https://doi.org/10.26898/0370-8799-2021-3-10
УДК: 619:615.371:579.842.14:636.2.082
Тип статьи: оригинальная
Type of article: original

ЦИТОГЕНЕТИЧЕСКИЕ НАРУШЕНИЯ У МОЛОДНЯКА КРУПНОГО РОГАТОГО СКОТА ПРИ ВАКЦИНАЦИИ ПРОТИВ САЛЬМОНЕЛЛЕЗА

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Изучен спектр и определены частоты цитогенетических нарушений у молодняка крупного рогатого скота, иммунизированного вакциной против сальмонеллеза телят. Исследования проведены в хозяйстве Новосибирской области на 10 клинически здоровых голштинизированных черно-пестрых телятах 10–17-дневного возраста. Использована концентрированная формолквасцовая вакцина против сальмонеллеза (паратифа) телят в дозе 2 мл (реиммунизация в дозе 2 мл) с интервалом 10 сут между инъекциями. Вакцина изготовлена из культуры бактерий штамма *Salmonella dublin* № 373, инактивированного формалином с добавлением алюмокалиевых квасцов и хлорида кальция. Цитогенетический анализ периферической крови у телят проведен до вакцинации (контроль), через 2 и 9 сут после вакцинации, через 2 и 9 сут после ревакцинации. Установлено, что спектр соматической хромосомной нестабильности в лимфоцитах периферической крови телят после вакцинации и ревакцинации представлен полиплоидией, гипоплоидией и гиперплоидией, хроматидными и хромосомными разрывами, одиночными и парными фрагментами хромосом. Выявлено, что спектр соматической хромосомной нестабильности после двукратных иммунизаций инактивированной вакциной против сальмонеллеза не отличался от спектра спонтанно возникающих мутаций у данного вида. Вакцинация и последующая ревакцинация телят в сравнении с довакцинационным периодом не приводили к достоверному увеличению частот анеуплоидных и полиплоидных клеток. При двукратной иммунизации телят в лимфоцитарных клетках крови животных отмечен волновой характер в вариации частот геномных мутаций от максимальных до минимальных значений аналогично продленному мутагенезу. Обнаружена тенденция увеличения частоты структурных нарушений хромосом через 2, 9 сут после вакцинации и 2 сут после ревакцинации. Отмечено достоверное возрастание в 2,9 раза частоты клеток с хромосомными аберрациями в лимфоцитах крови животных через 9 сут после их повторной иммунизации за счет разрывов и парных фрагментов хромосом. После вакцинации и ревакцинации хроматидные разрывы наиболее часто регистрировались в медиальных районах одной из хроматид, хромосомные разрывы в медиальных и теломерных районах обеих хроматид.

Ключевые слова: геномные мутации, хромосомные мутации, лимфоциты периферической крови, телята, вакцинация, ревакцинация, сальмонеллез

CYTOGENETIC ABNORMALITIES IN YOUNG CATTLE DURING VACCINATION AGAINST SALMONELLOSES

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The spectrum and the frequencies of cytogenetic abnormalities in young cattle immunized with a vaccine against salmonellosis of calves were investigated. The study was carried out on the farm of Novosibirsk region on 10 clinically healthy Holstein black-and-white calves of 10–17 days of age. A concentrated formol-alum vaccine against salmonellosis (paratyphoid) of calves was used at a dose of 2 ml (reimmunization at a dose of 2 ml) with an interval of 10 days between injections. The vaccine was made from the culture of bacteria of the *Salmonella dublin* strain № 373, inactivated with formalin with the addition of potassium alum and calcium chloride. Cytogenetic analysis of peripheral blood in calves was carried out before vaccination (control), 2 and 9 days after vaccination,

