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Development of protocols and efficiency of ozone-containing drugs for the treatment of livestock with reproductive pathologies

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Abstract. For animals with reproductive pathologies, a comprehensive program treatment that considers the principle of drug action is widespread. One of the essential points of the program is the use of antibacterial drugs. Available drugs have variable activities, some of which have adverse effects. Therefore, the search for the mentioned item of the program of new drugs that would meet the requirements of modern practice is an urgent problem in veterinary medicine that needs to be solved. In this regard, ozone therapy is promising due to its ability to affect the transport and release of oxygen into tissues, disinfectant action, and a wide range of ozone therapy for treating several diseases. Our work aimed at developing ozone-containing drugs for animal reproductive (obstetric, mammalogical, and andrological) pathologies treatment. In the standard protocol, we replaced antibacterial drugs with ozonated corn oil (OCO) and Prozon (complex preparation of ozonated corn oil and alcohol solution of propolis). The recovery process was assessed during and after the therapy by the duration and percentage of recovered animals. In treating animals with subclinical mastitis, the recovery criterion was the normalization of milk cytograms. In the treatment of cows and goats with acute postpartum catarrhal-purulent endometritis, the use of ozone-containing drugs reduced the period from the treatment beginning to the disappearance of clinical signs by 0.7 days (OCO) and 4.8 days (Prozon) and from birth to estrus – by 1.8 and 11.1 days, respectively; while fertility increased by 8.5% and 41.9%. Periods from the beginning of treatment of goats with OCO and Prozon to the disappearance of clinical signs decreased by 1.1 days and 2.8 days, respectively; while fertility increased by 17.2% and 37.2%. Treatment of cows with subclinical mastitis during the dry period with the use of ozone-containing drugs helped to reduce the duration of cure by 1.1 days (OCO) and 2.0 days (Prozon), and the effectiveness of treatment (percentage of recovered animals) increased by 5, 6% and 10.0%, respectively. Treatment of cows with subclinical lactational mastitis reduced the duration of cure by 0.2 days (OCO) and 0.8 days (Prozon), and its effectiveness (percentage of recovered animals) increased by 6.5% and 14.6%, respectively. The ozone-containing drugs for the treatment of nonspecific balanoposthitis in domestic boars reduced the period of recovery by 0.9 days (OCO) and 1.5 days (Prozon), bulls – by 1.1 and 2.7 days, and rams – by 0.8 and 2.2 days, respectively.

Keywords: cows; goats; domestic boars; bulls; sheep; ozone therapy; endometritis; mastitis; balanoposthitis.

Розробка схем та ефективність озонвмісних препаратів для лікування свійської худоби з репродуктивними патологіями

Анотація. Сьогодні щодо тварин з репродуктивними патологіями набуло поширення комплексне програмне лікування з урахуванням принципності дії препаратів. Один з важливих пунктів програми – це застосування препаратів антибактеріального спрямування. Відомі препарати відрізняються варіабельністю дії, а деякі з них мають негативні впливи. Тож пошук для згаданого пункту програми нових препаратів, які б відповідали вимогам практики на сучасному рівні є актуальною проблемою ветеринарної медицини, яка потребує вирішення. У цьому відношенні перспективу має терапія із застосуванням озону, яка отримала значного поширення, що пов'язано з його властивостями впливати на транспортування і вивільнення кисню в тканини, дезінфікуючою дією і широким діапазоном застосування озонотерапії за лікування низки захворювань. Мета роботи – оцінювання ефективності озонвмісних препаратів для лікування тварин з репродуктивними (акушерськими, мамологічними та андрологічними) патологіями та розроблення схем їх застосування, в яких пункт із використанням антибактеріальних препаратів замінено на препарати ОКО (озонована кукурудзяна олія) та Прозон (комплексний препарат озонованої кукурудзяної олії та спиртового розчину прополісу). Одужання тварин визначали впродовж курсу терапії та після неї за відсотком тварин, що одужали, і його тривалістю. За лікування тварин із субклінічним маститом критерієм одужання була нормалізація показників цитогам молока. За лікування корів і кіз з гострим післяродовим катарально-гнійним ендометритом використання озонвмісних препаратів дозволило скоротити тривалість лікування від його початку до зникнення клінічних ознак

