and fertility indices were calculated.

Results

Table 12.
Effect of prophylactic use of Lydium-KLP in pregnant cows (19, 21).

Itemization after delivery	Experimental group (n=60)	Control group (n=60)
Disease incidence (%)	13.3	38.3
Days from calving to firs estrus	53.8*	61.6*
Pregnancy index **	62.8*	57.6*
Insemination index	1.8	1.9
Interpregnancy period (days)	76.0*	79.8*
Culling (%)	7.7*	18.9*

Explanation:
*statistically significant difference; ** percent of cows pregnant after first insemination.

Puerperal disorders were observed in 13.3% of cows from the experimenthal group and in 38.3% of cows from the control group (Table 12). Retained placenta and puerperal metritis was rare in the experimental cows, and they showed faster uterine involution and an earlier onset of the ovarian cycle. Also, cows from the experimental group demonstrated a lower insemination index, shorter interpregnancy period and a better pregnancy index than those from the control group.

Conclusion

One injection of Lydium-KLP in dose of 0.02 mg/kg 10-7 days before parturation demonstrates a prophylactic effect against postparturient disorders in dairy cows.

Summary

Clinical and subclinical inflammatons of the mammary gland and reproduction disorders are the main causes of economic losses at dairy farms. Antibiotics and hormones are commonly used in the treatment and even prophylaxis of dairy cow diseases. However, the use of these drugs should be restricted because of the negative influence of their residue on human health.

Lydium-KLP is highly effective in the treatment of mastitis and reproductive disorders in dairy cows. One intavenous or intramuscular injection of Lydium-KLP in a dose of 0.02 mg of the lysozyme dimer per 1 kg of body weight ensures high efficacy in the treatment of clinical forms of mastitis in its early stages and in subclinical forms of mastitis when the somatic cell count does not exceed 3,000,000/ml in milk. A 0.01-mg/kg dose of Lydium-KLP increases the effectiveness of antibiotics administered intramammarily as treatment of clinical mastitis in cows. It also clearly affects systemic antibiotic therapy of chronic purulent form of mastitis. Studies have shown that the treatment of subclinical mastitis using Lydium-KLP does not cause the presence of inhibitory substances in milk (withholding time equals zero) and there is no prolongation of withdrawal time for antibiotics when used jointly. Intrauterine infusion of 2 mg per cow f the Lydium-KLP solution is highly effective in the treatment of bovine catarrhal inflammation of the uterus and cistic and cistic ovarian disease.

Two diseases, gastroenteritis and bronchopneumonia may affect health, normal growth, and the profitability od calf rearing. Financial losses arise from both mortality and from the cost of medication and labor needed to treat sick calves. Antibiotics that are applied in the treatment can be a source of antibiotic residue in veal.

The injection of Lydium-KLP increased the percentage of phagocyting cells, the phagocytic index, and the percentage of NBT-positive neutrophils in healthy and sick calves (37). Lysozyme dimer in different concentrations (from 0.25 to 0.5 μg/ml) stimulates the phagocytic activity of calf WBC in vitro (35). It was also (34) noted that Lydium-KLP does not change the calves' behavior and is totally safe for the animals.

EFFICACY OF LYDIUM-KLP IN THE TREATMENT OF GASTROENTERITIS AND BRONCHOPNEUMONIA IN CALVES

Introduction

Diarrhea is a symptom of gastroenteritis, which is the most common disease among newborns and sucklings. It causes death, and limits the suitability of some animals for further breeding. Studies indicate that the disease results from a number of conditions and has a complex pathogenesis. The etiological factors are: bacteria (such as Escherichia coli, Salomonella typhimurium, Clostridium perfringens, Camphylobacter sp., Yersinia enterolitica, Bacterioides fragilis), viruses (rota-, parvo-, corona-, entero-, adeno-, astro-, calici-, toro-, and retrovirus) and protozoa (Cryptosporidum). Infections cause inflammation of the mucous membrane of the intenstines, which leads to impeded absorption and excess discharge, and results in loss of fluids and electrolytes, matabolic acidosis, toxemia, damage to the parenchymatous organs, and ends frequently in death. The disease is treated with antibiotics (administered orally and parenterally), sulfonamides, acridine dyes, electro-

lyte solutions, sera, anti-protozoan, drugs, non-steroid anti-inflammatory drugs, vitamins, cardiac medications, etc. Attempts were also made to use interferon and monoclonal antibodies. The best results were achieved through casual and symptomatic treatment combined with improving the environment.

Bronchopneumonia is the most common disease in calves past 10 days of age. The greatest risk occurs when animals are kept under improper hygienic conditions, which facilitates the spread of infection. If it occurs in a healthy herd, the disease is usually acute. Bronchopneumonia frequently leads to death, but if the animal recovers, its growth and development are considerably inhibited.

The diseases which most frequently affect the respiratory system of calves are: pasteurellosis (Pasteurella multocida), enzootic bronchopneumonia (PI-3 virus), the VD-MD syn-drome, and the IBR-IPV infections; the latter two affect older calves. The types of bacteria that complicate viral infections are: Salmonella, Diplococcus, Staphylo-coccus, Streptococcus, Pasteurella, Corynebacterium, and others. Another etiological factor is Mycoplasma bovis. Most frequently, diseases of the respiratory system occur endemically and they typically peak during the fall-winter and winter-spring seasons ("crowding syndrome"). Viral and bacterial respiratory diseases are treated with injections of antibiotics, sulfonamides, immune sera, and immuostimulates. Efficacy depends on treatment timing and microorganisms' sensitivity to the chemicals used. Since treatment is often ineffective, prevention is very important.

Aside from widespread immunizations that increase specific resistance, preparations that stimulate non-specific immune mechanisms are also used. The following factors increase immunity:

- increased level of interferon that is produced to raise anti-viral immunity and to control the immune system mediators (interleukins),
- stimulation of Natural Killer (NK) cells and elimination of virus-infected cells,
- stimulation of lymphocyte proliferation,
- increased phagocytic activity of micro- and macrophages.

Material and methods

Studies were conducted at state and individual farms on 136 calves ages 3 days to 3 months. Seventy-seven calves were diagnosed with gastroenteritis and 59 with bronchopneumonia.

The animals did not receive any medication before they were treated with single or multiple (2-4 times every 12-24 hours), usually intravenous, injections of 0.02 mg/kg of Lydium-KLP. Clinical examinations were performed every 24 hours until the treatment was effective or other medications were used.

Results

Symptoms of acute gastroenteritis disappeared as soon as within 24 hours after the Lydium-KLP injection. Within that time, 50% of calves had normal stool and normal appetites. Diarrhea usually disappeared in the other calves had normal stool and normal appetites. Diarrhea usually disappeared in the other calves within 72 hours. The body temperature of the calves with fever returned to normal within the first 2 days, and those calves with below normal 24 hours later. Some calves had pneumoenteritis and severe symptoms of toxemia and dehydration. In these animals, symptoms disappeared more slowly and some calves required another treatment incorporating antibiotics. This was the only group in which deaths occurred. The animals with diarrhea (even bloody diarrhea) and with no dyspnea reacted very well to Lydium-KLP (recovery rate of over 95%). It must be emphasized that the animals received no other medication except Lydium-KLP (not even electrolytes given parenterally). Six to 12 hours following the Lydium-KLP injection, a limited amount of liquids was given orally. Diet was recommended and the consumption of milk was discouraged even if the appetite fully returned.

Table 13.
Efficacy of Lydium-KLP in the treatment of gastroenteritis and bronchopneumonia in calves (8, 63, 64).

Clinical diagnosis	Treatment method	No. of calves	Symptoms regression		Recovery rate (%)	Death rate (%)
			before 24h(%)	between 24-72h (%)		
Acute gastroenteritis	Lydium-KLP 1x	26	50	26.9*	84.6	3.8
	Lydium-KLP 2x & more	51	41.2	31.4*	82.3	3.9
Acute broncho-pneumonia	Lydium-KLP 1x	22	22.7	45.4*	81.8	0
	Lydium-KLP 2x & more	37	16.2	62.2*	81.1	0

Explanation:
*the remaining calves recovered after 72h.

Table 14.
Body temperature of calves with gastroenteritis and bronchopneumonia after treatment with Lydium-KLP (63, 64).

Temperature ranges (°C)	Time and percentage of calves							
	zero		24h		48h		72h	
	G	B	G	B	G	B	G	B
41,0	0	15,3	0	0	0	1,9	0	0
40,1-40,9	22,0	61,0	6,0	18,6	4,3	3,8	2,2	2,0
39,5-40,0	28,0	16,6	10,0	27,1	4,3	15,3	2,2	6,1
38,5-39,4	**32,0**	**10,2**	**82,0**	**50,8**	**91,5**	**67,3**	**95,6**	**87,8**
≤38,4	8,0	0	2,0	3,4	0	3,8	0	4,1

Explanation:
G - gastroenteritis; B - bronchopneumonia.

The studies firther indicate that similar effects were achieved with single and multiple (2-4) injections of Lydium-KLP (63, 64).

A characteristic result of Lydium-KLP administration in cases of acute bronchopneumonia was decreased fever (table 14), sometimes as soon as 12 hours after the injection. Usually, the temperature returned to the physiological norm between 24 and 72 hours after the injection and at that time the calves regained their appetite, became more mobile, dyspnea was less severe, and coughing was less frequent and less painful. Between days 3 and 5, coughing and dyspnea disappeared, discharge from the conjunctiva sac also disapperad, and nasal discharge became thicker and less profuse and it eventually regressed. No correlation was found between the disappearance of the symptoms and the number of injections (Table 13).

It must be emphasized that none of the calves died. Individual animals did not respond to treatment and showed repeated aggrevation after the original symptoms regressed. They recovered when antibiotics were administered.

It must be further emphasized that the calves that recovered due to Lydium-KLP were less susceptible to bronchopneumonia in the futere as opposed to the calves treated with antibiotics. Another important observation made by the animals' owners was that the calves that recovered from gastroenteritis and bronchopneumonia thanks to Lydium-KLP developed better than the ones that were never affected by these diseases.

Conclusion

Lydium-KLP shows high efficacy in the treatment of gastroenteritis and bronchopneumonia in calves.

One intravenous injection of 0.02 mg/kg of body wieght of Lydium-KLP is sufficient to achieve an 80% recovery rate from acute gastroenteritis and bronchopneumonia.

EFFECT OF LYDIUM-KLP ON THE EFFICACY OF ANTIBIOTICS IN THE TREATMENT OF BRONCHOPNEUMONIA AND GASTROENTERITIS IN CALVES

The study covered 124 ranging in age from 1 week to months that came from small and large farms. The group included included calves that had been treated carlier with Lydium-KLP and ones that received the combined treatment from the start. 0.02 or 0.01 mg/kg of Lydium-KLP was injected intravenously or intramuscularly only once, whereas antibiotics were administered for 2 or 3 days.

Tylosin, oxytetracycline or penicillin combined with streptomycin were used against bronchopneumonia. Oxytetracycline alone or streptomycin combined with penicilin were used intramuscularly and streptomycin or neomycin were used orally to treat gastroenteritis.

After the clinical examination was performed and treatment began, the following parameters were assessed every day for one week: body temperature, occurrence and intensity of coughing, amount and nature of discharge from the nose and eyes, lungs' activity, appetite, appearance of stool, bowel movement frequency, mobility, and degre of dehydration.

Results

As seen in Table 15, 72.4% of animals treated for bronchopneumonia with antibiotics recovered, and 10.3% died. Only one of the calves died in the group treated with the combined method (one injection of 0.02 or 0.01 mg/kg of Lydium-KLP plus 2 or 3 injections of antibiotics). Due to a relapse, one calf had to be treated with antibiotics again. Of all 37 animals that received Lydium-KLP in combinations with antibiotics, 35 recovered (94.6%) and only one-died (2.7%).

In the cases that did not respond to Lydium-KLP alone (relapse, exacerbation), Lydium-KLP had an unquestionable effect on the antibiotic treatment. Efficacy of antibiotics administered 72-96 hours after the Lydium-KLP injection was very high. In the group of 24 calves, the antibiotic had to be changed in only one case (4.2%). None of the animals died that received Lydium-KLP followed by antibiotics.