2 and 9 days after revaccination. It was found that the spectrum of somatic chromosomal instability in peripheral blood lymphocytes of calves after vaccination and revaccination is represented by polyploidy, hypoploidy and hyperploidy, chromatid and chromosomal breaks, single and paired fragments of chromosomes. It was revealed that the spectrum of somatic chromosomal instability after double immunizations with an inactivated vaccine against salmonellosis did not differ from the spectrum of spontaneously occurring mutations in this species. Vaccination and subsequent revaccination of calves in comparison with the pre-vaccination period did not lead to a significant increase in the frequency of aneuploid and polyploid cells. During double immunization of calves, a wave pattern in the variation of genomic mutation frequencies from maximum to minimum values in the lymphocytic blood cells of animals was noted, similar to prolonged mutagenesis. A tendency was found for the frequency of structural chromosome abnormalities to increase 2 and 9 days after vaccination and 2 days after revaccination. There was a credible 2.9-fold increase in the frequency of cells with chromosomal aberrations in the blood lymphocytes of animals 9 days after their repeated immunization due to breaks and paired fragments of chromosomes. After vaccination and revaccination, chromatid breaks were most often recorded in the medial regions of one of the chromatids, and chromosomal breaks in the medial and telomeric regions of both chromatids.

Keywords: genome mutations, chromosomal mutations, peripheral blood lymphocytes, calves, vaccination, revaccination, salmonellosis

Конфликт интересов
Авторы заявляют об отсутствии конфликта интересов.
Conflict of interest
The authors declare no conflict of interest.

Для цитирования: *Куликова С.Г., Логинов С.И., Назаренко Ю.С., Калинина Н.С.* Цитогенетические нарушения у молодняка крупного рогатого скота при вакцинации против сальмонеллеза // Сибирский вестник сельскохозяйственной науки. 2021. Т. 51. № 3. С. 92–103. https://doi.org/10.26898/0370-8799-2021-3-10
For citation: Kulikova S.G., Loginov S.I., Nazarenko Yu.S., Kalinina N.S. Cytogenetic abnormalities in young cattle during vaccination against salmonellosis. *Sibirskii vestnik sel'skokhozyaistvennoi nauki = Siberian Herald of Agricultural Science,* 2021, vol. 51, no. 3, pp. 92–103. https://doi.org/10.26898/0370-8799-2021-3-10

Благодарность
Авторы выражают благодарность и глубокую признательность аспиранту Новосибирского государственного аграрного университета Унагаевой Наталье Владимировне за оказанную помощь при проведении цитогенетических исследований.
Acknowledgments
The authors express their gratitude and deep appreciation to the post-graduate student of the Novosibirsk State Agrarian University Unagaeva Natalia Vladimirovna for her assistance in conducting cytogenetic research.

INTRODUCTION

An increase in livestock production in modern conditions is based on improving the genetic potential of animals and creating highly productive herds resistant to diseases[1] [1–4].

It has now been established that a number of infectious diseases are caused by pathogenic microorganisms. Their impact contributes to the appearance of abnormalities in the chromosomal apparatus of humans and laboratory animals. In medicine, numerous studies have been carried out to study the cytogenetic consequences of infectious diseases and vaccinations [5–8]. It has been suggested that antigens and toxins of some infectious agents and vaccines may be mutagenic. Reactive metabolites of oxygen and nitrogen, formed in the foci of inflammation and in the course of the immune response, can cause an increase in the frequency of DNA damage and cytogenetic disorders [5, 6].

The influence of infectious agents, including vaccines, on the instability of karyotypes in hu-

[1]Patent RU No. 2 083 102 C1 IPC A 01 K 67/02. The method of complex selection of bulls-producers for the resistance of offspring to diseases / V.L. Petukhov, L.K. Ernst, A.G. Nezavitin, A.I. Zheltikov, O.S. Korotkevich, S.G. Kulikova, V.G. Marenkov, N.N. Kochnev, V.P. Shishkov, V.T. Khristenko; applicant and patentee Scientific Research Institute of Veterinary Genetics and Breeding. No. 95113836/13; declared 08/01/1995; publ. 10.07.1997, Bul. No. 19. 10 p.

mans and laboratory animals is often ambiguous. According to N.N. Ilyinskikh [5], this is explained not only by the strain characteristics of infectious agents, but also by the specificity of the genotype of the organism, its age, the functional state of protection and resistance to the mutagenic influence of infectious factors.

