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Immunological control of aerosol phytotherapy of acute catarrhal bronchopneumonia for its effectiveness in calves

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ABSTRACT

Introduction. Respiratory diseases are widespread on livestock farms, especially in high-yielding animals, and they are particularly severe in young animals. Non-specific bronchopneumonia in calves is caused by a combination of factors including opportunistic respiratory microbiota, which can become pathogenic under unfavorable conditions, overcrowding, nutritional imbalances, stress, drafts, noise, other environmental stressors as well as compromised immunity in newborn animals.

Objective. Immunological control of aerosol phytotherapy of acute catarrhal bronchopneumonia for its effectiveness in calves.

Materials and methods. One – three month-old calves with acute catarrhal bronchopneumonia ($n = 60$) were used for the study. The calves were divided into three test groups, 20 calves per group. Blood samples were collected from the diseased animals before the start of treatment, as well as on day 7 and 12 after treatment and used for immunological tests.

Results. Aerosol administration of *Hypericum perforatum* extract, herbal product, in the complex treatment of calves with acute catarrhal bronchopneumonia demonstrated high efficacy compared to two other treatment regimens. In the test group receiving phytotherapy overall clinical improvement was observed as early as on (4.90 ± 0.64) day, which was 47.0% faster than in the group where animals were treated according to the treatment regime routinely used on the farm. Furthermore, the calves in this group demonstrated a faster recovery of appetite, consumed feed more readily, their coats became smooth and shiny, and their cellular and humoral immunity levels, as well as their pro-inflammatory cytokine levels reached the reference levels of clinically healthy animals by day 12 and day 7, respectively.

Conclusion. While all three regimens for acute catarrhal bronchopneumonia were effective, the aerosolized *Hypericum perforatum* extract produced the best results. Calves receiving this treatment showed the most significant improvements in cellular and humoral immunity, along with the reduction in pro-inflammatory cytokine levels.

Keywords: bronchopneumonia, therapy, aerosol treatment, herbal products, *Hypericum perforatum,* calves

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Иммунологический контроль эффективности аэрозольной фитотерапии острой катаральной бронхопневмонии у телят

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РЕЗЮМЕ

Введение. Респираторные заболевания широко распространены в животноводческих хозяйствах, особенно среди высокопродуктивных животных, при этом достаточно тяжело они протекают у молодняка. Возникновение неспецифической бронхопневмонии у телят связано с комплексом причин, включающим прежде всего условно-патогенную микробиоту дыхательных путей, которая при неблагоприятных условиях может стать патогенной, а также скученность содержания, несбалансированное кормление, стресс, сквозняки, шум, влияние негативных факторов окружающей среды, а также снижение резистентности и иммунной реактивности новорожденных животных.

Цель исследования. Проведение иммунологического контроля эффективности аэрозольной фитотерапии острой катаральной бронхопневмонии телят.
Материалы и методы. Исследование провели на 1–3-месячных телятах, больных острой катаральной бронхопневмонией ($n = 60$). Было сформировано три опытные группы по 20 особей в каждой. У больных животных до начала терапии, а также на 7-е и 12-е сут после лечения отбирали кровь для проведения иммунологических исследований.
Результаты. Установлено, что аэрозольное применение фитопрепарата «Экстракт зверобоя продырявленного» в комплексном лечении телят с острой катаральной бронхопневмонией продемонстрировало более высокую эффективность по сравнению с остальными двумя схемами. В опытной группе, где использовали фитотерапию, общее клиническое улучшение наблюдали уже на (4,90 ± 0,64) сут, что на 47,0% быстрее, чем в группе, где лечение животных проводили по общепринятой в хозяйстве схеме. При этом у телят указанной группы аппетит восстанавливался быстрее, они лучше поедали корм, шерсть становилась гладкой и блестящей, показатели клеточного и гуморального иммунитета на 12-е сут, а уровень провоспалительных цитокинов уже на 7-е сут приближались к референсным показателям клинически здоровых животных.
Заключение. Все три терапевтические схемы при борьбе с острой катаральной бронхопневмонией показали относительную эффективность, однако аэрозольное применение фитопрепарата «Экстракт зверобоя продырявленного» в комплексном лечении больных телят продемонстрировало наилучшие результаты, о чем свидетельствуют значительные позитивные сдвиги в клеточном и гуморальном звене иммунитета, а также снижение уровня провоспалительных цитокинов.