The calves treated according to the combined method and those that received antibiotics after a lack of response to Lydium-KLP recovered faster than those that did not receive Lydium-KLP at all. Fever dropped faster and coughing, dyspnea and visible discharge from the eyes and nose regressed sooner. Animals returned sooner to eating normally and they were less or not at all emaciated. Symptoms disappeared in a similar fashion in the calves that received antibiotics during a relapse or exacerbation after the initial symptoms regressed following the administration of Lydium-KLP by itself. In these cases, full recovery was observed within 24 hours after antibiotics were given.

Table 15.
Effect of Lydium-KLP on the efficacy of antibiotics in the treatment of pneumonia and gastroenteritis in calves (48, 49).

Diagnosis	Treatment	Number of calves	Symptoms regressed		Recovery rate (%)	Death rate (%)
			in 48h (%)	in 96h (%)		
Broncho-pneumonia	Antibiotics 3x24h i.m.	29	13.8	48.3	72.4**	10.3
	Lydium-KLP 0.02 mg/kg (1x) + antibiotics 2x24h i.m.	10	70.0	20.0	90.0	10.0
	Lydium-KLP 0.01 mg/kg (1x) + antibiotics 3x24h i.m.	16	37.5	50.0*	100.0	-
	Lydium-KLP 0.01 mg/kg (1x) + antibiotics 2x24h i.m.	11	45.4	36.4	81.8**	-
	Antibiotics 3x24h after ineffective injection of Lydium-KLP	10	40.0	50.0	90.0**	-
	Antibiotics 2x24h after ineffective injection of Lydium-KLP	14	64.3	92.8*	100.0	-
Gastroenteritis	Antibiotics 3x24h i.m. + per os	15	20	66.7*	86.7	13.3
	Lydium-KLP 0.02 mg/kg(1x) + antibiotics i.m. + per os 2x24h i.m.	10	100.0	-	100.0	-
	Antibiotics i.m. + per os (2x24h) after ineffective injection of Lydium-KLP	9	77.8	11.1	88.9	1.1
Total		124				

Explanation:
*the remaining calves recovered after 96h; ** the calves recovered as a result of the repeated antibiotic treatment.

Most of the calves that were treated with Lydium-KLP in combination with antibiotics or with Lydium-KLP followed by antibiotics recovered within 72 hours. Longer recovery periods were observed among calces that had chronic bronchopneumonia when Lydium-KLPalone was administered initially.

Table 15 shows very good results of the combined treatment of gastroenteritis. Clinical symptoms disappeared in all calves within 2 days. The effect of Lydium-KLP was also evident in the animals that had a recurrence after gastroenteritis disappeared when Lydium-KLP was administered. It must be emphasized that within 24 hours, the treatment eliminated the diarrhea that accompanied bronchopneumonia in some cases.

The study proves that 0.02 mg/kg and 0.01 mg/kg of Lydium-KLP increases the efficacy of antibiotics in the treatment of bronchopneumonia and gastroenteritis in calves. The effect of Lydium-KLP is evident in cases of the combined treatment and when antibiotics were used 3-4 days after Lydium-KLP has been administered. Two days of antibiotic administration was sufficient to recover from acute bronchopneumonia and gastroenteritis. The combined method may be recommended in the cases of suppurative pneumonia, chronic pneumonia, and pneumoenteritis when Lydium-KLP alone may not be sufficient. On the other hand, even if there is no response to Lydium-KLP, its administration accelerates antibiotic therapy and makes it more effective.

Conclusion

A single injection of 0.02 mg/kg or 0.01 mk/kg of Lydium-KLP increases the efficacy of antibiotics and decreases their dosage, which leads to a faster disappearance of symptoms and a higher recovery rate.

PROPHYLACTIC ACTIVITY OF LYDIUM-KLP AGAINST CALF DISEASES

Introduction

Lysozyme dimer stimultes cellular and humoral immunity and demonstrates prophylactic activity against some diseases of cows, sows, swine, horses and fowl. Injection of Lydium-KLP increases the prophylactic properties of the vaccine against Pasteurellosis in calves (130).

Material and methods

The field trial was conducted during one year on farm W, where calves were transferred from three herds (W, ST, O). The calves remained in the cow-barns for tree to four weeks. They were kept near their mothers and fed with mothers' milk, and then with bulk milk. Conditions in the barns were quite good. The temperature did not fall below 12°C, even when the temperature outside was well below freezing. The pens were lined with dry straw, and there was no excess concentration of gases. From there, the calves were transported to the calf-house where animals of various ages, including the sick ones, were kept inside three pens. Animals from adjoining pens were in contact with each other. The conditions in the calf house were closely related to the season of the year and the weather. The concentration of gases, such as ammonia and hydrogen sulfide, was high, and the humidity was also high, particularly in winter. The straw in the pens was always mixed with the animals' excrement.

During experiment I the temperature indoors remained between +2°C and +6°C. Calves had diarrhea of varying intensity, particularly during the first days following the transfer to the calf house. Respiratory system inflammations were dominant during the winter and spring, and the death rte was high.

Five experiments were conducted during different seasons of the year on 104 calves three to four weeks old with body weights between 50 and 60 kg. Twenty-four to 48 hours before transfer from the barns to the calf house, one half of the animals received a single i.m. injection of Lydium-KLP in dose of 0.02 mg/kg body weight. The calves that did not receive any medication constituted control groups. The calves were monitored for 30 days and treated if a disease arose. The following antibiotics were used: amoxicilin (with extended efficacy), norfloxacin (for administering every 24 hours), oxytetracicline (with extended efficacy), and penicilin combined with streptomycine (every 24 h for three days).

Results

The number and percentage of sick calves in the experimenthal and control groups in each trial is shown by Table 16. The data indicate that incidence of disease following transfer (from the barn) was directly associated with the conditions in the calf house. A particularly high disease incidence occurred during the winter when the temperature was low while humidity and gas concentrations were high. Diseases also occurred more frequently when temperatures were very high, and were combined with high humidity and lack of ventilation. During the remaining month (experiments III and IV), respiratory system inflammations were less frequent or did not occur at all (experiment V).

Table 16.
Results of prophylactic use of Lydium-KLP (110).

No. of experiment	Month of experiment	Conditions	Groups (n)	Incidence of disease			
				before 7th day	between 8 and 14 day	between 15 and 30 day	Totals
I	January - February	bad	E (14)	4 (28.6)	3 (21.4)	1 (7.1)	8 (57.1)
			C (14)	9 (64.3)	2 (14.3)	1 (7.1)	12 (85.7)
II	June - July	poor	E (12)	1 (8.3)	3 (25.0)	0	4 (33.3)
			C (2)	2 (16.7)	3 (25.0)	1 (8.3)	6 (50.0)
III	November - December	suff.	E (8)	0	0	0	0
			C (8)	3 (37.5)	0	1 (12.5)	4 (50.0)
IV	February - March	suff.	E (8)	0	2 (25.0)	0	2 (25.0)
			C (8)	1 (12.5)	2 (25.0)	1 (12.5)	4 (50.0)
V	June - July	good	E (10)	0	0	0	0
			C (10)	0	0	0	0
Total			E (52)	5 (9.6)	8 (15.4)	1 (1.9)	14 (26.9)
			C (52)	15 (28.8)	7 (13.5)	4 (7.7)	26 (50.0)

Explanation:
E - experimental group; C - control group; suff. - sufficient.

Prophylactic administration of Lydium-KLP as a single i.m. injection proved to be clearly favorable. The prophylactic effect was particularly visible during the first week following the transfer when healthy calves came in contact with the sick ones while under stress caused by a change in the environment and worsened feed. Under such conditions, the disease incidence was three times lower than in the control groups. The animals from experimental groups that became sick and were treated recovered faster. Death occurred only in experiment I when two animals from the experimental group died and three animlas from the control group died.

The observations conducted in the field prove that lysozyme dimer has prophylactic effects in calves.

Conclusion

A single injection of Lydium-KLP in a dose of 0.02 mg/kg b.w. demonstrates prophylactic activity against calf diseases.

Summary

Alimentary tract and respiratory system inflammations are the main causes that negatively affect health, normal growth, and the profitability of calf rearing. Financial losses arise both from mortality and from the cost of medication and labor needed to treat sick calves. Antibiotics are mostly applied in the treatment and they, apart from immunosupressing activity, can be a source of antibiotic residue in veal. Immunomodulators will become increasingly important drugs in the future. Lysozyme dimer activates the immune system in calves. One i.m. injection in a dose of 0.02 mg/kg b.w. is effective in treating acute cases of gastroenteritis and bronchopneumonia. Lysozyme dimer activates the immune system in calves. One i.m. injection in adose of 0.02 mg/kg b.w. is effective in treating acute cases of gastroenteritis and bronchopneumonia. Lysozyme dimer in a single dose of 0.02 or even 0.01 mg/kg increases the efficacy of antibiotics in treatment of calf diseases. Lysozyme dimer can also be used as a prophylactic tool in calves.

Alimentary tract and respiratory system infections are the most common causes of disease and death in foals. Infections also restrict of their growth periodically or permanently. As a result, the foals' value is lost more frequently than in other animals. Reproduction disorders cause a enormous losses for owners of adult horses. The condition of the immune system plays a very significant role in the diseases' development. Therefore, in an attempt to satisfy the needs of veterinary practitioners, many scientists are trying to develop effective immunomodulators. Lydium-KLP possesses such properties, among others. An evaluation conducted on clinically healthy foals showed that this preparation stimulates non-specific immunity by increasing phagocytosis, and is harmless to foals (39, 152). It also demonstrated prophylactic activity against bronchopneumonia of foals (113).

EFFICACY OF LYDIUM-KLP IN THE TREATMENT OF SOME HORSE DISEASES

Introduction

Gastroenteritis is the most frequent disease of newborn foals and bronchopneumonia affects both the foals and adult horses. Conditionally pathogenic microoganisms (bacteria, viruses, and fungi) are the most frequent causes of the diseases. Traditional methods of treatment are costly, but not always effective. The aim of field trials was to establish the usefulness and activity of Lydium-KLP in the treatment of some diseases in horses.

Material and methods

The study was conducted on 21 animals, some individually owned and some from a horse farm. Lydium-KLP was used in the treatment of 16 foals (7 days to 2 month old) with acute catarrhal enteritis, as well as 1 foal and 4 adult horses with bronchopneumonia. The preparation was administered once intramuscularly in a dose of 0.01 mg/kg and twice intravenously 24 hours apart in a dose of 0.02 mg/kg. The animals underwent detailed clinical examinations twice daily until symptoms disappeared.

Results

Table 17.
Effects of the Lydium-KLP treatment of selected diseases of foals and adult horses (153).

	Dose of Lydium-KLP	Number of animals	Recovery rate (%)		Death rate (%)
			before 24h	after 72h	
Acute gastroenteritis	0.01 mg/kg x1	11	72.7	27.3*	0
	0.02 mg/kg 2x24h	5	80.0	20.0	0
Bronchopneu-monia	0.02 mg/kg 2x24h	5	80.0	20.0	0

Explanation:
*2 foals recovered after the second injection of Lydium-KLP and 1 after antibiotics.

Following the first injection of 0.01 mg/kg of Lydium-KLP, diarrhea disappeared in 8 animals within 48 hours (72.7%). In 3 cases, Lydium-KLP was administered again 48 hours later due to a lack of response. Two foals recovered within 2-3 days and 1 recovered after it was hydrated and antibiotics were used. When 0.02 mg/kg of Lydium-KLP was administered twice 24 hours apart, all (5) foals recovered from catarrhal enteritis and 5 foals recovered from acute bronchopneumonia.

Conclusion

One intramuscular or intravenous injection of Lydium-KLP in a dose of 0.02 mg/kg is effective in the treatment of acute catarrhal enteritis and acute bronchopneumonia in foals.

