

EVALUATION OF LYDIUM KLP⁺- LYSOZYME DIMER USED FOR THE FIRST TIME IN THE TREATMENT OF BRONCHOPNEUMONIA AND GASTROENTERITIS IN CALVES

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INTRODUCTION

Bronchopneumonia, called also enzootic calf pneumonia, and gastroenteritis characterized by diarrhea in neonatal ruminants belong to the most common diseases despite the rise of preventive and therapeutic agents. These clinical pathologic syndromes are multifactorial with complex and varied etiology, and so far there are no fully satisfactory methods for their control. Beside a variety of environmental factors and infectious agents which may participate in the pathogenesis of the above syndromes, there are several predisposing host factors contributing to the development of the sickness, what to a great extent depends upon the immune status of animal body. In multifactorial antibacterial and also antiviral immune systems an important part plays lysozyme, known for a long time as a component of tissues and body fluids. The new dimeric form of lysozyme prepared from egg protein, inducing production of interferon alfa, modulating synthesis of tumor necrosis factor /TNF/ and stimulating phagocytosis /3/, seems to be a very useful product for the non specific immunomodulatory treatment of the above respiratory and alimentary syndromes, regardless of the kind of viral or bacterial infection.

MATERIALS AND METHODS

The treatment comprised 151 calves housed in several commune and small private farms: 82 animals 3-15 weeks old with bronchopneumonia, and 69 calves aged from 1 day up to 6 weeks with gastroenteritis including 10 cases of pneumoenteritis complex.

Among 82 cases of bronchopneumonia 59 animals have been affected by an acute or subacute forms of the disease. The sickness appeared 12-48 hours before the beginning of treatment and was characterized by depression, anorexia, cough, nasal and lacrimal seromucous or mucopurulent discharge, fever of variable intensity /38.8 - 41.7°C/, increased vesical murmur, and by mild diarrhea in 15 calves.

The remaining 23 animals showed the symptoms of less or more chronic bronchopneumonia which had lasted since 2 - 3 weeks. There were rough hair coat and a gaunt appearance, dyspnea, attacks of cough, a copious bilateral mucopurulent nasal and lacrimal discharge and a moderate fever about 39°C. Two months before starting these investigations several calves with similar symptoms died in the stocks in spite of treatment with the use of antibiotics and sultonamides. The necropsy and laboratory finding revealed *Pasteurella multocida* infection.

In the group of 69 calves with gastroenteritis and diarrhea of various degree of dehydration, 54 cases have been diagnosed as an acute form of disease, 10 as pneumoenteritis complex and the remaining 5 cases as chronic form of enteritis.

Acute gastroenteritis has been recognised usually on the first up to the third day of the disease, with primary diarrhea symptoms. Odor smelling faeces were watery, something white-gray, sometimes yellow-brown, sporadically with blood smears. The animals showed anorexia, various degree of dehydration which in some cases indicated peracute

enterotoxigenic E.coli infection. They remained weak, dull and lied down. In few cases they could not get up themselves, and it was necessary to pick up them for treatment. The temperature varied from subnormal range up to 40.8°C.

Ten mentioned above calves, beside diarrhea with accompanied symptoms of secondary pneumonia showed cough, dyspnea, serous nasal and lacrimal discharge and temperature ranging from 39.0 to 41.3°C.

The five remaining animals, 4 - 6 weeks old, with a gaunt appearance have been sick since about 2 weeks. In that time anorexia and diarrhea relapsed.

All 151 calves affected as well with bronchopneumonia as gastroenteritis have been treated on the beginning with Lydium KLP only. The product in the form of dimerous lysozyme solution has been applied intravenously in trial doses of active dimer from 0.02 up to 0.08 mg/kg b.w. Therapeutic effects of this treatment have been evaluated on the basis of daily clinical examination of sick animals.

The calves with respiratory complex received lysozyme at first in the doses of 0.05, 0.04 and 0.02 mg/kg b.w. at 24 or 12 hour intervals, and later in the dose of 0.02 mg/kg b.w. only once. Additional therapy with antibiotics /Tylosine, Oxytetracycline/ followed 2-3 days of an unsuccessful treatment with Lydium only and was recommended later in a few relapsed cases.