Ключевые слова: бронхопневмония, терапия, аэрозольная обработка, фитопрепараты, зверобой продырявленный, телята

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INTRODUCTION

Currently, respiratory diseases are widespread on livestock farms, especially among high-yielding animals, while they are quite severe in young animals [1, 2, 3, 4]. Respiratory diseases in livestock cause significant economic losses through animal mortality, reduced performance, stunted growth and development in survivors, and the costs of treatment and disease prevention [5, 6, 7]. Bronchopneumonia is reported in calves in almost all regions of the country and ranks second among all pathologies on farms, second only to gastrointestinal diseases, while reaching 30% of cases in the nosological profile of all pathologies [8, 9]. The etiological factors of nonspecific bronchopneumonia in calves represent a complex of causes, including, first of all, the opportunistic respiratory microbiota, which under unfavourable conditions can become pathogenic, overcrowding, imbalanced nutrition, stress, draughts, noise, other environmental stressors, as well as a compromised resistance and immune response of new-born animals [10, 11, 12, 13].

Under production conditions, antibiotics are widely used as antimicrobials for the prevention and control of factor diseases, including bronchopneumonia in calves, and are most often prescribed empirically [14, 15, 16]. Therewith, empirical and uncontrolled use of antibiotics promotes mutations as well as microbial resistance, it also leads to their accumulation in animal tissues and products, thereby contributing to the development of antibiotic-resistant microbiota in humans consuming such animal products. In addition, antibiotic use can result in systemic toxicity, which may culminate in multiple organ failure in animals. Therefore, the search for alternative tools for combating multidrug-resistant pathogenic bacteria is of current importance [17, 18, 19].

Studies on the immune system of calves with respiratory diseases often yield conflicting results, though they consistently indicate immune dysfunction and a reduced immune response [20, 21]. Therewith, the immunobiological responsiveness plays one of the key roles in the formation and progression of various infectious diseases, including acute catarrhal bronchopneumonia in calves. Therefore, immunological screening during the treatment of respiratory diseases in animals provides a critical method for monitoring therapeutic efficacy, representing, in our opinion, an urgent and promising area for further research.

The study was aimed at immunological control of the aerosol phytotherapy of acute catarrhal bronchopneumonia for its effectiveness in calves kept on livestock farms.

MATERIALS AND METHODS

The study was funded by grant of the Russian Science Foundation No. 24-26-00091 (https://rscf.ru/project/24-26-00091) and carried out on the "Babayevo" livestock farm located in the Sobinsky Raion of the Vladimir Oblast and "Delta-F" livestock farm located in the Sergiyev Posad municipality of the Moscow Oblast having the same animal keeping and feeding practices.

One-three month-old calves with acute catarrhal bronchopneumonia ($n = 60$) were used for the study. As the calves became diseased, they were randomly