In veterinary medicine and farm animal genetics, there are few publications on the subject, despite the need for research due to the widespread use of vaccination in agriculture[2,3] [9].

Salmonellosis (paratyphoid fever) is one of the most common infectious diseases of young cattle in Siberia [10]. It is caused by bacteria of the genus *Salmonella* (*S. dublin*, less often *S. typhimurium* and bacteria of other serological types), which primarily affect young animals aged from 10 days to 5 months. In young animals, the acute course of the disease is characterized by fever, septicemia, toxicosis and diarrhea, subacute and chronic - pneumonia and arthritis; in adult females, abortion. Vaccination is still the most effective way to prevent the spread of infectious diseases in farm animal populations. To date, the cytogenetic consequences of vaccinations against salmonellosis in cattle have not been investigated.

The aim of the work is to study cytogenetic disturbances in young cattle when vaccinated against Salmonellosis.

The research objectives are:

– determination of the spectrum of cytogenetic disorders in peripheral blood lymphocytes in calves at different periods of immunization against salmonellosis,

– investigation of the effect of double immunizations with an inactivated vaccine against salmonellosis on the frequency of cytogenetic disorders in immunocompetent cells in young cattle.

MATERIAL AND METHODS

The studies were conducted on 10 clinically healthy 10-17-day old Holsteinized black-motley calves in a farm in Novosibirsk district, Novosibirsk region. Blood for cytogenetic analysis was taken from each animal five times: before vaccination (control), 2 and 9 days after vaccination, 2 and 9 days after revaccination with the salmonellosis vaccine.

A concentrated formolvac vaccine against salmonellosis (paratyphoid) of calves was used in a dose of 2 ml (reimmunization in a dose of 2 ml) with an interval of 10 days between injections. The vaccine is made from bacterial culture of *Salmonella dublin* strain No. 373 inactivated with formalin (0.4% by volume) with the addition of potassium alum and calcium chloride (0.1% by volume) as an adjuvant.

The material for the cytogenetic study was the peripheral blood lymphocytes of animals stimulated by phytohemagglutinin. Preparations of metaphase chromosomes were prepared according to the method of P.S. Moorchead et al. [11] with modifications. The preparations were stained with Giemsa stain. The classification of somatic mutations was carried out according to the criteria proposed by N.P. Bochkov and A.N. Chebotarev [12]. As a result of a cytogenetic study of calves in different periods, 9472 metaphase plates were analyzed in detail. The frequencies of numerical and structural chromosome abnormalities were calculated per 100 cells. Frequencies of cytogenetic abnormalities are given in tables with percentage errors.

The research results were processed by standard methods of variation statistics using Microsoft Office Excel 2010. The significance of differences between the frequencies of cytogenetic indicators in the groups was evaluated by Fisher's method with φ-transformation of fre-

[2]Nazarenko Yu.S., Kulikova S.G., Loginov S.I. The influence of vaccinations on somatic chromosomal instability in animals and humans // The role of agricultural science in the sustainable development of rural areas: collection of articles. V All-Russian (national) scientific. conf. (Novosibirsk, December 18, 2020). Novosibirsk: RC NSAU "Zolotoy Kolos", 2020. P. 516–519.

[3]Kulikova S.G., Loginov S.I., Nazarenko Yu.S. The influence of vaccination against salmonellosis on the associative ability of acrocentric chromosomes in cattle // Theory and practice of modern agricultural science: collection of articles. IV national (All-Russian) scientific. conf. from international participation (Novosibirsk, February 26, 2021). Novosibirsk: RC NSAU " Zolotoy Kolos ", 2021. P. 908-912.

quencies. For the zero-frequency value the error was calculated by the method of B.L. Van der Waerden [13].