In the treatment of all 69 calves with diarrhea complex dimeric lysozyme was injected intravenously to begin with 6 various doses: 0.08, 0.06, 0.05, 0.04, 0.03 and 0.02 mg/kg b.w. 2, 3 or 4 times at 12 and 24-hour intervals. Then the dose of 0.02 mg/kg b.w. has been given only once. Single animals affected with prolonged or relapsed sickness received additionally Streptomycin orally and Oxytetracycline parenterally. Ten calves were watered with electrolyte solution following treatment with lysozyme and restriction of milk intake.

RESULTS DISCUSSION AND CONCLUSIONS

In the group of 59 calves affected by an acute or subacute form of bronchopneumonia 49 animals /83%/ responded to Lydium therapy quite positively. Ten animals improved then relapsed and recovered after additional treatment with the use of antibiotics. Sick animals showed a pronounced improvement in general condition already on the 1st-2nd day after the first lysozyme injection, followed by decreasing fever, increase of appetite and progressive retreating respiratory disorders. The cough disappeared after 3-4 days. There were no differences in therapeutical effects of various lysozyme doses repeated in different intervals, in comparison with the results obtained after only one single dose of 0.02 mg/kg b.w. .

Twenty three cases with the symptoms of chronic respiratory disorders responded to lysozyme treatment less positively. Therapeutical effect of Lydium was unsatisfactory and it was necessary to treat the calves additionally with antibiotics. Necropsy findings in died animals discovered gross lesions in the form of fibrinous pleuritis and pulmonary abscessation what confirmed chronic pathologic processes.

Very promising therapeutical effects of Lydium have been achieved in 54 calves affected with an acute form of gastroenteritis with diarrhea symptoms; full recovery rate was reached up to 94.4%. In this group only 2 calves died, and beside lysozyme additional antibiotic successful treatment has been applied in 6 relapsed cases only. A clear pronounced improving in sick calves was been seen already in 24-48 hours after the injection of Lydium. In this time diarrhea disappeared, the temperature started to shift into physiological range and the majority of animals seemed to be in good condi-

-tion.

In 10 calves affected by pneumoenteritis complex satisfactory recovery after Lydium administration was obtained in 4 animals and some improvement in 3 calves. In the remaining animals Lydium injections were followed by the application of antibiotics; 1 calf died.

Five cases with prolonged symptoms of alimentary disorders, diagnosed as chronic form of enteritis, recovered after application of antibiotics which followed primary injections of Lydium.

The presented results of clinical investigations of calves with acute form of enzootic respiratory syndrome and with diarrhea complex showed a very promising therapeutical usefulness of the new product Lydium KLP containing an active dimeric form of lysozyme. The prolonged chronic forms of these disorders and a few relapsed cases required additionally antibiotic application.

In the pathogenesis of respiratory also gastrointestinal diseases some authors emphasize significance of lysozyme in local immunity of the mucous membrane, pathogenic effect of toxins produced by bacteria and necrotic tissue, reduced phagocytic activity of lymphocytes and multiplication of the infectious agents /1/. Lydium immunomodulatory features found in other trials like tumor necrosis factor /TNF/ modulation, phagocytosis activation and interferon alfa induction - may explain therapeutical effects of this products in the treated calves presented in this paper. The product has been also positively evaluated in other animals affected by some infectious diseases /2/.

In conclusion the new product Lydium KLP - lysozyme dimer may be recommended for calves in treatment of gastroenteritis with diarrhea complex and of acute form of enzootic bronchopneumonia, in a single intravenous dose of dimeric lysozyme 0.02 mg/kg b.w.