EFFECT OF LYDIUM-KLP ON THE EFFECACY OFANTIBIOTICS IN SELECTED HORSE DISEASES

Introduction

Antibiotics are the first tools in treating alimentary tract and respiratory system inflammations. The treatment, especially of newborn diarrhea, is often ineffective. Subcutaneous phlegmon is the inflammation of the connective tissue and lymphatic vessels, which is caused by infection of the area surrunding the wound. Pyogenic and putrescent bacteria are the primary agents. Treatment with the use of systemic and local injections of antibiotics is usually and often ineffective. Phlegmon can result in abscesses, elephantiasis and even death. The purpose of the study was to evaluate the effect of lysozyme dimer on efficacy of conventional therapy of bronchopneumonia and subcutaneous phlegmon in horses.

I. Treatment of bronchopneumonia

Material and methods

The study was conducted on 31 foals, 3-6 months old, with acute bronchopneumonia. In these cases, 0.01 mg/kg of body weight of Lydium-KLP was administered once and antibiotics (mostly gentamycin) were used for 5 days. The control group consisted of 20 foals which were treated without Lydium-KLP.

Results

The combined (table 18) method resulted in a higher recovery rate and a faster regression of the symptoms than that of the control group. Fever dropped 24 hours after Lydium-KLP was injected. It took the control animals 48 to 72 hours to regain normal body temperature. Persistent coughing for the longest period of time.

Table 18.
Effect of Lydium-KLP on the efficacy of antibiotics in diseases of foals and adult horses (113).

Clinical diagnosis	Treatment method	No. of animals	Recovery rate (%)	Regression of symptoms	Death rate (%)
Broncho-pneumonia	Antibiotics 5x24h	20	80*	up to 21 days	10
	Lydium-KLP 0.01 mg/kg + antibiotics 5x24h	11	100	up to 14 days	0

Explanation:
*the remaining 10% of the foals required a repeated administration of the antibiotic.

II. Treatment of subcutaneous phlegmon

Material and methods

The study was conducted on 35 horses sick with phlegmon of the legs (mostly phlegmona serosa et purulenta). The control horses were treated conventionally, i.e. with antibiotics, NSAIDs and vitamins with minerals. Antibiotics, mainly compound LA products were injected 3-6 times every 48-72 hours. The experimental horses, apart from conventional therapy, received Lydium-KLP once i.m. a dose of 0.01 mg/kg b.w.

Results

The effect of Lydium-KLP was particularly evident in the treatment of phlegmon. Its characteristic symptoms are high temperature and swelling of the legs. In all horses, the swelling regressed in up to 7 days, i.e. 2-3 times faster than with traditional treatment. Abscesses and fistulas were generated in three horses from control group, and in only one from the experimental group.

Table 19.
The effect of Lydium-KLP on the efficacy of subcutaneous phlegmon treatment in horses.

Therapy method	Number of animals	Recoveries (%)			Abscesses (%)
		to 7th d	to 14th d	to 21st d	
Conventional	10	33.3	40	33.3	33.3*
Combined	25	76	24	-	4*

Conclusion

Lydium-KLP in a dose of 0.01 mg/kg increases the efficacy of antibiotics in the treatment of bronchopneumonia and subcutaneous phlegmon of the legs in horses.

APLICATION OF LYDIUM-KLP IN THE TREATMENT OF METRITIS IN MARES

Introduction

Endometritis is a common cause of infertility in mares, and it is the third most frequently occuring medical problem in adult horses. The causal organisms of endometritis are Streptococcus spp., E. coli, Klebsiella pneumoniae, Staphylococcus spp., Rhodococcus spp., Actinobacillus equili and numerous others including fungi and yeast. An insufficient immune system of the uterus can be the main cause of the disease. Older and multiparous females appear to have disturbances in the local defensive system, which is mostly based on the activity of phagocyting cells.

The diagnosis of endometritis is often difficult because of a history of infertility coupled with a positive uterine culture.

Therapy of acute bacterial metritis is based on the use of uterus contraction agents and appropriate antibiotics and on the reinforcement of local defense mechanisms. Satisfactory results have not been obtained in the treatment of acute

metritis yet. It has been determined that intrauterine therapy with the use of high doses of antibiotics leads to destructive changes in the endometrium. The treatment of chronic endometritis is particularly difficult, labor intensive, and frequntly inffective.

Lydium-KLP demonstrate good results in the therapy of endometritis in cows and sows due to an intrauterine application dose of 2 mg of lysozyme dimer per animal. The use of Lydium-KLP can bring profitable results in the treatment of both acute and chronic endometritis in mares.

Material and methods

Experiment 1

Examinations were carried out on 90 mares suffering from endometritis and free from other diseases related to the reproductive system. They were from 4 to 20 years old, in good condition, and were owned by stables or individual farms. Mares were clinically examined before the treatment. Smears from endometrium for cytological and bacteriological examinations were taken aseptically. Special sterile sets made by the French firm I.M.V (BP81-L'AIGLE-FRANCE) were used. Samples were placed in a transport medium, and within 24 hours bacteriological examinations were undertaken, which included isolation of bacteria as well as their antibiotic-resistance. The material for cytological examinations was placed on a basal glass and preserved with an aerosol-fixing agent, Cytofix. After drying, the preparation was dyed according to the Papanicolaou's method.

The animals were divided into 3 groups. The age of mares, intensity of inflammation, and the time between parturition and the treatment of endometritis in each group was the same. All mares were treated topically with intrauterine infusions of selected preparations diluted in 50 ml of warm buffered fluid of physiological saline (PBS). Antibiotics were used according to the indiciation of the antibiogram in commonly recommended doses. When the presence of inflammation discharge in the uterus was evident, the uterus was irrigated with physiological saline warmed to 40ºC before the infision. For the study, 2 mg in 10 ml vials of Lydium-KLP were used (Lot. 644696).

Mares from the first experimental group received only Lydium-KLP in a dose of 2 mg of lysozyme dimer per animal, twice every 48 hours. A combination of Lydium (2-mg/animal) and antibiotics was applied in the second experimental group, also twice every 48 hours. In the third (control) group, the conventional antibiotic therapy was used, three times every 48 hours. Both in the control group and in the second experimental group, gentamycin, streptomycin, Ciprobay, Augmentin, penicilin, ampicilin and Zinacef were used most frequently.

The follow-up examinations were carried out in a period of 10-14 days after the therapy. The non-recovered animals were treated again with the use of identical methods.

Experiment 2

Field trials were carried out during 2 years in the same stable. The study was conducted on 144 mares with symptoms of endometritis. The animals received intrauterine treatments with an antibiotic solution twice or three times every 24 hours (53 mares) or once with a 2 mg Lydium-KLP solution (91 mares). Bacteriological tests were conducted prior to treatment. The antibiotics and Lydium-KLP were suspended in 200 ml of PBS. Pregnancy rate among the mares was the best indicator of recovery.

Results

Endometritis was diagnosed clinically in all 90 mares from experiment 1, and it was confirmed by the cytological examination in 89 animals. The clinical diagnosis of one mare, cytologically negative, was confirmed by the ultrasonografic examination, and this animal was included in the control group. The following bacteria were found in the smears from 18 mares (60.6%) from the second experimental group and in 23 mares (76.6%) from the control group.

Results of control tests (Table 20) indicate, that after the first treatment, clinical symptoms of endometritis persisted in 2 mares only (6.6%) from the first experimental group, six mares (20%) remained positive cytologically, and in 14 cases (46.6%) previously appearing micro-organisms were still isolated. Regression of endometritis in 28 mares (93.3%) was noted, and than estrus appeared at the same time. As an effect of the treatment, 20 mares (66.6%) became pregnant. The second treatment of two mares produced a negative result, but the third therapy with Lydium-KLP resulted in the impregnation of one animal. However, one mare remained cytologically and bacteriologically positive. The final outcome of the triple treatment with Lydium-KLP was regression of endometritis in all animals (100%) and the pregnancy of 22 mares (73.3%).

Estrus and regression of endometritis in 24 mares (80%) occurred due to the effect of the combined therapy in the first experimental group. Fifteen animals (50%) from this group became pregnant. As a result of the repeated therapy of 6 mares from the second experimental group, disease symptoms disapeared in all of the animals that showed the estrus. Four mares remained cytologically positive and three were bacteriologically positive. A total of 19 (63.3%) mares became pregnant as the result of double treatment.

Treatment with antibiotics caused regression of endometritis together with estrus appearance in 9 mares (20%) from the control group and 5 (16.6%) were pregnant. Of the 21 animals, which were twice treated with antibiotics, 13 mares were impregnated (43.3%). A total of 18 mares (60%) became pregnant after double treatment. Clinical symptoms of metritis did not disappear in 3 animals. However, 9 mares remained cytologically positive and 19 bacteriologically positive.

Table 21 contains the results of the second experiment. Pregnancy rates were 79.2% in the antibiotic group and 76.9% in the Lydium-KLP group. There were no statistically significant differences between the efficacy of tratment relative to etiological agents of endometritis. It may be said that treatment of endometritis in mares with Lydium-KLP is effective and that it is less expensive than with antibiotics.

Table 20.
Efficacy of intrauterine treatment of endometritis in mares (156).

Therapy method (n)	Examination	Positive mares (%)			Result of treatment (%)		
		clinically	cytologically	bacteriologically	endometritis regression	estrus	pregnancy
Lydium-KLP (30)	I	100	100	60	93.3	93.3	66.7
	II	6.7	20	46.7			
	III	6.7	6.7	3.3			
Antibiotics + Lydium-KLP (30)	I	100	100	96.7	100	100	63.3
	II	20	60	66.7			
	III	0	13.3	10			
Antibiotics (30)	I	100	96.7	76.7	90	93.3	60
	II	70	76.7	70			
	III	10	30	63.3			

Explanation:
I - before treatment; II - 10-14 days after first treatment; III - 10-14 days after second treatment.

Results of these studies demonstrate that positive results of the treatment of endometritis in mares was obtained after intrauterine infusion of Lydium-KLP in a dose of 2 mg of lysozyme dimer applied twice every 48 hour, or even once. Such a procedure resulted in the recovery of 93.3% of mares, while in the combined therapy (Lydium-KLP with antibiotics) group, the result was worse (80% recovery rate). The use of antibiotic therapy alone (3 times every 48 h) seemed the least effective, bacause the inflammation of endometrium after the first treatment disappeared only in 30% of the animals (experiment 1).

Similar to Lydium-KLP, the efficacy of antibiotics was noted only after the second treatment (90%). A higher percentage of recoveries (100%) was obtained due to the second use of Lydium-KLP together with antibiotics. Therefore, the final result after the second treatment was best when combined therapy was used and worst when antibiotic-therapy alone was used. However, the percentage of recoveries in the second experiment was high, regardless of the drug used (Lydium-KLP or antibiotics).

Table 21.
Effect of treatment of endometritis with Lydium-KLP or antibiotics in mares (56).

Etiological agent	Antibiotics 2-3x		Lydium-KLP once	
	n	recovery rate*	n	recovery rate*
E. coli	9	55.6	29	72.4
Str. haemolyticus	17	88.2	15	100
Other	27	81.5	47	70.2
Total	53	79.2	91	76.9

Explanation:
* percent of pregnant mares as effect of treatment.

Conclusion

The intrauterine infusion of 2 mg of lysozyme dimer twice every 48 h causes regression of endometritis in mares.

Summary

Alimentary tract and respiratory system inflammations are the most common diseases of foals. Infections cause death and also restrict their growth periodically or permanently. Reproduction disorders in mares and diseases of legs cause enormous losses for owners of adult horses. The condition of the immune system plays a very significant role in the diseases' development. Therapy with antibiotics is becoming more and more expensive and often ineffective. Lysozyme dimer positively affects the horse immune system. This drug, in a dose of 0.02 mg/kg b.w., treats gastroenteritis and bronchopneumonia in foals. Lysozyme dimer increases the percentage of recoveries of bronchopneumonia and subcutaneous phlegmon cases treated according to conventional methods. Intrauterine therapy of endometritis in mares with the infusion of Lysozyme dimer in a dose of 2 mg per animal is particularly efficacious.