assigned to test groups, placed in separate isolated rooms, and treated according to the presented treatment regimes. Three test groups of animals ($_1$T, $_2$T and $_3$T) were formed, 20 calves with bronchopneumonia per group. The animals of test group 1 ($_1$T) were treated according to the scheme commonly used on farms: indoor aerosol treatment of animals with iodoethylene glycol solution (3 mL/m^3 the room + 10% glycerine, v/v) using industrial "Hi-Fog" cold mist generator for 30 minutes once a day during 7 days. As an antibacterial therapy, "Penstrep 400" (1 mL/10 kg) was administered intramuscularly to calves of $_1$T group once a day for three days. The calves of test group 2 ($_2$T) were also subjected to indoor aerosol treatment with iodoethylene glycol solution (3 mL/m^3 the room + 10% glycerine, v/v) using industrial "Hi-Fog" cold mist generator for 30 minutes once a day during 7 days. "Marbofloxacin" (fluoroquinolone), 10% solution, administered at a dose of 8 mg/kg, once a day, three times, was used for antibacterial therapy based on the results of microbiological tests and tests of the isolated pathogens for their susceptibility to antibiotics performed earlier. The animals of test group 3 ($_3$T) were subjected to indoor aerosol treatment with *Hypericum perforatum* extract, herbal product, demonstrating high antibacterial activity against the bronchopneumonia initiators in calves that was experimentally selected previously [22]. In addition, 10% "Marbofloxacin" (fluoroquinolone) solution was also administered at a dose of 8 mg/kg once a day, three times.

Blood samples were collected from diseased animals (10 animals from each group) before treatment and on day 7 and day 12 after treatment for immunological tests. The total number of T-lymphocytes was determined by spontaneous rosette formation using common methods. Therewith, T cells were tested for their susceptibility and resistance to theophylline. Number of T-suppressors was calculated as the difference between the total number of T-lymphocytes and the number of T-helpers. The immunoregulatory index (IRI) was calculated by dividing the number of T-helper cells by the number of T-suppressor cells. The number of natural killer (NK) cells was calculated by subtracting the total count of T-lymphocytes and B-lymphocytes from the total number of lymphocytes, using a complementary rosette formation method to distinguish and quantify these cell types. The structure of circulating immune complexes (CICs) was determined by molecular weight. The levels of pro-inflammatory IL-1*α*, IL-6, IL-8 interleukins and TNF-1*α* (tumour necrosis factor) were determined with enzyme-linked immunosorbent assay. Blood collected from clinically healthy calves (n = 10) once on day 1 of the study was used as a control.

The animals were handled in accordance with the European Convention (ETS No. 123).

The results were statistically processed using the STATISTICA 7.0 program (StatSoft, USA). Before the study, the Shapiro – Wilk test was used to check the dataset for normal distribution. With a normal distribution of quantitative variables, an ANOVA test was used to compare the two groups. Mann – Whitney test was used for assessment of significance of differences between the indicators before and after treatment of animals (* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$).

RESULTS AND DISCUSSION

Optimal treatment outcomes are achieved through dynamic monitoring of the animals' state and timely adjustment of treatment regimens. In this context, comparative assessment of three different treatment regimens for acute catarrhal bronchopneumonia in calves for their effectiveness was carried out including monitoring the animals' state.

It should be noted that mean time to clinical improvement in calves in test group $_1$T was (9.25 ± 0.91) days, complications were reported in six cases during the treatment course, the final recovery rate was 90.0% (18/20), 2 calves (10.0%) died. In test group $_2$T overall clinical improvement was observed as early as on day (7.20 ± 0.61), and the final recovery rate was 100.0% (20 animals). Therapeutic monitoring in test group $_3$T showed a mean time to clinical improvement of (4.90 ± 0.64) days. This was 47.0% faster than in group $_1$T, and all 20 calves (100.0%) recovered.

The clinical outcome of an infectious process – encompassing both disease severity and animal convalescence – depends as much on the virulence of the infecting microflora as well as on the resistance and immunological competence of the host organism. Cellular immunity indicators in calves with acute catarrhal bronchopneumonia during the treatment are given in Table 1.