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SUMMARY

Clinical evaluation of therapeutical properties of the new product Lydium KLP containing immunomodulatory biologically active dimeric form of lysozyme, has been performed on 151 calves affected with respiratory syndrome and diarrhea complex. Eighty-two cases of bronchopneumonia and 69 cases of gastroenteritis were examined. Over 70% of calves suffered from an acute or subacute form of the sickness. All animals have been treated at first with Lydium only, by intravenous doses of dimeric lysozyme ranging from 0.02 up to 0.08 mg/kg b.w. repeated 2-4 times in 12- and 24-hour intervals, or in a single dose of 0.02 mg/kg injected once. The most promising and prompt therapeutical effects with the use of Lydium only have been achieved in 54 calves affected with the acute form of gastroenteritis; the recovery rate was 94.4%. Among 59 animals with acute and subacute symptoms of bronchopneumonia 83% recovered. The chronic forms and a few relapsed cases required additional treatment with antibiotics. In advanced and prolonged sickness the results were not quite satisfactory. In conclusion, the presented results with Lydium KLP indicate practical usefulness of this product which may be recommended for the treatment of calves suffering from gastro-

-enteritis and acute bronchopneumonia. A single intravenous injection of 0.02 mg/kg b.w. of dimeric lysozyme seems to be effective therapeutic dose.

ZUSAMMENFASSUNG

Klinische Beurteilung therapeutischer Eigenschaften des neuen Präparates Lydium KLP, welches eine immunstimulierende Wirkung eines dimerisierten Lysozym enthält, wurde bei 151 Kälbern mit respiratorischem Syndrom und Durchfall-Komplex, durchgeführt. Über 70% Kälber litten an einer akuten oder subakuten Krankheitsform. Alle kranken Tiere wurden zuerst nur mit Lydium /Lysozymdosen von 0.02 bis 0.08/kg k.g./ intravenös behandelt. Injektionen wurden 2-4 mal in 12-24 stündigen Abständen wiederholt oder nur einmalig gegeben. Die besten frühzeitigen Behandlungserfolge wurden bei 54 an akute Form von Gastroenteritis erkrankten Kälbern erreicht; positiver Erfolg in 94.4%. Unter den 59 Tieren mit den akuten und subakuten Symptomen von Bronchopneumonie wurden die Kälber in 83% geheilt. Die chronischen Krankheitsformen und einzige Rückfälle erforderten zusätzliche Behandlung mit Antibiotika. Im Falle fortgeschrittener und länger dauernder Krankheit waren die Erfolge nicht so befriedigend. Zum Schluss, auf Grund vorgestellten Ergebnissen darf man Lydium KLP als ein brauchbares Produkt anerkennen und es zur Behandlung der Gastroenteritis und Bronchopneumonia acuta, empfehlen. Einmalige intravenöse Lysozymdose von 0.02 mg/kg k.g. wird als wirkungsvoll bezeichnet.

RÉSUMÉ

L'évaluation clinique des propriétés thérapeutiques d'un nouveau médicament Lydium KLP a été exécutée chez les 151 veaux atteints de syndrome respiratoire et diarrhéique. Le Lydium KLP contient la forme biologique active de dimeric Lysozym à propriété d'immunomodulation. Parmi les 151 veaux malades on a constaté 82 cas "respiratoires" et 69 cas de diarrhée. Plus que 70 pourcent de veaux présentaient la forme aiguë ou subaiguë de deux maladies. Tous les animaux malades ont été traités par le Lydium KLP, administré par la voie intraveineuse en doses de 0.02 mg/kg à 0.08 mg/kg de poids d'animal. Les injections ont été appliquées 2-4 fois dans l'intervalle de 12-24 heures ou une seule fois en dose de 0.02 mg/kg de poids d'animal. Les meilleurs résultats thérapeutiques, après l'application de Lydium, ont été obtenus chez les 54 veaux avec la forme gastroentérique aiguë. On a observé un effet positif dans 94.4 pourcent de veaux. Parmi les 59 animaux malades avec la forme aiguë ou subaiguë de la bronchopneumonie une guérison concernait 83 pourcent d'animaux. Il faut ajouter que les formes chroniques de la maladie ou les cas de récurrence nécessitaient au plus un traitement par des antibiotiques. Dans les cas avancés ou de durée prolongée de la maladie les résultats de traitement n'étaient pas si satisfaisants.

D'après les résultats obtenus avec le Lydium dans le traitement des formes aiguës de la gastroentérite et de la bronchopneumonie on peut apprécier ce médicament comme profitable; il mérite d'être recommandé au traitement. Une dose de Lydium en quantité de 0.02 mg/kg de poids d'animal appliquée une fois par voie intraveineuse s'avère comme efficace.

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