RESULTS AND DISCUSSION

Studies of peripheral blood lymphocyte cultures of clinically healthy Holsteinized black-motley calves found that the spectrum of cytogenetic abnormalities in animals after vaccination and revaccination against salmonellosis is represented by polyploidy, hypoploidy and hyperploidy cells, chromatid and chromosome breaks, single and paired chromosome fragments regardless of the time since the vaccine administration. Polyploid and aneuploid cells were detected among the numerical abnormalities in individuals both before and after vaccination and revaccination against salmonellosis (see Table 1.).

It was found that vaccination and revaccination of young cattle against salmonellosis did not lead to a significant increase in the frequency of genomic mutations in the somatic cells of animals. On the contrary, a tendency was found for a gradual decrease in the frequency of cells with an altered chromosome number 2 and 9 days after vaccination of calves against salmonellosis. 9 days after revaccination of animals, a significant decrease in the frequency of cells with genomic mutations to 7.18% was noted, control - 9.62% ($p < 0.05$).

The maximum frequency of cells with a changed number of chromosomes (14.0%) was found 2 days after revaccination of calves against salmonellosis, which exceeded the same indicator in animals 9 days after their vaccination and revaccination by 1.7 and 2.0 times, respectively ($p < 0.05$-0.01).

Among the cells with an altered chromosome number, aneuploid cells with hypoploid sets predominated (35.6-51.8%). The average frequency of hypoploid cells in calves before vaccination was 4.98%. The frequency of hypoploid cells was 1,9 times lower in the animals 9 days after revaccination against Salmonellosis

Табл. 1. Частота клеток с измененным числом хромосом у молодняка крупного рогатого скота до и после вакцинации, ревакцинации против сальмонеллеза, %

Table 1. Frequency of cells with changed number of chromosomes in young cattle before and after vaccination, and revaccination against salmonellosis, %

Indicator	Period of study				
	before vaccination (control)	after vaccination		after revaccination	
		after 2 days	after 9 days	after 2 days	after 9 days
Polyploid cells	3,40 ± 0,57	4,40 ± 0,75	3,16 ± 0,63	6,00 ± 1,68	2,52 ± 0,47
Aneuploid cells, including:	6,22 ± 1,10	4,47 ± 1,06	4,94 ± 1,10	8,00 ± 2,71	4,66 ± 0,91
hypoploid cells, including types:	4,98 ± 0,99	3,16 ± 0,90	3,38 ± 0,92	6,00 ± 2,37	2,61 ± 0,69*
2*n*-1	1,04 ± 0,46	2,11 ± 0,74	1,30 ± 0,58	1,00 ± 0,99	1,12 ± 0,45
2*n*-2	2,49 ± 0,71	0,00 ± 0,26***	1,30 ± 0,58	4,00 ± 1,96	0,56 ± 0,32**
2*n*-3 and more	1,45 ± 0,54	1,05 ± 0,52	0,78 ± 0,45	1,00 ± 0,99	0,93 ± 0,41
hyperploid cells, including types:	1,24 ± 0,51	1,32 ± 0,58	1,56 ± 0,63	2,00 ± 1,40	2,05 ± 0,61
2*n*+1	1,04 ± 0,46	0,53 ± 0,37	1,04 ± 0,52	2,00 ± 1,40	1,68 ± 0,55
2*n*+2	0,00 ± 0,21	0,53 ± 0,37*	0,52 ± 0,37*	0,00 ± 0,97	0,19 ± 0,19
2*n*+3 and more	0,21 ± 0,21	0,26 ± 0,26	0,00 ± 0,26	0,00 ± 0,97	0,19 ± 0,19
Cells with an altered number of chromosomes	9,62 ± 0,93	8,87 ± 1,04	8,10 ± 0,99	14,00 ± 2,45	7,18 ± 0,77*

Hereinafter *$p < 0,05$.
**$p < 0,01$.
***$p < 0,001$.