The data show that significant increase in T-helper cells by 29.27%: from (12.30 ± 0.89) to (15.90 ± 0.94)% (*↑) was recorded on day 7 when the calves were subjected to the treatment routinely used on tested farms (test group $_1$T). More significant shifts in the cellular immunity: 1.87-fold increase in the level of T-helper cells, from (11.90 ± 0.69) to (22.30 ± 1.31)% (***↑), and 1.30-fold and 1.19-fold decrease in the level of T-suppressors (**↓) and NK cells (**↓), respectively, was observed in the treated calves of test group $_2$T on day 7. It should be noted that the most significant positive changes in cellular immunity were recorded in calves of test group $_3$T: an increase in total T cells by 18.41%, from (39.10 ± 1.04) to (46.30 ± 1.34)% (***↑), and increase in T-helper cells by 111.72%, from (12.80 ± 0.87) to (27.10 ± 1.36)% (***↑), and significant decrease in serum T-suppressor levels by 1.37 times, from (26.30 ± 1.36) to (19.20 ± 1.15)%, and decrease in NK cell levels by 1.45 times, from (42.00 ± 1.81) to (29.00 ± 2.03)%, as compared to the indicators for the calves before the treatment was started. Further favourable changes in cellular immunity indicators were recorded in all test groups on day 12 after the start of treatment, but only in calves of test group $_3$T these indicators approached the reference ones of healthy animals. Thus, a highly significant increase in total T-lymphocytes and T-helper cells by 29.92% and by 188.28%, respectively, and a significant decrease in T-suppressors and NK cells by 1.79 and 1.68 times, respectively, were observed in calves of test group $_3$T.

Table 1
Cellular immunity indicators in calves with acute catarrhal bronchopneumonia during the treatment

Indicators	Healthy calves ($n = 10$)	Groups	Calves with bronchopneumonia		
			before treatment ($n = 10$)	day 7 ($n = 10$)	day 12 ($n = 10$)
T-lymphocytes, total number, %	50.40 ± 1.49	$_1$T	39.80 ± 1.31	40.50 ± 1.20	43.60 ± 1.21*↑
		$_2$T	39.30 ± 1,.49	43.40 ± 1.35	48.20 ± 1.33***↑
		$_3$T	39.10 ± 1.04	46.30 ± 1.34***↑	50.80 ± 1.58***↑
T-helpers,%	35.50 ± 0.98	$_1$T	12.30 ± 0.89	15.90 ± 0.94*↑	22.60 ± 1.21***↑
		$_2$T	11.90 ± 0.69	22.30 ± 1.31***↑	32.80 ± 1.03***↑
		$_3$T	12.80 ± 0.87	27.10 ± 1.36***↑	36.90 ± 1.71***↑
T-suppressors, %	14.90 ± 1.01	$_1$T	27.50 ± 1.12	24.60 ± 1.08	21.00 ± 1.94**↓
		$_2$T	27.40 ± 1.37	21.10 ± 1.58**↓	15.40 ± 0.79***↓
		$_3$T	26.30 ± 1.36	19.20 ± 1.15***↓	14.70 ± 1.27***↓
NK cells,%	25.10 ± 1.41	$_1$T	41.50 ± 1.81	40.30 ± 1.69	35.80 ± 1.34*↓
		$_2$T	42.50 ± 1.51	35.60 ± 1.38**↓	28.10 ± 1.59***↓
		$_3$T	42.00 ± 1.81	29.00 ± 2.03***↓	25.00 ± 1.50***↓

↑ – significant increase in indicators; ↓ – significant decrease in indicators; * $p < 0,05$; ** $p < 0,01$; *** $p < 0,001$ as compared to the indicators before treatment.

The immunoregulatory index is one of the main laboratory indicators of the satisfactory immune state, which makes it possible to give an objective assessment of immune response intensity, IRI dynamics in calves with acute catarrhal bronchopneumonia is given in the Figure.