The main causes of economic losses at small and large hog farms are diseases of the alimentary tract and the respiratory system. The most common diseases of the alimentary tract are various forms of colibacillosis (newborn colibacillosis and weaning period colibacillosis) and edema disease.

The most common disease of the pig's respiratory system is, undoubtedly, mycoplasmal pneumonia, caused by Mycoplasma hyopneumoniae. Until recently, it was known as enzootic bronchopneumonia. The disease is common anywhere hogs are raised on a large scale.

Three pathologic conditions may affect sows during the perinatal period: disorders in the expulsion of the fetus and the placenta, infectious diseases, and inflammations of the uterus and the udder, usually accompanied by agalactia. The latter is the most frequent disorder and is known as the MMA (Mastitis-Metritis-Agalactia) syndrome.

EFFICACY OF LYDIUM-KLP IN THE TREATMENT OF SELECTED DISEASES AFFECTING PIGS UNDER DIFFERENT FARMING CONDITIONS

Introduction

Etiopathogenesis of piglet colibacillosis depends on whether colibacilli possess the fimbria antigens (K88, K99, 987P, F41) that allow them to colonize the mucous membrane epithelium of the small intestine and to generate thermostable enterotoxin (ST) and thermolabile enterotoxin (LT). The etiological factors of the edema disease are mainly the 0139-, 0141-, and 0138-serotypes of colibacilli. These microorganisms generate toxins, now called verotoxin and Shiga-like toxin, which are capable of damaging the capillary vessels. As a result, the exudate penetrates tissues and swelling occurs.

Infections with M. hyopneumoniae causes of the disease, with a significant inhibition of growth and poor utilization of feed, but relatively few death. Also important are the immunosuppressing properties of M. hyopneumoniae that cause other bacterial and viral respiratory diseases in herds affected by mycoplasmal pneumonia.

In the establishments with high concentrations of pigs, Mastitis-Metritis-Agalactia syndrome (MMA) may affect up to 40% of farrowing sows. Partial or total lack of lactation is the main cause of death among piglets prior to weaning.

A number of factors may cause perinatal disorders, such as the type of breeding, the herd size, and the type of nutrition, especially during the perinatal period. Etiopathogenesis also includes important bacterial factors, such as Escherichia coli, other intestinal bacilli, streptococci, and staphylococci.

Many authors consider Escherichia coli to be the main cause of postpartum agalactia syndrome. These bacteria and their endotoxins, normally present in the alimentary canal, do not penetrate the cardiovascular system because they are blocked by the intestinal mucous membrane and the properly functioning reticuloendothelial system. The stress triggered by labor and unfavorable environmental factors may lower the immunity and increase the number of bacteria and the level of endotoxins they generate. Due to decreased immunity, they are capable of penetrating the intestinal mucous membrane. Once they enter the cardiovascular system, they poison the body.

The diseases are dealt with through specific prophylaxis, chemoprophylaxis, and antibiotic treatment. It seems advisable to utilize another method, i.e. non-specific stimulation of the immune system. Lysozyme dimer influences cellular and humoral mechanisms of the immunity. It activates phagocytosis in adult pigs and some other immunological mechanisms in piglets.

Material and methods

The study was conducted in several environments, i.e. breeding farms, production farms, and small and large individually owned farms.

After each adult animal and a representative sample of piglet litters underwent a clinical examination, they received 0.02 mg/kg of Lydium-KLP once or twice. It was given intramuscularly to piglets and intravenously to weaned piglets and sown. Monitoring tests (including measurements of body temperature) were done every 24 hours until all symptoms disappeared.

Results

Treatment of acute gastroenteritis, usually caused by E. coli, achieved the best results. Diarrhea normally disappeared within 24 hours. It persisted in isolated cases, but the stool became thicker. The animals regained their appetite and their

Table 15.
Effect of Lydium-KLP on the efficacy of antibiotics in the treatment of pneumonia and gastro-enteritis in calves (48, 49).

Disease	Treatment	Number of animals	Recovery rate (%)	Death rate (%)
Piglet colibacillosis	Lydium-KLP 1x	700	96,9*	1,4
	Lydium-KLP 2x24h	139	97,8*	2,2
	Chemotherapeutics	550	81,1	x
Edema disease	Lydium-KLP 1x	125	84,0*	9,6
	Lydium-KLP 2x24h	70	85,7*	11,4
	Chemotherapeutics	60	60,0	x
Enzootic broncho-pneumonia	Lydium-KLP 1x	140	89,0*	4,3
	Lydium-KLP 2x24h	25	88,0*	8,0
	Chemotherapeutics	95	80,0	x
Pospartum agalactia (MMA)	Lydium-KLP 1x	70	90,0*	4,3
	Lydium-KLP 2x24h	10	90,0*	0
	Chemotherapeutics	60	80,0	x

Explanation:
*the remaining animals recovered after 1 or 2 injections of antibiotics; x - no data.

overall condition did not show any signs of the disease. The effects of treating edema disease were surprisingly good. Some animals that had already been lying down regained their appetite within 6-12 hours. When their body temperature was above or below the norm, it returned to normal 24 or even 12 hours after treatment began.

The efficacy of Lydium-KLP in the treatment of colibacillosis and edema clearly surpassed the efficacy of antibiotics. The effects of Lydium-KLP were also very good in the treatment of bronchopneumonia. Only the chronic cases ended in death.

Lydium-KLP was particularly effective and useful in the treatment of the MMA syndrome. Ninety percent of sows recovered after 1 or 2 injections. Fever dropped within 24 hours or, in some cases, within 6-12 hours. The animals regained appetite, the swelling of inflamed gland sections decreased, the amount of inflamed discharge from the reproductive organs also decreased, and lactaction increased. Piglets did not appear hungry and their diarrhea atopped (it had appeared in some litters of diseased sows). Forty eight hours after treatment began sows ate normally,

had a normal body temperature, and showed no disease symptoms. The animals that were sick for more than 48 hours recovered after receiving antibiotics. There were only 2 deaths associated with toxemia. The results of treating postpartum agalactia with Lydium-KLP were better than the results of traditional treatment, which consists of injections of antibiotics and oxytocin, intravenous infusions of glucose, and administration of laxatives.

The efficacy of Lydium-KLP was identical after 1 i.m. or i.v. injection, or after 2 injections given 24 hours apart.

Conclusion

One intramuscular or intravenous injection of Lydium-KLP in dose of 0,02 mg/kg of body weight ensures high efficacy in the treatment of diseases of the alimentary tract and the respiratory system and postpartum agalactia (MMA) in pigs.

USEFULNESS OF LYDIUM-KLP IN THE TREATMENT OF POSTPARTUM DISEASES IN SOWS

Experiment 1

Material and methods

The study was conducted in 2 large herds. One hundred sows with clinical symptoms of the MMA syndrome were included in the study. The animals received full portions of feed in accordance with the generally accepted guidelines. Deliveries occurred in individual pens where the temperature remained at 20-25°C. The experimental group consisted of 50 females selected at random that received Lydium-KLP once intrauterinely (40 sows) or intramuscularly (10 sows). The control group consisted of 50 females that were treated according to methods based on antibiotics and vitamins traditionally followed at a given establishment. Lydium-KLP was administered intramuscularly in doses of 0.02 mg/kg of body weight and intrauterinely in doses of 2 mg per animal in 20 ml of physiological NaCl solution. Clinical examinations consisted of 2 daily measurements of body temperature beginning 2 days prior to delivery and ending 5 days following delivery, observation of the overall symptoms (appetite, depression), the amount, nature and smell of discharge from the reproductive organs, and inflammatory changes in the mammary gland. The convalescence period was closely monitored and selected reproductive indices for both groups were analyzed. The death rate among piglets younger than 7 days was also analyzed. Bacteriological tests were done on smears collected from the reproductive organs of 10 randomly selected sows from both groups prior to the administration of Lydium-KLP or antibiotics, and 24-36 hours following their administration.

Results

Inflammation of the reproductive organs was observed in 73% of sows, mammary gland inflammation in 13%, and both diseases in 7%. At 24-36 hours after Lydium-KLP was administered intrauterinely or parenterally, the body temperature decreased (Figure 7). The discharge from the reproductive organs also decreased and its nature and smell changed to normal. On day 2 after treatment began, the body temperature ranged between 39.2 and 39.4°C, interest in the young increased and so did the appetite. In the sows suffering from mammary gland inflammation, sensitivity to touch decreased and disappearance of inflammatory changes and presence of milk were observed. In the sows with large inflammations of the mammary gland and the reproductive organs, obvious overall symptoms and lack of lactation, the changes regressed more slowly and the body temperature also decreased more slowly. The temperature returned to normal in 48-56 hours and inte-

rest in the young and in food grew. On day 4, the amount of discharge from the reproductive organs decreased and its consistency and smell changed. The symptoms regressed faster after intramuscular injections than after intrauterine infusions.

In the control sows that received antibiotics (mostly from the tetracycline group), The body temperature decreased more slowly and it returned to normal as late as 5 days after treatment began. Inflammations of the mammary gland and the reproductive organs also receded more slowly. The reproductive organ's discharge persisted longer and its amount, nature, and smell indicated the inflammation was acute. In the sows with obvious inflammations of the mammary gland and the reproductive organs and lack of lactation, the course of the disease was slower, the convalescence period was 10-14 days longer than in the experimental sows, and the treatment efficacy rate, defined as capability to resume the reproductive function, was lower: 94% in the experimental group and 74% in the control group. The analogical efficacy rate in the sows with full-blown MMA syndrome was, respectively, 66.7% and 25%.

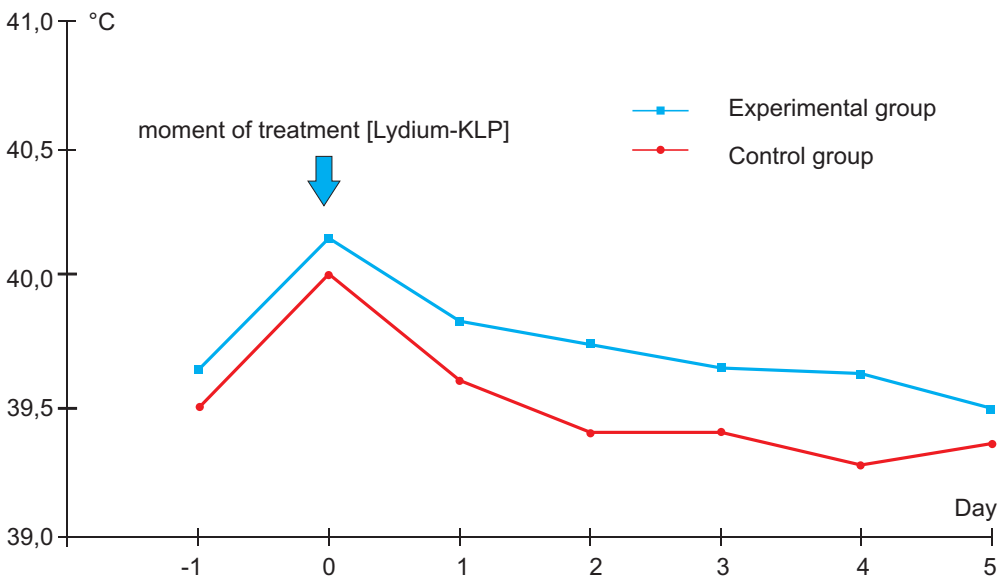

Figure 7.
Average body temperature of sows with the MMA syndrome (11).

Both intrauterine and parenteral administration of Lydium-KLP caused significant quantitative and qualitative changes in the bacterial flora of the reproductive tract. At 36 hours after the preparation was administered, 80% of sows had no bacteria and 20% had mixed flora, the majority being coli bacteria. During this time, the control animals that received antibiotics parenterally also showed quantitative and qualitative changes in the bacterial flora of the reproductive tract.

Table 23 presents the effect of sows' overall health on the losses of piglets younger than 7 days. The death rate among the experimental piglets was 8.5% and 21% among the control piglets. These data reflect the intensity of the disease and the course of convalescence among sows in different groups. The decrease of body temperature and disease recession were faster in the experimental sows than in the control sows. Interest in the young and lactation also returned faster. The high death rate in the control group was the result of slower recovery among sows and decreased lactation.