Significant differences are indicated in comparison with the period before vaccination (control).

compared with the control (p <0,05). There was no significant increase in the frequency of hyperploid cells in animals after their vaccination and revaccination after 2 and 9 days compared with the period before drug administration (see Table 1), but there was a clear tendency for a gradual increase in the frequency of this cell type after primary and repeated calf immunization (p > 0.05).

Different types of hypoploid and hyperploid cells were detected, the frequencies of which varied in different periods of study in young cattle (see Table 1). The frequency of cells with a loss of two chromosomes was found to decrease in 2 days after vaccination and in 9 days after revaccination of calves against Salmonellosis, to 0,0 and 0,56%, respectively, in the prevaccination period - 2,49% (p < 0,01-0,001). The highest frequency (4.0%) of cells with a deficiency of two chromosomes was observed 2 days after revaccination of animals, which was 7.14 times higher than 9 days after revaccination of calves against Salmonellosis (p < 0.05).

No significant differences were found in the frequency of cells with an excess of one or three or more chromosomes in calves before vaccination compared with animals vaccinated and revaccinated against Salmonellosis. Cells with an excess of two chromosomes (2n+2) were detected 2 and 9 days after vaccination of calves against Salmonellosis, with the frequency of 0.53 and 0.52%, respectively, while they were absent in controls (p < 0.05).

Another type of genomic mutation reported in the present studies is polyploidy (see Table 1). No significant differences were found in the frequency of polyploidy cells in calves at all periods after vaccination and revaccination against salmonellosis compared to controls (p > 0.05). At the same time, a 2.38-fold reduction in the frequency of polyploid cells was found in calves 9 days after revaccination, compared with animals examined 2 days after revaccination against Salmonellosis (p < 0.05).

Analysis of the polyploid cell spectrum (see Table 2) showed that tri- and tetraploid cells were detected in the animals without exception in all periods of the study (before vaccination, 2 and 9 days after vaccination and revaccination against salmonellosis). Cells with higher ploidy (5n and/or 6n) were recorded only in calves before vaccination and 2 days after their vaccination and revaccination against salmonellosis. The proportion of tetraploid cells was 75.7-95.9% of the total number of polyploid cells.

Along with genomic abnormalities in young cattle before vaccination, after vaccination and revaccination with inactivated vaccine against salmonellosis, chromosomal mutations were revealed. In the present studies, the spectrum of chromosomal aberrations is represented by single and paired fragments, chromatid and chromosomal breaks (see Table 3).

The frequencies of cells with aberrations and the total number of chromosome aberrations in the examined young calves had a tendency to

Табл. 2. Спектр и частота полиплоидных клеток у молодняка крупного рогатого скота до и после вакцинации, ревакцинации против сальмонеллеза, %

Table 2. Spectrum and frequency of polyploid cells in young cattle before and after vaccination, and revaccination against salmonellosis, %

Period of study	Cell ploidy			
	3*n*	4*n*	5*n*	6*n* and more
Before vaccination (control)	0,40 ± 0,20	2,80 ± 0,52	0,10 ± 0,10	0,10 ± 0,10
After vaccination:				
after 2 days	0,40 ± 0,23	3,33 ± 0,66	0,27 ± 0,19	0,40 ± 0,23
after 9 days	0,13 ± 0,13	3,03 ± 0,62	0,00 ± 0,13	0,00 ± 0,13
After revaccination:				
after 2 days	0,50 ± 0,50	5,00 ± 1,54	0,00 ± 0,50	0,50 ± 0,50
after 9 days	0,36 ± 0,18	2,16 ± 0,44	0,00 ± 0,09	0,00 ± 0,09

a gradual increase in 2, 9 days after vaccination and in 2 days after calf revaccination, in 9 days after revaccination the animals significantly exceeded the control in 2,9 and 2,5 times ($p < 0,01$). This increase was due to an increase in the frequency of cells with chromosome breaks and their total number in vaccinated and revaccinated calves against salmonellosis. Before vaccination, the frequency of cells with chromosome breaks was 1.04 ± 0.46%, but 9 days after vaccination it was 1.82 ± 0.68% ($p > 0.05$), and 9 days after revaccination it was 2.98 ± 0.73% ($p < 0.05$).