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хвороби на 0,7 доби (ОКО) та 4,8 доби (Прозон) і від родів до прояву еструсу – на 1,8 та 11,1 діб, та підвищити заплідненість на 8,5 та 41,9 % відповідно. За лікування кіз із використанням препаратів ОКО та Прозон тривалість періодів від початку лікування до зникнення клінічних ознак хвороби скоротилася відповідно на 1,1 та 2,8 доби, а заплідненість підвищилася на 17,2 та 37,2 %. Лікування субклінічного маститу у корів сухостійного періоду з застосуванням озонвмісних препаратів сприяло скороченню тривалості періоду від початку терапії до одужання на 1,1 доби (ОКО) та 2,0 доби (Прозон), а ефективність лікування (відсоток тварин, що одужали) підвищилася на 5,6 та 10,0 % відповідно. За лікування корів із субклінічним маститом лактаційного періоду скоротилась тривалість періоду від початку лікування до одужання на 0,2 доби (ОКО) та 0,8 доби (Прозон), а ефективність лікування (відсоток тварин, що одужали) підвищилася на 6,5 та 14,6 % відповідно. Застосування озонвмісних препаратів у способі лікування кнурів із неспецифічним баланопоститом забезпечило скорочення тривалості періоду від початку лікування до одужання на 0,9 доби (ОКО) та 1,5 доби (Прозон), бугаїв – на 1,1 та 2,7 доби і баранів – на 0,8 та 2,2 доби відповідно.

Ключові слова: корови; кози; кнури; бугаї; барани; озонотерапія; ендометрит; мастит; баланопостит.

Introduction

One of the urgent tasks of veterinary medicine is the development of modern methods of therapy and prevention of diseases (Makarov, 2007; Stekolnikov, 2007; Skliarov et al., 2021). Due to the growing allergies of humans and animals, reduced sensitivity to antibiotics, and rising drug prices, non-drug methods are becoming increasingly popular. Therefore, along with efficiency, such a criterion as safety is put forward (Brejne et al., 2017; Canning et al., 2017; Gorjuk, 2021).

Nowadays, comprehensive treatment protocols for highly productive animals with reproductive (obstetric, mammological, gynecological, and andrological) diseases based on the drugs' action features are widespread in world practice. One of the essential points of the protocols is the use of antibacterial drugs. Available drugs have variable kinds of actions, and some also have adverse effects. Therefore, the search for new drugs that would meet the safety requirements of modern practice is an urgent problem in veterinary medicine, and it needs to be solved (Koshevojet et al., 2014; Ūnal & Sel, 2019; Nikolaev & Konopelcev, 2021).

Ozone therapy meets these criteria because therapeutic concentrations of ozone have several desirable properties – immunomodulatory, anti-inflammatory, antiviral, antifungal, analgesic and others. However, its antibacterial activity should be singled out (Di Paolo et al., 2004; Elvis & Ekta, 2011; Shaganenko et al., 2020). Therefore, veterinary medicine has introduced ozone therapy (Bocci, 2002; Repciuc et al., 2016; Sciorsci et al., 2020; Orlandin et al., 2021).

There are examples of the use of ozone in the treatment and prevention of reproductive pathologies in animals, such as retained foetal membrane, mastitis, and diseases of the uterus and other reproductive organs (Djuricic et al., 2012; Samardžija et al., 2017; de Souza et al., 2021).

In this regard, ozone gas therapy, which has deservedly become widespread, has prospective potential (Balljuzek et al., 2005; Re et al., 2008; Koshevoj et al., 2014). It is caused by the properties of ozone to affect the transport and release of oxygen into tissues, its disinfectant effect and causes a wide range of ozone therapy – in the treatment of many diseases, including obstetrics and gynecology (Kachalina & Grechkanev, 2007; Balmagambetova, 2011; Smith et al., 2017).