Table 23.
Piglet losses during the perinatal period (11).

Sows	Number of animals	Piglets		
		born	died before 7 days of age	death rate (%)
Experimental	50	483	41	8.5
	x	9.7±1.3		
Control	50	481	101	21.0
	x	9.6±1.1		

Explanation:
x - average size of litter.

The course of the disease and the length of the convalescence period had an effect on the reproductive readiness of sows after piglets had been weaned. Forty-seven of the experimental sows (94%) were designated for further reproduction and 80% of them were in heat in 7-10 days after piglets were weaned. The success rates of covering the females were 89.4% in the experimental group and 59.4 % in the control group.

Experiment 2

Material and methods

Lydium-KLP was used in the treatment of 74 sows, multiparae and primigravidae, with a body weight of 110-280 kg, owned by individual farmers. The animals had been diseased for 12 hours to 7 days. Eight sows received antibiotics earlier. Fifteen cases were directly associated with delivery (miscarriage, dystocia, retained placenta), 3 sows became ill during the last week of pregnancy, and the remaining ones had the postpartum agalactia syndrome. The most common symptoms were those of metritis, toxemia, loss of appetite, weakening, and lack of lactation. The pigles from sick mothers were uneasy, hungry, and most of them were emaciated. Diarrhea was observed in 26 litters and in 5 cases it affected all piglets. Isolated death cases occurred in 7 litters.

Lydium-KLP was administered intravenously or intramuscularly in a dose of 0.02 mg per 1 kg of body weight. It was given twice every 24 hours in combination with oxytocin (4 animals) and without oxytocin (5 animals). It was also given once after an ineffective treatment with antibiotics (8 animals), in combination with oxytocin (13 animals), or with antibiotics that were given only once (25 animals), and with no other medications (15 animals).

Control tests were performed 24 and 48 hours after the treatment began and, on some animals, 72 and 96 hours after it began. All animals were examined 7 and 14 days after treatment began.

Results

Single injections of Lydium-KLP, with or without oxytocin, and 2 injections of Lydium-KLP (Table 24) proved to be very effective in the traetment of postpartum agalactia and metritis associated with the retention of fetuses or placentae that were removed manually, with forceps, or through cesarean section. One of the sows that received Lydium-KLP with oxytocin died 48 hours after the injection. An autopsy revealed intestinal volvulus. It was necessary to slaughter one sow 8 hours after the injection due to persistent circulatory failure and fever. In this case, autopsy revealed the presence of dead fetuses and peritonitis. Symptoms of the disease persisted in 2 sows for 48 hours after the first injection. The recovered after antibiotics were given. Single injections of Lydium-KLP in combination with antibiotics also proved to be effective in the treatment of postpartum agalactia.

Table 24.
Efficacy of Lydium-KLP in postpartum diseases in sows (69).

Treatment	Number of sows			Recovered (%)		Died (%)
	overall	MMA	other	1st treatment	2nd treatment**	
Lydium-KLP	22	19	3	19 (86.4)	2 (9.1)	1 (4.5)
Lydium-KLP + oxytocin	19	15	4	17 (89.5)	1 (5.3)	1 (5.3)
Lydium-KLP + antibiotics*	25	22	3	22 (88.0)	2 (8.0)	1 (4.0)
Lydium-KLP after antibiotics	8	1	7	3 (37.5)	-	5 (62.5)

Explanation:
*oxytetracycline or penicillin in conjunction with streptomycin or neomycin; ** only antibiotics were used.

Table 24 further shows that a single Lydium-KLP injection caused the symptoms to disappear in 3 out of 8 sows unsuccessfully treated with antibiotics. Autopsy of the animals that died revealed lung abscesses and pleurisy (1 animal), pneumonia with pleural and pericardial adhesions (1 animal), and peritonitis, metritis and putrefactive fetuses (2 animals). An autopsy was not conducted on one animal.

The recovery process was almost identical in all subgroups. Within the first 24-hours period, and sometimes even within 6-12 hours, fever diminished, the appetite returned, lactation increased, swelling of the glands decreased, the amount of ichorous-suppurative discharge from the reproductive tract decreased, and the symptoms of circulatory failure regressed. The piglets were calm, did not appear hungry, and diarrhea disappeared in 20 litters where it was evident before treatment of the sows began. Of particular significance was the recovery of 3 sows with severe circulatory failure and body temperatures below normal (less than 37°C) that had been receiving antibiotics for 3-5 days in addition to other medications.

Early within the second 24-hour period, one half of the animals showed poor appetite and moderate discharge from the vagina. Some animals had insufficient lactation and a slight swelling and hardening of the inflamed glands.

At 48 hours after treatment began, the sows ate normally, their body temperature was normal, and they had no other disease symptoms except a slight hardening of the glands (2 animals) and a moderate, odorless discharge from the reproductive tract (3 animals). Symptoms of enteritis with diarrhea disappeared in more piglets and isolated deaths occurred in only 4 litters.

The efficacy of treating pathological perinatal conditions in sows with Lydium-KLP did not differ from other methods used in the veterinary practice, such as chemotherapeutics, oxytocin, intestinal peristalsis stimulants, the reproductive tract lavage, and general strengthening drugs. These traditional methods are effective, but more labor-intensive and more costly.

What must be particularly emphasized is the importance of beginning treatment as early as possible. In diagnosing the postpartum agalactia syndrome, especially its subclinical form, it is very important to measure the sows' body temperature during the first 3 days following delivery. Initially, the appetite may frequently remain unaffected and there are no clinical symptoms. Fever, which may be the only symptom, is accompanied by diarrhea in piglets. In cases where the body temperature exceeds 39°C, treatment must start immediately. In such cases, Lydium-KLP may be used as the only drug or it may be used in combination with antibiotics and oxytocin.

Conclusion

In the treatment of postpartum diseases in sows, Lydium-KLP should be administered once in a dose of 0.02 mg/kg. It may be combined with an injection of oxytocin. If there is no improvement within 24 hours, 1 or 2 injections of antibiotics give satisfactory results.

Lydium-KLP shows high efficacy in the treatment of the MMA syndrome in sows by shortening the convalescence period to 2-3 days and favorably affecting the reproductive capability of the females.

Administration of Lydium-KLP restrics losses caused by MMA among piglets and sows by 2.5 times.

LYDIUM-KLP IN THE PROPHYLAXIS OF SELECTED PERINATAL DISEASES IN SOWS

Experiment I

Material and methods

The study covered 120 randomly selected pregnant Polish White Breed sows (60 in the experimental group and 60 in the control group) with an average body weight of 208 kg. The study was conducted at an establishment with high rates of postpartum agalactia. The animals received full-portion feed in accordance with the generally accepted criteria and were kept under average cleanliness conditions. Deliveries took place in delivery rooms in individual pens where the temerature was 20-25°C. Ten days before delivery, the experimental animals (n=60) received one i.m. injection of Lydium-KLP in a dose of 0.02 mg/kg of body weight. The control group (n=60) consisted of sows within the same production cycle that were kept in an identical environment. The effects of Lydium-KLP were evaluated based on the results of clinical examinations, including the MMA incidence, death rates among piglets of the sows of the sows affected with MMA, and reproductive readiness after piglets have been weaned. In addition, 2 blood tests were performed before treatment and 10 days after delivery on 20 sows from each group to assay selected indices of cellular and humoral immunity.

Results

In the experimental group, 1.7% of the sows were diagnosed with full-blown MMA syndrome, 3.4% had metritis with no changes in the udder, and 5.1% had clinical mastitis. In the control group, the respective disease rates were higher: 10%, 13.3%, and 10.2%; the symptoms were more severe, and they persisted longer. Five experimental sows with postpartum agalactia received single injections of Lydium-KLP and 2 received 2 injections. The effects were satisfactory. When the preparation was administered to 13 sick sows from the control group, the body temperature dropped within 24-36 hours and improvements were noted in the amount, nature, and smell of the discharge. In some of the animals in this group, administration of Lydium-KLP proved insufficient and they recovered after a tetracycline-type antibiotic was used. Therapeutic efficacy among the sows that did not receive Lydium-KLP before delivery was 88.3% (Table 25). Various degrees of disease intensity among sows were associated with different death rates among their young. In the experimental group, 4.9% of 590 piglets died during the first 7 days after delivery, whereas in the control group, 12.2% of 588 piglets died. The difference in death rates was statistically significant. Administration of Lydium-KLP before delivery also had a favorable effect on the heat onset after piglets had been weaned. The time period before heat was shorter by almost one half than that of the control animals.

The experimental sows had greated immunity: phagocytic activity increased by 65.2% and neutrophil (NBT+) activity increased by 37.2%. Unlike in the control sows, there was also a statistically significant increase of the percentage of lymphocytes transforming under the influence of LF-1 (82% on average). There was also a significant increase of the total protein with an increased level of albumins and globulins, which was especially marked in the gamma fraction.

Table 25.
Effects of prophylactic use of Lydium-KLP in sows (15).

Itemization	Groups	
Sows	Experimental	Control
Disease incidence (%)	11.7	41.7
Piglet deaths before 7 days of age (%)	4.9	12.2*
Heat in sows after piglets weaning (days)	7-10	16-25

Explanation:
*statistically significant difference ($p<0.05$).

Experiment 2

Material and methods

The effectiveness of Lydium-KLP in preventing post-partum agalactia syndrome was evaluated in a trial performed in great commercial farms A, W and P, all affected by MMA, on 90 multiparous large white sows, each at 140 to 190 kg of body weight. Thirty sows were used in the experiment in farm A, 40 in farm W and 20 in farm P. In each farm, the animals were subdivided into group E (experimental pigs) and group C (control animals). The experimental animals were given an intramuscular injection of Lydium-KLP at a dose of 0.02 mg/kg b.w., 5-7 days prior to the expected farrowing, whereas the control sows received water for injection as a placebo, during the same period of time.

The sows were placed in individual farrowing pens approximately 7 days before parturition. Clinical observations of the sows were made over period of 7 consecutive days following farrowing. The effect of Lydium-KLP on animal organisms was estimated on the basis of clinical observations during which the following parameters were measured: body temperature (b.t.), loss of appetite, agalactia, discharge from the genital tract, mastitis, and the number of born and weaned piglets, as well as the number of suckling piglets that were affected with diarrhea.

The experimental sows had greated immunity: phagocytic activity increased by 65.2% and neutrophil (NBT+) activity increased by 37.2%. Unlike in the control sows, there was also a statistically significant increase of the percentage of lymphocytes transforming under the influence of LF-1 (82% on average). There was also a significant increase of the total protein with an increased level of albumins and globulins, which was especially marked in the gamma fraction.

Results

Table 26.
Efficacy of Lydium-KLP in the prevention of post-partum agalactia syndrome in sows (127).

Group (n)	Percentage of sows ith the following items under observation					Piglets		
	body temp. >39.9°C	loss of appetite	agalactia	metritis	mastitis	born (n)	weaned (%)	diarrhea (%)
E (45)	0	6.7	0	4.4	-	470	90.8	7
C (45)	15.5	15.5	17.8	8.9	8.9	485	83.7	17.1

Explanation:
E - experimental, C - control.

The frequency at which at least one of the MMA symptoms appeared clinically varied from 20% (for farms W and P) to 26.7% (in farm A) in the control groups, compared to 6.7-15.0% sows from the experimental groups. The average MMA frequency decreased from 22.2% to 11.1%. The improvement in the health of the sows caused the diarrhea of piglets to be less pronounced in the experimental groups (4.8% - farm W to 10.7% - farm P) than in control groups (respectively 11.2% to 24.2%). The average percentage of piglets with diarrhea decreased from 17.1% in the control groups to 7.0% in the experimental groups (Table 26).

Conclusion

Administration of Lydium-KLP 10-7 days prior to delivery helps prevent postpartum agalactia among sows, and it decreases losses among piglets. Lydium-KLP also has favorable effect on the course of the postpartum period and on earlier resumption of reproductive activity after piglets have been weaned.