Chromatid and chromosomal aberrations were recorded in calf lymphocytes during the whole period of observation, both before vaccination and after vaccination and revaccination against Salmonellosis. There was no significant increase in the frequencies of each of these types of chromosome aberrations separately in the postvaccination and revaccination periods compared to the pre-vaccination period. On the whole, a significant increase in the frequency of these aberrations in 9 days after revaccination of animals against Salmonellosis in comparison with control was found. It should be noted that 2 days after calf vaccination against Salmonellosis no chromatid chromosome breaks were detected in comparison with the pre-vaccination period, where their incidence was 0.62 ± 0.36%.

Analysis of the chromosome breaks localization showed that they were recorded in large and medium chromosomes in the pericentromeric, medial and telomeric regions of the long arms of one or both chromatids. Chromosome breaks of the chromatid type are found mainly in the medial regions of one of the chromatids (almost 80% of all chromatid breaks). Breaks in telomeric regions were found in calves only before vaccination with a frequency of 0.41 ± 0.29%, in near-centromeric regions of chromatids - only 9 days after revaccination of young animals against salmonellosis with a frequency of 0.56 ± 0.32%. Breaks of the chromosomal type were most often localized in the medial (43% of cases) and telomeric (46%) regions of both chromatids, much less frequently (11%) in the pericentromeric regions. In the studied animals, both before and after vaccination and revaccination, cells with one and two chromosome breaks were recorded, and lymphocytes with one break prevailed, the proportion of which varied from 80 to 100%. No cells with

Табл. 3. Частота аберраций хромосом у молодняка крупного рогатого скота до и после вакцинации, ревакцинации против сальмонеллеза, %

Table 3. Frequency of chromosome aberrations in young cattle before and after vaccination, and revaccination against salmonellosis, %

Indicator	Period of study				
	before vaccination (control)	after vaccination		after revaccination	
		after 2 days	after 9 days	after 2 days	after 9 days
Cells with chromosome aberrations	1,66 ± 0,58	2,11 ± 0,74	2,86 ± 0,85	3,00 ± 1,71	4,84 ± 0,93**
Chromosome aberrations	2,07 ± 0,65	2,37 ± 0,78	2,86 ± 0,85	4,00 ± 1,96	5,21 ± 0,96**
Cells with fragments of chromosomes	0,83 ± 0,41	1,05 ± 0,52	1,04 ± 0,52	1,00 ± 0,99	1,86 ± 0,58
Fragments of chromosomes Including:	0,83 ± 0,41	1,05 ± 0,52	1,04 ± 0,52	1,00 ± 0,99	1,86 ± 0,58
single fragments	0,62 ± 0,36	0,53 ± 0,37	0,52 ± 0,37	0,00 ± 0,97	0,56 ± 0,32
paired fragments	0,21 ± 0,21	0,53 ± 0,37	0,52 ± 0,37	1,00 ± 0,99	1,30 ± 0,49*
Cells with chromosome breaks	1,04 ± 0,46	1,32 ± 0,58	1,82 ± 0,68	3,00 ± 1,71	2,98 ± 0,73*
Chromosome breaks Including:	1,24 ± 0,51	1,32 ± 0,58	1,82 ± 0,68	3,00 ± 1,71	3,36 ± 0,78*
chromatid breaks	0,62 ± 0,36	0,00 ± 0,26*	0,52 ± 0,37	2,00 ± 1,40	1,68 ± 0,55
chromosomal breaks	0,62 ± 0,36	1,32 ± 0,58	1,30 ± 0,58	1,00 ± 0,99	1,68 ± 0,55

three or more chromosome breaks were detected. There was a 3.1-fold higher frequency of cells with one chromosome break 9 days after calf revaccination against Salmonellosis, compared with the period before vaccination ($p < 0.05$).