It was detected that clinical manifestations of acute catarrhal bronchopneumonia in animals of all test groups were accompanied by a significant IRI decrease. However, it should be noted that on day 7 the IRI increased by 44.44% (*↑) in calves of the test group $_1$T, by 143.73% (***↑) in calves of test group $_2$T and by 188.24% (***↑) in calves of test group $_3$T (the most significant IRI increase as compared to the initial data). On day 12, highly significant (***↑) increase in IRI was reported in calves of all test groups as follows: 2.71 times increase in calves of test group $_1$T, from (0.45 ± 0.04) to (1.22 ± 0.18) conventional units (CU); 4.98 times increase in calves of test group $_2$T, from (0.44 ± 0.03) to (2.19 ± 0.16) CU; 5.35 times increase in calves of group $_3$T, from (0.51 ± 0.05) to (2.73 ± 0.32) CU, which approached the reference levels.

The data shown in Table 2 clearly demonstrate changes in the humoral immunity of calves with acute catarrhal bronchopneumonia during the treatment.

Acute catarrhal bronchopneumonia in calves was shown to trigger a major shift in humoral immunity characterized by decrease in B-lymphocyte counts and significant rise in pathogenic, medium- and small-molecular CICs. On day 7, significant positive changes were observed only in animals of test group $_3$T: increase in total B cells by 30.69%, from (18.90 ± 0.84) to (24.70 ± 0.88)% (***↑), and significant decrease in total CICs by 39.61%, from (481.40 ± 10.37) to (290.70 ± 11.26) AU (***↓), due to decrease in large-molecular CICs by 40.10%, from (60.10 ± 1.53) to (36.00 ± 0.73) AU (***↓), medium-molecular CICs by 22.49%, from (97.80 ± 3.36) to (75.80 ± 1.58) AU (***↓), and small-molecular CICs by 44.70%, from (323.50 ± 8.31) to (178.90 ± 10.94) AU (***↓) as compared to the initial data. It was found that on day 12, positive changes in the specified immunological indicators were recorded in calves of all test groups, but only in calves of test group $_3$T the humoral immunity indicators approached the reference indicators of clinically healthy calves: increase in total B-lymphocytes by 1.28 times, from (18.90 ± 0.84) to (24.20 ± 0.55)% (***↑), decrease in total CICs by 2.10 times, from (481.40 ± 10.37) to (228.80 ± 3.88) AU (***↓): large-molecular CICs – by 1.81 times, from (60.10 ± 1.53) to (33.20 ± 0.61) AU (***↓), medium-molecular CICs – by 1.43 times, from (97.80 ± 3.36) to (68.60 ± 1.68) AU (***↓), and small-molecular CICs – by 2.55 times, from (323.50 ± 8.31)