LYDIUM-KLP IN THE PROPHYLAXIS OF WEANING PERIOD DISEASES AMONG PIGLETS

Experiment 1

Material and methods

The study covered a total of 580 clinically healthy 6-week-old piglets with a body weight of approximately 12-kg each. The experimental group and the control group consisted of 290 piglets each. On the day they were weaned, the experimental animals received Lydium-KLP as an intramuscular injection of 0.02 mg/kg og the active substance per 1 kg of body weight. Piglets from both groups were kept under identical environmental conditions and received the same full-portion feed that met their nutritional needs.

An evaluation of the effects of Lydium-KLP was based on the results of clinical observations conducted during 4 weeks following the administration of the preparation with particular attention given to incidents of disease, death, use of feed, and weight increases. Litter disease incidence and group disease incidence indices were calculated. The prophylactic efficacy was calculated as a quotient of the number of disease-free piglets to the number of piglets that received Lydium-KLP. If there was transient improvement or no improvement, antibiotics were used in combination with Lydium-KLP. The results were analyzed statistically according to the two-parameter method with the Student's t-test.

Results

Body weight increases were over 13% larger in the experimental group than in the control group. Better utilization of food among the piglets that received Lydium-KLP corresponded to greater weight increases. The experimental animals had a statistically significant 11% lower use of feed per 1 kg of weight increase. Disease incidence was 3 times lower among the experimental piglets. There were no death among the 10.3% of experimental piglets that developed diarrhea, whereas almost 6% died in the control group despite antibiotics or antibiotics combined with Lydium-KLP. It was also noted that administration of antibiotics in combination with Lydium-KLP was more effective than administration of pure antibiotics. After both medications were administered, disease symptoms receded faster, which was evident through increased mobility and faster return of the appetite. Shortening of the convalescence period diminished body weight losses that normally occur during disease and treatment.

Table 27.

Prophylactic effects and economic results of administering Lydium-KLP to piglets (16).

Itemization	Groups	
	Experimental	Control
Disease incidence per litter (%)	1034	32.43**
Death rate (%)	0	5.7
Body weight on the day of weaning (kg)	11.5-12.8	10.8-11.9
Average daily weight increase (g)	473,0* (393.0-518.0)	418.0 (325.0-486.0)
Average feed utilization kg/kg of increase	3,08 (2.90-3.30)	3.46** (3.1-3.8)

Explanation:
*statistically significant difference; ** statistically highly significant difference.

Experiment 2

Material and methods

The field trials were carried out in 4 large commercial farms (Z, P, S, T) on a total of which 265 were tested in farm Z, 880 in farm P, 495 in farm S and 254 in farm T. In each farm, the animals were randomly subdivided into 2 groups, more or less equal in number of heads: an experimental group and a control group, composed, in turn, of equal number of males and females. Both the experimental and control piglets were kept in the same comfortable conditions and fed the same, complete feed. The piglets were weaned on the day 35 of life in farms Z, P and T, and on the day 21 of life in farm S. The experimental piglets (altogether 956 heads) received a single i.m. injection of Lydium-KLP, at a dose of 0.02 mg of lysozyme dimer/kg b.w., 3-5 days before weaning. At the same time, all of 0.02 mg of lysozyme dimer/kg b.w., 3-5 days before weaning. At the same time, all of the 929 control piglets received a placebo injection (sterile water). Any case of diarrhea, in the experimental and control groups, was treated with antibiotics (efficacious in the given farm) and hydration fluids mixed in the feed.

In order to evaluate effectiveness of Lydium-KLP in the prophylaxis of diarrhea in piglets during the post-weaning period, the following parameters were considered: the percentage of piglets with symptoms of scours during 14 days following weaning, growth rate over the same period of time, and mortality during the experiment. The animals were under clinical observation throughout the entire experiment, twice a day (in the mornings and in the evenings).

Results

The post-weaning diarrhea was a noticeable problem in all farms. The number of affected piglets ranged from 25% (farms S and T) to 67.7% (farm Z). Bacteriological examinations of the feces of infected animals revealed the presence of enterotoxic strains of E. coli. Swine rotaviruses were also isolated. We assume that these micro-organisms were but a few of the factors responsible for diarrheic symptoms.

The application of Lydium-KLP markedly limited the incidence of diarrhea linked with the weaning period. The best results were obtained in the farms (S and T) where the state of health of the animals was evidently better than that in the remaining 2 farms. In the control groups at these farms, clinical diarrhea was noted in 25% of piglets, whereas in the experimental groups it amounted to 6.5% and 4.0%. All in all, the use of lysozyme dimer decreased the diarrhea in the weaning period from 40.5% to 19.2%. Losses due to mortality dropped from 8.3% to 5.1%. Fewer piglets were diseased and, consequently, their average daily growth rate improved in a period of 14 days after weaning, reaching 247.5g in the experimental group, as compared to 217.5g in the control group.

Table 28.

Efficacy of Lydium-KLP in the prevention of diarrhea in weaned piglets (127).

Group	Number of piglets	Number of piglets with diarrhea during 14 days after weaning	Average daily growth rate during 14 days after weaning			Mortality n (%)
			min.	average	max.	
E	956	184 (19.2%)	151.5	247.5	306.0	49 (5.1)
C	929	376 (40.5%)	101.7	217.7	278.5	77 (8.3)

Explanation:
E - experimental; C - control.

Conclusion

Administration of Lydium-KLP to piglets before weaning demonstrates prophylactic effects through less frequent alimentary tract inflammations and better utilization of feed.

Summary

Alimentary tract inflammations in piglets, respiratory system inflammations of swines after weaning and mastitis-metritis-agalactia syndrome in sows are the main causes of economic losses at small and large hog farms. The diseases are dealt with through specific prophylaxis, chemoprophylaxis, and antibiotic treatment. It seems advisable to utilize another method, i.e. non-specific stimulation of the immune system.

Lydium-KLP is particularly useful in the therapy and prophylaxis of diseases affecting swines. One intramuscular injection of 0.02 mg/kg of Lydium-KLP ensures high efficacy in the treatment of the diseases of the alimentary tract and the respiratory system in suckling and weaned piglets. This dose of the prepartion is also highly effective in the treatment of the MMA syndrome in sows.

When administered 10 days prior to delivery, the same dose prevents MMA in sows, and when given to piglets on the day they are weaned, it prevents diseases and death. Lastly, Lydium-KLP increases the efficacy of antibiotics in pig diseases.

Inflammations of the alimentary tract, the respiratory system and the skin are the most common diseases affecting carnivores. Each of these disordes has a complicated etiology and pathogenesis, and is dependent on intricate environmental and genetic factors. Inflammations of the alimentary tract are usually acute and are frequently accompanied by abrupt dehydration. Inflammations of the respiratory system are acute with high fever, or are chronic and prolonged. Skin inflammations are generally chronic and the causes are sometimes difficult to identify. In each case, susceptibility to bacterial and viral infections is a consequence of reduced immune system efficiency. Lysozyme dimer increases the WBC count and phagocytic activity of neutrophils in healthy, adult dogs as a result of a single or double i.m. application (38, 148). It has been proven that Lydium-KLP can be safely administered to dogs (44, 51).

EFFICACY OF LYDIUM-KLP IN TREATMENT OF SELECTED DISEASES AFFECTING CANINES

Introduction

The treatment of diseases affecting dogs is difficult, costly, lengthy, and frequently ineffective. Most commonly, it involves antibiotics. In addition, depending on the disease and the time that treatment begins, the following therapeutic agents are also used: sera, vaccines, electrolyte solutions, glucose solutions, vitamins, corticosteroids, non-steroid anti-inflammatory drugs, cardiac drugs, diuretics, hormones, and stimulating and homeopathic drugs. Inflammations of the alimentary tract are often associated with bloody diarrhea, and frequently cause death. Many cases of pneumonia with complications can also end in death. Skin and ear diseases are characterized by frequent relapses.

Material and methods

The study was conducted on 141 male and female dogs of various breeds, ages 2 month to 15 years. The length of sickness ranged from several hours to 7 days or longer. Most of the dogs did not receive any treatment with the exception of isolated cases of ear, skin, or respiratory system inflammations. Lydium-KLP was administered twice, 24 hours apart, or once in a dose of 0.02 mg/kg of body weight. Clinical examinations were performed prior to treatment and, in some cases, samples were taken for laboratory testing. Follow-up testes were conducted every 24 hours until symptoms disappeared, or additional treatment was instituted. The animals were treated for problems with the alimentary tract, respiratory system, and skin. Some of the dogs affected with gastroenteritis suffered from severe overall symptoms, vomiting, and bloody diarrhea. Viral enteritis, including parvovirus, was suspected in these cases. The majority of dogs with respiratory system diseases had elevated body temperatures. Auscultatory examination revealed bronchopneumonia in 50% of the animals, and bronchitis, tracheitis and laryngitis in the other 50%.

The cases of skin inflammations included folliculitis and skin fold inflammations. Most of the infections were caused by Staphylococcus aureus. Samples collected from ears revealed Staphylococcus aureus, Staphylococcus epidermidis, and Streptococci.

Results

Approximately 70% of the animals recovered after Lydium-KLP was administered once or twice. Death rates were similar in both subgroups. The remaining animals recovered in response to supplementary treatment with antibiotics given parenterally and orally, solutions of glucose and electrolytes, and vitamin preparations.

In the cases of successful treatment of gastroenteritis, fever disappeared within a few hours, and in approximately 33% of the dogs, vomiting and diarrhea regressed within 24 hours. In the remaining animals, loose stool was observed for 2-3 days. Thirst and appetite usually returned to normal between days 4 and 6, although there were cases when appetite returned on day 2 or 3. The preparation proved more effective in the fresh cases, i.e. when treatment began within 12-24 hiurs of the apperance of the first symptoms. Chronic cases in which vomiting and bloody diarrhea persisted for 2-3 days were less susceptible to the lysozyme dimer and it was necessary to supplement it with antibiotics, glucose, and electrolytes.

Table 29.
Efficacy of Lydium-KLP in selected diseases affecting dogs (128).

Clinical diagnosis	Number of iniecjons	Number of animals	Percentage of:		
			Recovery		Death
			Lydium-KLP	Additional drugs	
Acute gastroenteritis	2x24h	45	64.4	20.0	15.6
	1	28	75.0	17.9	7.1
Acute and chronic bronchopneumonia	2x24h	26	57.7	38.5	3.8
	1	12	66.7	33.3*	0
Acute and chronic skin inflammation	2x24h	20	65.0	35.0	0
	1	10	70.0	30.0	0

Explanation:
*2 dogs required long-term treatment.

Treatment of respiratory tract inflammations progressed similarly, regardles of the number of Lydium-KLP injections and the inclusion of other medications. Body temperature dropped, and the overall condition improved within the first 24 hours. Symptoms such as coughing, dyspnea, and auscultatory changes regressed rather slowly. The efficacy of Lydium-KLP in the treatment of regressed rather slowly. The efficacy of Lydium-KLP in the treatment of pneumonia, bronchitis, tracheitis, and laryngitis was exceptional. There were only 3 death due to complications from lung distemper.

High efficacy was also achieved in the treatment of skin inflammations. Itching disappeared quickly, and in new cases where small skin areas were affected, the suppurative exudate disappeared and acabs formed promptly. Surprisingly good efficacy was observed in acute and chronic external otitis. The treatment consisted of injecting Lydium-KLP, introducing and antibiotic peparation into the cleaned-out external canal, and administering antibiotics for 3-4 days.

Conclusion

Lydium-KLP in a single dose of 0.02 mg/kg of body weight is effective in the treatment of gastroenteritis, bronchopneumonia, and skin inflammations in dogs.

USEFULNESS OF LYDIUM-KLP IN TREATING SELECTED FORMS OF TUMORS IN DOGS AND CATS

Introduction

The treatment of tumors in dogs, cats and other animals that act as companions to humans is becoming more and more important regarding both theory and the practice of the veterinary science. The most common method of therapy is surgery. The objective of clinical observations is to evaluate the usefulness of Lydium-KLP (NIKA) in the treatment of selected tumors in pets.