There were no significant differences in the frequencies of single and paired chromosome fragments in calves in all periods of the study compared to controls (see Table 3). No differences were found after vaccination and revaccination when comparing these parameters between them, except for the frequency of cells with paired chromosome fragments, which was 6.2 times higher 9 days after revaccination than before vaccination ($p < 0,05$). It was found that cells with only one fragment were found in calves before vaccination and then at all periods after their vaccination and revaccination against salmonellosis.

As a result of the conducted studies of cattle, the mutagenic effect of routine vaccinations against salmonellosis of calves was assessed.

It was found that in peripheral blood lymphocytes of young cattle the spectrum of cytogenetic disorders induced by the inactivated vaccine against salmonellosis of calves is represented by polyploid, hyperploid and hypoploid cells, single and paired fragments of chromosomes and chromatid and chromosomal breaks.

It was revealed that the spectrum of somatic chromosomal instability after double immunizations with an inactivated vaccine against salmonellosis did not differ from the spectrum of spontaneously occurring mutations in this species [14–17].

To date, the mutagenic properties of many viral and bacterial vaccines have been studied in humans, in particular against measles, smallpox, poliomyelitis, influenza, rabies, mumps, yellow fever, herpes simplex, tick-borne encephalitis, brucellosis, typhoid fever and others [5–8, 18]. These studies showed that in most cases live vaccines had a pronounced mutagenic effect, while inactivated vaccines did not cause an increase in the frequency of cytogenetic disorders in the lymphocytes of vaccinated people. But according to J. Chun et al. [19], no increase in the number of cytogenetic disorders was found in 7 children vaccinated with a live measles vaccine.

The results of these studies indicate an ambiguous effect of vaccination and repeated revaccination after 10 days with an inactivated vaccine against salmonellosis on the frequency of genomic and structural mutations in clinically healthy Holsteinized black-and-white calves. There was no increase in the frequency of aneuploid and polyploid cells after vaccination and revaccination of calves with an inactivated salmonellosis vaccine in comparison with the pre-vaccination period. A tendency towards a gradual decrease in the frequency of cells with altered chromosome number in calves in all periods following vaccination against salmonellosis has been detected. A sharp increase in the frequency of these cells (both aneuploid and polyploid cells) was noted 2 days after revaccination, followed by a significant decrease in the frequency of cells with genomic mutations 9 days after revaccination in comparison with the period before vaccination. A significant change in the frequency of polyploid cells in different periods after revaccination of animals against salmonellosis was established. The significant variations in the frequencies of genomic mutations in young cattle revealed in studies after repeated immunization are consistent with the statement that with prolonged mutagenesis, which is possible during revaccinations, its intensity is characterized by a wave character with fluctuations in aberration levels from maximum to minimum [20].

The fact that the frequency of cells with an altered number of chromosomes in young cattle decreased significantly 9 days after revaccination against salmonellosis in comparison with intact animals, established in the study, may be caused by age features and/or different functional state of the immune system of the studied calves, responsible for the elimination of cells with cytogenetic abnormalities. An enhancement of the genome-protective system and other mechanisms cannot be excluded [18].

The results of these and earlier studies [15] and data from other scientists [17, 21] indicate that spontaneous and agent-induced mutagenesis of various nature in cattle most often revealed cells with a tetraploid set of chromosomes among polyploid cells.

At the same time, with regard to chromosome aberrations, it was found that immunization of calves with inactivated vaccine against Salmonellosis tended to gradually increase the frequency of chromosome structural disorders in 2, 9 days after vaccination and in 2 days after revaccination. This resulted in a significant increase in the frequency of cells with chromosome aberrations in animal blood lymphocytes 9 days after re-vaccination due to breaks and paired chromosome fragments. A similar result was obtained by N.N. Ilinskikh [5] during cytogenetic examination of healthy donors vaccinated against brucellosis. As early as 2 days after vaccine introduction, a significant increase in chromosome structural disorders was detected: the frequency of cells with chromosome breaks to 0.9 ± 0.2% vs. 0.1 ± 0.06% in the control and 2.3 ± 0.2% with chromatid breaks to 1.0 ± 0.01% in the control.