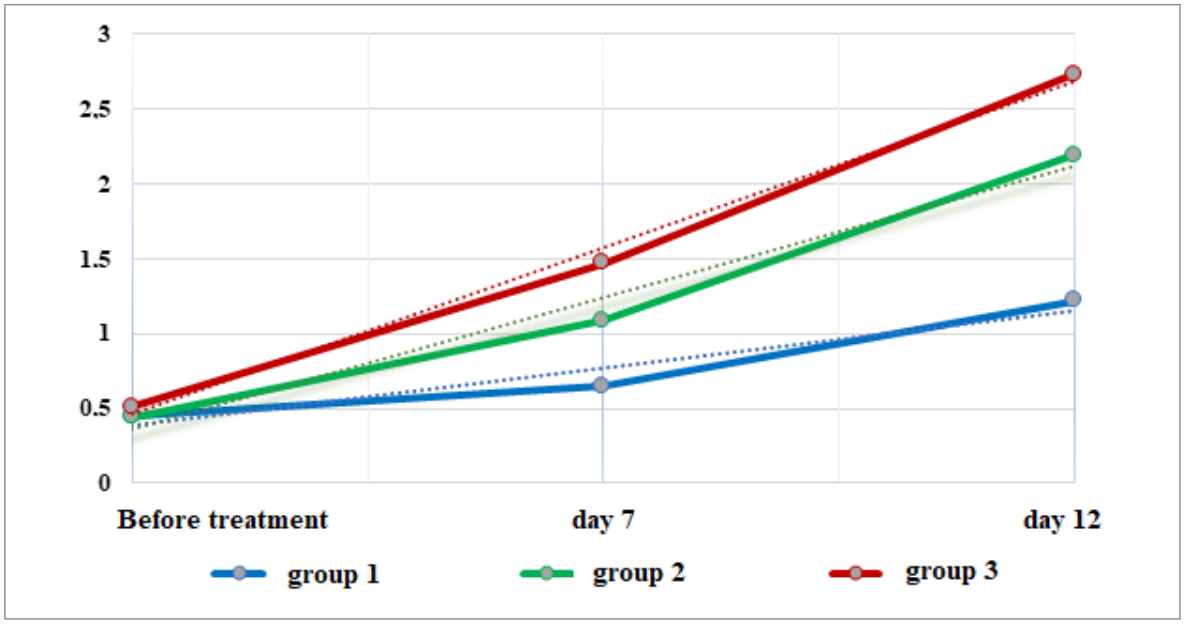

Fig. The immunoregulatory index in calves with acute catarrhal bronchopneumonia during the treatment

Table 2
Humoral immunity indicators in calves with acute catarrhal bronchopneumonia during the treatment

Indicators	Healthy calves ($n = 10$)	Groups	Calves with bronchopneumonia		
			before treatment ($n = 10$)	day 7 ($n = 10$)	day 12 ($n = 10$)
B cells, total count, %	24.50 ± 0.85	$_1$T	18.70 ± 0.66	19.20 ± 0.64	20.60 ± 0.52*↑
		$_2$T	18.20 ± 0.81	21.00 ± 0.64*↑	23.70 ± 0.77***↑
		$_3$T	18.90 ± 0.84	24.70 ± 0.88***↑	24.20 ± 0.55***↑
CICs total, AU	229.10 ± 4.34	$_1$T	464.60 ± 9.68	436.40 ± 8.63*↓	397.20 ± 7.70***↓
		$_2$T	459.70 ± 10.83	403.00 ± 8.03***↓	292.30 ± 6.38***↓
		$_3$T	481.40 ± 10.37	290.70 ± 11.26***↓	228.80 ± 3.88***↓
CICs large, AU	34.80 ± 0.81	$_1$T	51.50 ± 1.43	49.40 ± 1.62	43.10 ± 2.07**↓
		$_2$T	53.60 ± 1.17	47.30 ± 1.34**↓	34.80 ± 0.51***↓
		$_3$T	60.10 ± 1.53	36.00 ± 0.73***↓	33.20 ± 0.61***↓
CICs, medium, AU	67.10 ± 1.53	$_1$T	98.80 ± 3.24	93.10 ± 2.96	83.40 ± 2.05***↓
		$_2$T	97.10 ± 3.14	79.60 ± 2.33***↓	71.60 ± 2.17***↓
		$_3$T	97.80 ± 3.36	75.80 ± 1.58***↓	68.60 ± 1.68***↓
CICs small, AU	127.20 ± 3.83	$_1$T	314.30 ± 10.35	293.90 ± 9.61	270.70 ± 7.94**↓
		$_2$T	309.00 ± 8.58	276.10 ± 6.74**↓	185.90 ± 5.97***↓
		$_3$T	323.50 ± 8.31	178.90 ± 10.94***↓	127.00 ± 3.49***↓

↑ – significant increase in indicators; ↓ – significant decrease in indicators; * $p < 0,05$; ** $p < 0,01$; *** $p < 0,001$ as compared to the indicators before treatment.