Known mechanisms of biological activity of ozone determine its therapeutic effects in reproductive medicine. They are: bactericidal, fungicidal, and viricidal activity against the most common types of both gram-positive and gram-negative bacteria, viruses, pathogenic fungi, and protozoa; activation of oxygen-dependent processes; strengthening metabolic processes of energy substrates production; immunomodulatory effect; improving microhemocirculation and gas exchange at the tissue level (Bocci, 1999; Grishhenko et al., 2005; Kachalina & Grechkanev, 2007).

Based on the above, our work aimed to assess the efficiency of drugs for domestic livestock with reproductive pathologies and to develop treatment schemes, in which the ozone-containing drugs replace the antibacterial ones.

Materials and methods

We assessed drug efficiency and development of ozone therapy methods at the Department of Veterinary Surgery and Reproductology of the State Biotechnological University (Kharkiv) and the Department of Low-Temperature Equilibrium Plasma Chemistry of the National Research Center «Kharkiv Institute of Physics and Technology» (Kharkiv). Center for Plant Breeding and Animal Husbandry of the State Biotechnological University (Kharkiv), implementation – in farms of various forms of ownership in the eastern, southern, and central regions of Ukraine.

We treated the animals according to the developed protocol with the ozone-containing drugs OCO (ozonated corn oil) and Prozon (complex preparation of ozonated corn oil and alcohol solution of propolis). The focal development is the replacement of antibacterial drugs with ozone-containing ones.

In the method of treatment of cows and goats with acute postpartum catarrhal-purulent endometritis, Combi-Kel (benzyl penicillin + dihydro streptomycin; Kel, Belgium) and Gynobiotic (neomycin sulfate + oxytetracycline hydrochloride; Lek/Sandoz/Novartis, USA) were used according to the instructions, ozone-containing drugs were administered intrauterinely, at a dose of 100–150 ml – for cows, and 10–15 ml – for goats, with an interval of 24 hours 5–7 times – OCO and 3–4 times – Prozon.

Cows with subclinical mastitis during the dry period were treated with Mastilex according to the instruction. Ozone-containing OCO and Prozon were administered as 3–4 intracisternal injections in a dose of 10–20 ml with an interval of 24 hours.

In treating pigs, bulls, and rams with nonspecific balanoposthitis, the drugs were administered intrapreputially: gentamicin – according to the instructions, OCO and Prozon – at a dose of 10–20 ml per injection, 3–4 times, with a 24-hour interval.

Animal recovery was determined as the percentage of the recovered animals and the convalescence process duration. The recovery criterion of animals treated for subclinical mastitis was the normalization of milk cytograms.

Results

A method of treating cows and goats with acute postpartum catarrhal-purulent endometritis

In treating animals with endometritis, the problem with the lack of adequate and acceptable practice of veterinary medicine methods of therapy remains. The main requirements should be:

- its high therapeutic and economic efficiency;
- easiness of execution;
- availability and cheapness of selected drugs.

The following principles should also be followed:

1. Normalization of metabolism and increase of immunobiological reactivity of an organism, stimulation of cardiovascular and immune systems.
2. Rehabilitation of the uterine cavity, the use of antibacterial drugs.

Table 1 – Efficacy of therapy of cows and goats with postpartum catarrhal-purulent endometritis

Group of animals	Duration of the period from the beginning of treatment to the disappearance of clinical signs of the disease, days (M ± m)	The period from childbirth to the manifestation of estrus, days (M ± m)	Fertilization after the first insemination, %
Cows			
Control (Combi-Kel, Gynobiotic), n = 5	10.4 ± 0.51	45.2 ± 1.9	20.0
Experimental I (OCO), n = 7	9.7 ± 0.42*	43.4 ± 1.65***	28.5
Experimental II (Prozon), n = 21	5.6 ± 0.19***	34.1 ± 0.54***	61.9
Goats			
Control (Combi-Kel, Gynobiotic), n = 7	9.2 ± 0.39	–	42.8
Experimental I (OCO), n = 5	8.1 ± 0.28*	–	60.0
Experimental II (Prozon), n = 5	6.4 ± 0.56***	–	80.0

Note: *** $p < 0.001$; * $p < 0.05$.