Material and methods

The research concerned a group of 118 dogs and 18 cats with neoplastic changes that differed in progress and malignancy level. The animals were divided into three groups: one control group and two experimental groups. The control group (41 animals) was treated with the conventional mathod consisting of a surgical procedure (removing tumors and other affected tissue) and applications of protective and palliative drugs. The first experimental group, consisting of 37 dogs and cats was treated with a surgical procedure followed by injections of Lydium-KLP (at least 8 times) in doses of 20-40mg/kg b.w. or s.c. (combined method). The second experimental group was made up of 40 dogs and cats. In this case, the conservative method (only Lydium-KLP injections) was implemented. The effectiveness was monitored for a period of 6-24 month after the therapy ended.

Results

The results of tumor treatment with the use of lysozyme dimer are shhown in Table 30. The combined method appears to be the most effective (67.6% of recovery) when compared with conventional (62.2%) and conservative (45%). Lysozyme dimer injections led to the quicer recoverirs of surgically treated animals. As a consequence of combined therapy, there were fewer recurrences, metastases, and postoperative complications, as compared to the conventional treatment. The conservative therapy resulted in the termination of tumors, or even the regression of tumor like adenocarcinoma, adenofibroma, seminoma and papilloma.

The results of these observations indicate the validity of continuing research on the application of lysozyme dimer in the treatment of animals affected by neoplasm.

Table 30.
Results of the surgical, combined and conservative treatment methods of tumors in dogs and cats (52).

Animals	Diagnosis		Method and results of treatment*					
			surgical		combined		conservative	
	clinical	histological	n	cured	n	cured	n	cured
Dogs	mammary gland tumor	adeno-carcinoma	14*	9	13	9	15	6
		adeno-fibroma	2	2	2	2	3	3
	tumor of perianal gland	adeno-carcinoma	4	2	3	1	2	2
	tumor of testis	seminoma	4	2	2	2	4	2
	tumor of gums	epulis neoplasmaticus	5	2	5	3	4	1
	cystomatous hyperplasma	cystis epidermoidales	5	3	2	1	3	1
	ovary tumors	fibroma, cystoadenoma	-	-	4	2	4	-
Total dogs			34	20	31	20	35	15
Cats	tumor of testies, skin and ears	seminoma, adenoma, papilloma	7	5	6	5	5	3
Total		n	41	25	37	25	40	18
		%	100	62.2	100	67.5	100	45.0

Explanation:
*in 5 cases cytostatics were used.

EFFECT OF LYDIUM-KLP ON THE EFFICACY OF TRADITIONAL TREATMENT

The study was conducted on 98 male and female dogs of various breeds, ages 3 month to 16 years. Most of the animals did not receive any earlier treatment. The disease was observed for several hours (enteritis with boody diarrhea) or up to several days (skin and ear diseases, metritis). Treatment began after a clinical examination was conducted, and laboratory test (bacteriology and hematology) samples were collected from some animals. There were two treatment variants. Variant I involved administering Lydium-KLP twice, 24 hours apart, in conjunction with antibiotics (penicilin, streptomycin, tetracycline, lincomycin, ampicillin, etc.). The antibiotucs were continued for 2-3 days. In cases of severe dehydration, glucose or electrolyte solutions were administered i.v. or s.c. In variant II, Lydium-KLP was administered once and antibiotics were given again after 24 hours. If an obvious improvement or regression of the symptoms was observed, antibiotics were discontinued. In the treatment of ear inflammations, in addition to the injection, antibiotics were also administered topically. Pyometritis was treated with antibiotics administered intravenously and intrauterinely as emulsion. Treatment involving Lydium-KLP was also compared with treatments traditionally utilized in selected diseases affecting puppies, dogs, kittens, and fox cubs.

Results

The combined treatment was effective, because it resulted in high recovery rates in all diseases. One injection of Lydium-KLP was no less effective than two injections given 24 hours apart. The overall health of the animal and the time of the first injection had a significant effect on the response. In comparison with traditional treatment methods, the efficacy of Lydium-KLP was greater by 10-25%. Poor efficacy of Lydium-KLP in combination with intravenous administration of electrolytes was also observed. This was not the case in regards to the administrtion of glucose or multi-electrolyte fluids before or after the Lydium-KLP injection. It seems that Lydium-KLP should be injected as first, and then liquids can be applied in cases of dehydrated animals (46).

Table 31.
Effect of Lydium-KLP on treatment with antibiotics in dog diseases (128).

Clinical diagnosis	Dose of Lydium-KLP	Number of dogs	Percentage	
			of recovery	of death
Acute gastroenteritis	0.02x2	12	75.0*	16.7
	0.02x1	21	80.9*	9.5
Acute and chronic inflammation of the respiratory tract	0.02x2	10	70.0	30.0
	0.02x1	12	83.3*	8.3
Acute and chronic skin inflammation	0.02x2	7	71.4	0
	0.02x1	15	80.0*	0
Otits external	0.02x2	5	60.0	0
	0.02x1	16	87.5*	0

Explanation:
*recovered after additional treatment.

These studies and clinical observations prove the indisputable effects of Lydium-KLP used in conjuction with antibiotics in the treatment of carnivorous animals. Fever and other typical symptoms (such as pain due to ear inflammations and itching due to skin diseases) disappeared faster. The animals regained their appetites sooner and bacame more mobile and eager to interact with their environments. It must be emphasized that a recovery of 4 out of 9 females with pyometritis is not common. When administered after a hysterectomy, the preparation shortened convalescence and helped in the faster healing of the postoperative wound. It must be noted that non-resorptive materials must be used to close the wounds.

Table 32.
Effects of conventional treatment versus conventional treatment plus Lydium-KLP in animals (50).

Clinically diagnosed disease	Conventional treatment		With the use of Lydium-KLP	
	Number of animals	Number (%) of recoveries	Number of animals	Number (%) of recoveries
Parvovirus in puppies	14	8 (57.1)	21	16 (76.2)
Panleukopenia in kittens	11	4 (36.4)	18	4 (50.0)
Nutrition-related diarrheas in dogs	10	7 (70.0)	8	8 (100.0)
External otitis in dogs	4	2 (50.0)	6	4 (66.7)
Paratyphus in silver fox cubs	30	18 (60.0)	26	20 (76.9)
Paratyphus in polar fox cubs	10	3 (30.0)	8	6 (75.0)
Total	79	42 (53.2)	77	58 (75.3)

Conclusion

A single injection of 0.02 mg/kg of Lydium-KLP increases the efficacy of antibiotics in the treatment of inflammations of the alimentary tract, the respiratory system, and the skin in dogs.

Summary

Inflammations of the alimentary tract, the respiratory system, the skin, and ears are the most common diseases affecting dogs, cats and other carnivores. The treatment of tumors in dogs, cats and other pets is becoming increasingly important regarding both theory and practice. In each case, susceptibility to bacterial and viral infections is a consequence of reduced immune system efficiency. Treatment of canine diseases is difficult, costly, lengthy, and frequently ineffective. Most commonly, it involves antibiotics. Lysozyme dimer is effective as the sole medicine in treatment of enteritis and bronchopneumonia, as well as skin diseases. The same dose (0.02 mg/kg) increases therapeutic efficacy of antibiotics. It appears that Lydium-KLP can be useful in the treatment of several tumors in dogs and cats.

Industrial-scale raising of domestic fowl involves very large populations where viral and bacterial diseases may cause tremendous econimic losses. The most common viral diseases are the Newcastle disease (NDV), infections inflammation of the bursa of Fabricius (IBDV), Marek's disease (MD), and Derzy's disease. The most common among the bacterial diseases are infections caused by: Pasteurella multocida (pasteurellosis), Escherichia coli, Salmonella enteritidis, and Staphylococcus aureus. The most crucial consideration is disease prevention through vaccinations and programs developed by various companies. Despite the precautions, the death rate from, for instance, Marek's disease may be as high as 80%. Treatment of the viral and bacterial diseases is difficult and expensive.

Administration of Lydium-KLP in a dose of 0.02 mg/kg b.w. to vaccinate laying geese against Derzy's disease increases antibody production, improves and prolongs humoral response in adult birds as well as guarabtees the transmission of maternal antibodies to egg yolk, thus protecting progeny against the disease (132, 133). Lysozyme dimer also stimulates the activity of the vaccine against Marek's disease (131).

INITIAL RESULTS OF USING LYDIUM-KLP IN RAISING CHICKENS

Material and methods

Two experiments were conducted. Experiment I involved 1,188 one-day-old Astra P hens that were observed for 6 weeks. The average initial weight of each hen was 34 grams. The chickens were randomly divided into 3 groups of 396 each.

During the 6 weeks, each group received the same full-portion DKM-1mixed feed. Lydium-KLP was administered to the hens in groups II and III. The birds in group II received the medication once (a subcutaneous injection) when they were one day

old and still at the incubation department, whereas the birds in group III received it when they were 7 days old. In both cases, the dose was 0.02 mg per 1 kg of body weight. Group I was the control and did not receive the preparation. The following criteria were adopted in evaluating the usefulness of Lydium-KLP: the health of the hens (defined by the number of deaths), body weight increases that were monitored every week, the amount of feed consumed (also monitored every week), and the index of feed utilization per unit of weight increase. The differences between groups were measured according to the Statgraf program with the level of significance at $p<0.05$.

Experiment II was designed to ewaluate the usuefulness of Lydium-KLP in rasing chickens for meat (broilers). The population consisted of 1,200 one-day-old avian chicks that were tested according to the Japanese method to obtain analogical sex distribution in both experimental groups. On the 8th day, the chicks from group II were inoculated subcutaneously with Lydium-KLP in a dose of 0.02 mg per 1 kg od body weight. Group I was the control. The chicks in botth groups were fed the same. The effects of Lydium-KLP were mesuared by examining the overall health of the chicks (determined throught the number of deaths), weekly body weight increases, and weekly feed consumption per growth unit. The results were statistically analyzed with the Statgraf program and the significances was measured with the significance level of $p<0.05$.

Results

Table 33 shows that the poorest results were obtained in the control group (I). The chicks in this group were the lightest at 394.8 grams, on average. The index of feed utilization was also the least favorable at 2.75, as was the overall health, because a total of 17 birds (4.3%) died. The birds from group II received Lydium-KLP at one day of age and after 6 weeks they weighed 403.1 grams on average (2% more than the control). Feed consumption was also better by 2%, and there were 9 deaths (2.3%). The chicks from group III received the prepartion at 7 days age and their growth was the best. At the conclusion of the experiment, their average body weight was 405.9 grams and the difference between this group and the control was statistically significant ($p<0.05$). The feed utilization index (2.68) was lower than that of the control group by 3%, and overall health was the best in group III because only 6 birds (1.5% of the flock) died.

Table 34 shows that a favorable outcome due to Lydium-KLP was observed in the chickens raised for meat, just as it was evident in the egg-laying hens. The average weight of the chicks inoculated at 8 days of age (group II) was 1,881.5 grams after 49 days of the experiment (5% more than the control). On average, the feed utilization index (consumption of food per one unit of weight increase) was 5% better than in the control group. There were considerably fewer deaths in group II (4.7%) than in the control group (6.8%) and the differences were significant.

Table 33.
Effect of Lydium-KLP on the growth of Astra P hens (129).

Group	Body mass in 6 weeks (g/hen)	Feed consumed per 1 kg of growth	Number of deaths	Death rate (%)
I (control) n = 396	394.8 a 100%	2.75 a 100%	17	4.3
II (Lydium-KLP on day 1) n = 396	403.1 ab 102%	2.71 ab 98%	9	2.3
III (Lydium-KLP on day 7) n = 396	405.9 b 103%	2.68 b 97%	6	1.5

Explanation:
a, b - statistically significant difference.

Table 34.
Influence of Lydium-KLP on the effects of raising chickens for meat for 49 days (129).

Group	Body mass (g)	Feed consumed per 1 kg of growth	Number of deaths	Death rate (%)
I (control) n = 600	1,794.8 a 100%	2.32 100%	41	6.8
II (Lydium-KLP n = 600	1,881.5 b 105%	2.21 95%	28	4.7

Explanation:
a, b - statistically significant difference.