Table 3
Pro-inflammatory cytokine levels in sera from the calves with acute catarrhal bronchopneumonia during the treatment

Indicators	Healthy calves ($n = 10$)	Groups	Calves with bronchopneumonia		
			before treatment ($n = 10$)	day 7 ($n = 10$)	day 12 ($n = 10$)
IL-1α, pg/mL	17.35 ± 0.41	$_1$T	37.50 ± 0.92	29.42 ± 0.61***↓	24.47 ± 0.74***↓
		$_2$T	35.97 ± 1.22	22.54 ± 0.51***↓	19.67 ± 0.29***↓
		$_3$T	36.55 ± 1.21	19.08 ± 0.31***↓	18.11 ± 0.27***↓
IL-6, pg/mL	13.14 ± 0.47	$_1$T	46.55 ± 1.14	37.51 ± 1.13***↓	25.03 ± 0.65***↓
		$_2$T	44.68 ± 1.36	26.78 ± 1.23***↓	17.74 ± 0.52***↓
		$_3$T	45.11 ± 1.31	15.39 ± 0.38***↓	13.48 ± 0.45***↓
IL-8, pg/mL	12.51 ± 0.50	$_1$T	30.67 ± 0.87	24.19 ± 1.23***↓	14.19 ± 0.47***↓
		$_2$T	30.04 ± 0.83	20.65 ± 0.48***↓	16.28 ± 0.40***↓
		$_3$T	30.67 ± 0.77	13.67 ± 0.25***↓	12.06 ± 0.33***↓
TNF-1α, pg/mL	44.55 ± 0.92	$_1$T	93.20 ± 2.05	82.43 ± 1.37***↓	55.18 ± 1.41***↓
		$_2$T	94.40 ± 1.96	58.35 ± 1.18***↓	44.04 ± 0.51***↓
		$_3$T	94.14 ± 1.68	46.23 ± 1.13***↓	41.66 ± 0.45***↓

↑ – significant increase in indicators); ↓ – significant decrease in indicators; * $p < 0,05$; ** $p < 0,01$; *** $p < 0,001$ as compared to the indicators before treatment.

to (127.00 ± 3.49) AU (***↓), when compared to indicators before the start of treatment.

Cytokines are known to be critical regulators of the host immune response during inflammation and infection. Cytokines are small proteins that facilitate intercellular communication and form an independent regulatory system that directs fundamental body functions, particularly in maintaining homeostasis following microbial challenge or tissue injury. Systemically, cytokines integrate the immune, nervous, endocrine, and hematopoietic systems, thereby organizing a complex defence against antigens and regulating protective reactions [20].

According to data given in Table 3, calves develop a cytokine storm accompanied with marked upregulation in pro-inflammatory cytokine synthesis during the clinical manifestation of acute respiratory pathology as compared to clinically healthy animals. Sharp decrease in interleukin levels was observed in animals of all test groups as early as on day 7, and in calves of test group $_3$T, these indicators approached the reference values. Thus, a significant decrease (***↓) of the following indicators were reported in tested sera on day 7 as follows: in calves of test group $_1$T: decrease in IL-1α – by 1.27 times, IL-6 – by 1.24 times, IL-8 – by 1.27 times, TNF-1α – by 1.13 times; in calves of test group $_2$T: decrease in IL-1α – by 1.60 times, IL-6 – by 1.67 times, IL-8 – by 1.45 times, TNF-1α – by 1.62 times; in calves of test group $_3$T the most significant positive changes were recorded: decrease in IL-1α – by 1.92 times, from (36.55 ± 1.21) to (19.08 ± 0.31) pg/mL, in IL-6 – by 2.93 times, from (45.11 ± 1.31) to (15.39 ± 0.38) pg/mL, in IL-8 – by 2.24 times, from (30.67 ± 0.77) to (13.67 ± 0.25) pg/mL and in TNF-1α increased by 2.04 times, from (94.14 ± 1.68) to (46.23 ± 1.13) pg/mL, when compared to indicators before the start of treatment. It should be noted that on day 12, the animals showed a further decrease in pro-inflammatory cytokine levels. In calves of test group $_1$T receiving standard treatment it was accompanied by decrease in IL-1α by 1.53 times only, in IL-6 – by 1.86 times, in IL-8 – by 2.16 times, and in TNF-1α – by 1.69 times. More significant interleukin shifts were detected in sera from calves of test groups $_2$T and $_3$T: IL-1α – by 1.83 and 2.02 times, IL-6 – by 2.52 and 3.35 times, IL-8 – by 1.85 and 2.54 times, TNF-1α – by 2.14 and 2.26 times, respectively, when compared with the initial data.