Studies by a number of scientists have shown that mutagenic factors are capable of specifically affecting individual chromosomes and their zones [5, 18]. When studying the mechanisms of the karyopathogenic effect of a brucellosis vaccine (strain 19 BA) in humans, large chromosomes of group A were affected more frequently, and disorders in small chromosomes of groups F and G were extremely rarely observed [5]. A similar pattern was detected in the present studies. The specificity of lesions of large and medium chromosome groups and their regions in young cattle after vaccination and revaccination against salmonellosis has been established. According to N.N. Ilinskikh [5], the biochemical structure of the infectious agent itself and its immunogenicity are of great importance in chromosome lesions. It was found that in calves after vaccination and re-vaccination against salmonellosis, chromatid breaks were most often registered in the medial regions of one of the chromatids, while chromosomal breaks were found in the medial and telomere regions of both chromatids. Apparently, the specificity of lesion of some chromosome regions by antigenic factors of inactivated vaccines as well as by some infectious agents is associated with peculiarities of structure and functioning of these chromosome regions. Some studies have shown that infectious agents, by altering cell metabolism, can initiate a chain of reactions that lead to visible damage to chromosomes [22].

Consequently, revaccination with inactivated salmonellosis vaccine induces cytogenetic abnormalities in reimmunized calves, causing a significant increase in the frequency of cells with chromosomal aberrations in peripheral blood lymphocytes of the animals. A cumulative effect of double vaccination with inactivated bacterial vaccine in cattle seems to be observed, resulting in an increased frequency of DNA damage due to the mutagenic properties of the vaccine antigens during the formation of the immune response.

CONCLUSION

As a result of studying the spectrum and frequency of cytogenetic disorders in somatic cells in clinically healthy Holsteinized black-and-white calves before vaccination, after vaccination and revaccination with an inactivated vaccine against salmonellosis, the mutagenic effect of routine immunizations against this disease in cattle was evaluated.

The spectrum of cytogenetic disorders induced by the inactivated vaccine against salmonellosis in young cattle in peripheral blood lymphocytes is represented by polyploid, hyperploid and hypoploid cells, single and paired chromosome fragments and chromatid and chromosomal breaks. The spectrum of cytogenetic disorders caused by double immunization with the vaccine against salmonellosis of calves did not differ from the spectrum of spontaneously occurring mutations in this species.

Different effects of vaccination and re-vaccination after 10 days with an inactivated vaccine against salmonellosis on the frequencies

of genomic and structural mutations in immunocompetent cells in young cattle were found. Vaccinations and subsequent revaccinations of calves with an inactivated vaccine against salmonellosis in comparison with the pre-vaccination period did not cause an increase in the frequencies of aneuploid and polyploid cells.

The intensity of prolonged mutagenesis during revaccination of calves against salmonellosis was characterized by a wave character with fluctuations in the frequencies of cells with genomic mutations from maximum to minimum values.

Revaccination with an inactivated salmonellosis vaccine has a mutagenic effect on the chromosomal apparatus of re-immunized calves, causing a significant increase in the frequency of cells with chromosomal aberrations in the peripheral blood lymphocytes of animals due to breaks and paired fragments of chromosomes.

The specificity of damage to certain regions of chromosomes in young cattle after vaccination and revaccination against salmonellosis was revealed. In calves after double immunization, chromatid breaks were most often recorded in the medial regions of one of the chromatids, and chromosomal breaks - in the medial and telomeric regions of both chromatids.

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Дата поступления статьи / Received by the editors 11.02.2021
Дата принятия к публикации / Accepted for publication 21.04.2021
Дата публикации / Published 26.07.2021