The study indicates that Lydium-KLP has favorably affected selected parameters of egg-laying hens and chickens raised for meat (fewer deaths, larger weight increases, and lower feed consumption). Inoculating chicks at 7-8 days of age seems to be more favorable than at one day of age. This may, perhaps, be explained by the precence of yolk antibodies during the first days of life. The yolk sac is reabsorbed within 6-7 days of hatching. It must be emphasized that this was an initial study and certain conclusions may not be drawn.

Conclusions

A subcutaneous injection of 0.02 mg/kg of lysozyme dimer induces: fewer death, greater body weihgt increases, and lower feed utilization with regard to wieght increases in egg-laying hens and chickens raised for meat.

Administering Lydium-KLP to chicken at 7-10 days of age should be considered to have important prophylactic signifaicance.

EFFICACY OF LYDIUM-KLP IN COMBINED TREATMENT OF PASTEURELLOSIS IN TURKEYS

Material and methods

The study was conducted on a total of 14,000 11-week-old turkeys raised for meat in 4 flocks. At the end of week 10, dyspnea, difficulty with walking (limping), and increased thirst were observed. Twenty to 30 birds died each week. Pasteurella multocida was identified in the internal organs. When treatment with enrofloxacin proved ineffective, Paracilline (amoxicilin) was given in combination with Lydium-KLP in a dose of 0.04 mg per bird.

Results

During 4 days of Enrobioflox administration, the death rates in 4 groups were very high, i.e. 9.71%, 5.10%, 4.76%, and 4.62%. After Paracilline and Betamox were given, the death rate dropped to 4-6 birds on day 5 and 2-4 birds in the groups that received Lydium-KLP as a supplement. During the next 10 days of observation, the disease relapsed in the groups that did not receive Lydium-KLP and the total drath rates were 8.58% and 6.11%. In the groups that did receive Lydium-KLP, the death rates were 1.52% and 1.24%. The latter groups showed no need for additional medical intervention.

Conclusion

An intramuscular injection of Lydium-KLP in a dose of 0.04 mg per bird (0.02 mg/kg) has a favorable effect on the final efficacy of antibiotics in the treatment of pasteurellosis in turkeys raised for meat.

Summary

Viral and bacterial diseases of domestic fowl may cause tremendous economic losses. The most common viral diseases are the Newcastle disease (NDV), infectious inflammation of the bursa of Fabricius (IBDV), Marek's disease (MD), and Derzy's disease. Infections caused by Pasteurella multocida (pasteurellosis), Escherichia coli, Salmonella enteritidis, and Staphylococcus aureus are the most frequent among the bacterial diseases. The crucial consideration is disease prevention through vaccinations and programs developed by various companies. Lydium-KLP in a dose of 0.02 mg/kg b.w. stimulates the activity of the vaccine against Marek's disease and Derzy's disease. Lysozyme dimer itself demonstrates prophylactic activity against chicken diseases. An injection of Lydium-KLP increases the efficacy of antibiotic therapy.

GENERAL REMARKS

Lydium-KLP (Lysozyme dimer) is a new tool the hands of veterinary doctors. It is the tool that facilitates treatment and, quite possibly, it is the only tool that affords doctors the opportunity to effectively deal with some diseases. The medication is available on the market now, at a time when antibiotics are losing their efficacy and there is widespread discussion of the problems associated with the presence of antibiotics in animal-origin food products and its consequences for human health.

Table 35.
Therpeutic activity of Lydium-KLP in selected animal diseases.

Animals	Disease	Recovery percent
Cows	Subclinical mastitis	60-80[X]
	Endometritis (E-1, E-2)[XX]	90
	Cystic ovarian disease	70
Calves	Gastroenteritis	80-90[X]
	Bronchopneumonia	80
Horses	Influenza, Bronchopneumonia	70-80[X]
	Endometritis[XX]	70-80
Foals	Enteritis	70-90[X]
	Bronchopneumonia	70-90[X]
Sows	Metritis-mastitis-agalactia	85-95[X]
Piglets	Edema disease	70-90[X]
	Enzootic bronchopneumonia	80
	Gastroenteritis (colibacteriosis)	90-98[X]
Dogs	Bronchopneumonia	75-85[X]
	Bacterial dermatitis	70-90[X]
	Gastroenteritis	65-80[X]

Explanation:
X - by different authors; XX - intrauterinealy in a dose of 2 mg of lysozyme dimer as an aqueous solution.

The lysozyme dimer is not an enzyme that has been altered. It is a new compound with entirely unique properties. The lysozyme dimer is the main component of Lydium-KLP, which is harmless to sick and healthy animals and shows no positive results in tests for the presence of inhibiting substances in milk.

In vivo, lysozyme dimer demonstrates antibacterial, antiviral and antiinflammatory activity. It acts very fast in new cases of disease. Sometimes the effects are visible within to hours, and the animal begins to noticeably improve. Lydium-KLP helps the animal fight the disease without doing it for the animal. The medication activelyworks against the pathogenic mechanisms that are active during its course and are responsible for the clinical symptoms.

Lydium-KLP acts without additional support when the body itself fights the disease, which is particularly visible in subacute and acute diseases. Its effects are less spectacular when the body is passive. Lydium-KLP must have approximately 6-9 hours to develop machanisms directed at eliminating etiological factors, although its effects on the symptoms do become visible earlier. If the animal has no chance of survivig, the medication may prove ineffective and it may even hasten death in certain extreme cases. Therefore, it is not recommended to disregard life-saving drugs in cases of pulmonary edema, circulatory failure, liver degeneration, and ascites. It seems no response can be expected in cases of post-distemper changes in the central and peripheral nervous systems, as well as in cases of encephalitis and meningitis.

Lydium-KLP alone is not sufficient for cows to recover from suppurative, fibrous, and serous mastitis. After the preparation has been injected, previously invisible encysted abscesses may appear in the udder. As a result, the abscess will open into the sinus or through the skin, a fistula will appear, and then a scar will form.

In acute diseases, Lydium-KLP shows both symptomatic and causative properties. It has a wide range of properties that has not been found in other medications to date. In observing the course of the disease an animals, one will note that the properties of Lydium-KLP are similar to those of etiological drugs (e.g. antibiotics), liquids (including glucose), cardiac drugs, and pain killers combined. Lydium-KLP creates conditions for a better response to such drugs as antibiotics because it eliminates their immunosuppressing activity, which allows lower doses to be more effective.

The first injection of Lydium-KLP leads to therapeutic results in acute, subacute and subclinical form of diseases (Table 35). Subsequent administration of the medication in doses of 0.02 mg/kg is harmless and seems to complement the effects of the initial injection.

The study also indicate a positive interaction between Lydium-KLP and well-known and widely used chemical agents. Synergism between Lydium-KLP and antibiotics is visible in fighting bacterial infections. Synergism is also likely between Lydium-KLP and antiviral medications (Table 36). There is no antagonism between Lydium-KLP and oxytocin, cardiac drugs, and glucose solutions. It seems. However, that intravenous administration of Lydium-KLP in combination with multi-electrolyte liquids may restrict the drug's action. The delayed action of Lydium-KLP as not observed in cases of oral and intravenous administration of the liquids 2-3 hours after the preparation was injected.

Table 36.
The effect of lysozyme dimer on the course and efficacy of conventional therapy.

Animals	Disease	Dose mg/kg	The effect
Cows	Acute mastitis	0.01	faster regresion of clinical signs, increase of recoveries
	Icchoroid metritis	0.02	as above
	Chronic purulent mastitis, summer mastitis	0.02	increase of the systemic therapy with antibiotics
Horses	Subcutaneous phlegmon	0.01	increase of efficacy of antiobiotics more than 20% faster recovery
Calves	Gastroenteritis, bronchopneumonia	0.01	increase of efficacy of antiobiotics faster regression of symptoms
Foals	Enteritis, bronchopneumonia	0.02	faster regression of symptoms, increase of recovery rate
Sows	MMA, pneumonia	0.02	shortening of the use of antibiotics
Piglets	Bronchopneumonia, edema disease	0.02	faster regression of symptoms, better growth
Dogs	Pyometritis, inflammations of skin, ears, respiratory system and alimentary tract	0.02	acceleration of symptoms regression, increase of recovery rate
Foxes	Paratyphus	0.02	as above
Turkeys	Pasteurellosis	0.02	as above

Despite the fact that Lydium-KLP increases treatment efficacy and has prophylactic (Table 37) properties, veterinarians and owners must continue to maintain proper procedures in caring for animals. Most of all, strict adherence to the principles of zoohygiene is required during treatment with the lysozyme dimer.

During treatment of subclinical mastitis with Lydium-KLP, particular attention must be paid to proper milking technique, cleanliness of the udder and the milking cups, pre-milking disinfection, and post-milking teat baths in proper solutions. During the studies, it was noted that herds with satisfactory cleanliness showed better treatment efficacy and were less susceptible to recurring infections. Equally important is proper nutrition of the animals that underwent treatment with Lydium-KLP for alimentary tract inflammations. Overfeeding leads to severe relapses of the disease. It must be remembered that the animal suffered severe damage to the alimentary tract's mucous membrane and must be treated as a convalescent even though no symptoms may be visible.

Table 37.
Usefulness of lysozyme dimer in prophylaxis of animal diseases.

Animals	Disease (syndrome)	Dose and time of applicattion
Cows	Postpartum diseases	0.02 mg/kg 10-7 days before parturition
Calves	Bronchopneumonia	0.02 mg/kg 1-2 days before transfer to calf-shed
Horses	Influenza	0.02 mg/kg while vulnerable
Foals	Bronchopneumonia	0.01 mg/kg while vulnerable
Sows	MMA syndrome	0.02 mg/kg 10-7 days before parturition
Piglets	Postweaning diseases	0.02 mg/kg on day of weaning
Chickens	Developmental period diseases	0.02 mg/kg on day 8 of life

The animals that were treated with Lydium-KLP for respiratory system inflammations should note come in contact with calves or piglets with pneumonia during the recovery period, particularly during the 3-5 days after symptoms have regressed. Under improper conditions (humidity, drafts, poor nutrition), recurrences of the disease may develop.

Lydium-KLP is a drug dispensed at the discretion of the physician. In addition to knowledge, the ability to fully take advantage of the therapeutic and prophylactic properties of Lydium-KLP involves following scientific literature.

An increasingly popular conviction is that further developments in therapy and prophylaxis of animal diseases will be possible as a result of introducing medications which affect defensive mechanisms (resistance, immunity). The compounds of natural origin which as intermediaries between cells and organs will become particularly significant. Lydium-KLP is a medication based on a substratum of natural origin. Lydium-KLP matches those criteria very well.

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Usefulness of lysozyme dimer in prophylaxis of animal diseases.

Animals	Disease (syndrome)	Dose and time of applicattion
Cows	Postpartum diseases	0.02 mg/kg 10-7 days before parturition
Calves	Bronchopneumonia	0.02 mg/kg 1-2 days before transfer to calf-shed
Horses	Influenza	0.02 mg/kg while vulnerable
Foals	Bronchopneumonia	0.01 mg/kg while vulnerable
Sows	MMA syndrome	0.02 mg/kg 10-7 days before parturition
Piglets	Postweaning diseases	0.02 mg/kg on day of weaning
Chickens	Developmental period diseases	0.02 mg/kg on day 8 of life

The animals that were treated with Lydium-KLP for respiratory system inflammations should note come in contact with calves or piglets with pneumonia during the recovery period, particularly during the 3-5 days after symptoms have regressed. Under improper conditions (humidity, drafts, poor nutrition), recurrences of the disease may develop.

Lydium-KLP is a drug dispensed at the discretion of the physician. In addition to knowledge, the ability to fully take advantage of the therapeutic and prophylactic properties of Lydium-KLP involves following scientific literature.

An increasingly popular conviction is that further developments in therapy and prophylaxis of animal diseases will be possible as a result of introducing medications which affect defensive mechanisms (resistance, immunity). The compounds of natural origin which as intermediaries between cells and organs will become particularly significant. Lydium-KLP is a medication based on a substratum of natural origin. Lydium-KLP matches those criteria very well.

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