Thus, the treatment was shown to be effective for calves with acute catarrhal bronchopneumonia in all three test groups. However, the best results were achieved with the aerosol administration of *Hypericum perforatum* extract, herbal product, in combination with antibacterial treatment, as evidenced by significant positive changes in cellular and humoral immunity, as well as decrease in the of pro-inflammatory cytokine levels.

CONCLUSION

Aerosol administration of *Hypericum perforatum* extract, herbal product, within the complex treatment of calves with acute catarrhal bronchopneumonia demonstrated high efficacy compared to two other treatment regimens. Therewith, in test group $_3$T overall clinical improvement was observed as early as on (4.90 ± 0.64) day, which was 4.35 days faster than in calves of test group $_1$T; the calves in this group demonstrated a faster recovery of appetite, consumed feed more readily, their coats became smooth and shiny, and their serum immunological parameters reached the reference levels of clinically healthy animals by day 12. Calves receiving routine treatment (group $_1$T) demonstrated 29.27% increase in T-helper cells only on day 7. More significant shifts in the cellular immunity: a 1.87-fold increase in T-helper levels, and decrease in T-suppressor levels by 1.30 times and NK cells by 1.19 times were observed in calves of test group $_2$T on day 7. The most significant positive changes in cellular immunity were reported in calves of test group $_3$T: an increase in total T cells by 18.41% and T-helper cells by 111.72% and decrease in T-suppressor and NK cell levels by 1.37 and 1.45 times, respectively. Further positive changes in cellular immunity indicators were noted in all test groups on day 12, but only in calves of test group $_3$T they reached the reference values. Thus, increase in total T-lymphocytes and T-helper cells by 29.92% and by 188.28%, respectively, and decrease in T-suppressors and NK cells by 1.79 and 1.68 times, respectively, were observed in calves of test group $_3$T. On day 7 IRI increased in test group $_1$T by 44.44%, in test group $_2$T – by 143.73%, and test group $_3$T – by 188.24%. On day 12 calves of all test groups demonstrated highly significant increase in IRI: in calves of test group $_1$T – by 2.71 times, test group $_2$T – by 4.98 times; test group $_3$T – by 5.35 times (in $_3$T group it was reaching the reference values). Acute catarrhal bronchopneumonia in calves was shown to trigger a major shift in humoral immunity characterized by decrease in B-lymphocyte counts and significant rise in pathogenic medium- and small-molecular CICs. Clinically manifested acute respiratory pathology in calves can lead to a cytokine storm, where the immune system's overreaction causes an overproduction of pro-inflammatory cytokines. On day 7 a sharp drop in interleukin levels was observed in calves of all test groups, and in calves of test group $_3$T these indicators reached the reference values: IL-1*α* decreased by 1.92 times, IL-6 – by 2.93 times, IL-8 – by 2.24 times, and TNF-1*α* – by 2.04 times. It should be noted that on day 12, the animals showed a further decrease in pro-inflammatory cytokine levels. In calves of test group $_1$T receiving routine treatment it was accompanied by decrease in IL-1*α* by 1.53 times, in IL-6 – by 1.86 times, in IL-8 – by 2.16 times, and in TNF-1*α* – by 1.69 times only. More significant interleukin shifts were detected in sera from calves of test groups $_2$T and $_3$T: IL-1α – by 1.83 and 2.02 times, IL-6 – by 2.52 and 3.35 times, IL-8 – by 1.85 and 2.54 times, TNF-1*α* – by 2.14 and 2.26 times, respectively, when compared with the initial data.

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