3. Correction of animal hormonal status.
4. The use of tonomotor and anti-inflammatory drugs.
5. Rehabilitation of the structure and function of the uterus.

The most responsible was the choice of antibacterial drugs, which do not always provide the expected effect.

Treatment of cows and goats with acute postpartum catarrhal-purulent endometritis was carried out according to a targeted protocol motivated by the action of drugs.

The method was put into practice at the training and production center of crop and livestock of the State Biotechnological University (Kharkiv), LLC «Delta» Novovodolazsky district, LLC «Alpha» Zolochiv district, LLC JE «Rodina» Bogodukhiv district of Kharkiv region, personal farms in the service area Svativ District State Hospital of Veterinary Medicine of Luhansk region and Verzhynsk State District Hospital of Veterinary Medicine of Bilmatsk district of Zaporizhia region.

The results are shown in Table 1.

According to the data obtained, the use of ozone-containing drugs instead of antibiotics (Combi-Kel and Gynobiotic) decreased the duration of treatment just to the disappearance of the disease clinical signs by 0.7 days (OCO) and 4.8 days (Prozon), the term from childbirth to estrus – by 1.8 and 11.1 days, and increased fertility by 8.5% and 41.9%, respectively.

The treatment of goats with the OCO and Prozon decreased the treatment course duration by 1.1 days and 2.8 days and increased fertility by 17.2% and 37.2%, respectively.

A method of treating cows with subclinical mastitis during dry and lactation period

Subclinical mastitis that occurs in the dry period is a widespread livestock disease. Inflammatory processes of the breast during the dry

period lead to dysfunction of this organ, which negatively affects the quality of the colostrum.

Pre-lactation mastitis can turn into lactation one with all possible negative consequences. Treatment of cows with subclinical mastitis during the dry period was carried out according to a purposeful protocol motivated by the principle of action of drugs. We replaced antibiotics, nitrofurans, and sulfonamides with ozone-containing medications OCO and Prozon.

The treatment protocol for cows with subclinical mastitis during the dry and lactation period was implemented in the training and production center of plant and animal husbandry of the State Biotechnological University (Kharkiv), LLC «Alpha», Zolochiv district, LLC JE «Rodina», Bogodukhiv district, LLC «Vostok», Izyum district, and the Dairy Farm of Dergachiv Correctional Colony № 109 in Kharkiv region. The results are shown in Table 2.

The obtained data show that treating cow subclinical mastitis during the dry period with ozone-containing drugs reduced the recovery duration by 1.1 days (OCO) and 2.0 days (Prozon), contrary to the antibacterial drug Mastilex treatment. In addition, the effectiveness of the treatment in terms of the percentage of recovered animals increased by 5.6% and 10.0%, respectively.

The treatment of cows with subclinical mastitis during lactation reduced the duration of the period from the beginning of treatment to recovery by 0.2 days (OCO) and 0.8 days (Prozon) compared to the control (Mastilex). It also increased the effectiveness of the treatment by 6.5% and 14.6%, respectively.

A method of treating males with nonspecific balanoposthitis

Conventional antibacterial drugs (disinfectants, antibiotics, nitrofurans, and sulfonamides) are usually used for nonspecific balanoposthitis treatment in males. Such antibacterial therapy varies;

Table 2 – Efficacy of therapy of cows with subclinical mastitis during dry and lactation periods

Group of animals	Duration of the period from the beginning of treatment to recovery, days (M ± m)	The effectiveness of treatment		
		number of recovered cows	number of not-recovered cows	%
Subclinical mastitis during the dry period				
Control (Mastilex), n = 15	7.4 ± 0.16	13	2	86.7
Experimental I (OCO), n = 26	6.3* ± 0.12	24	2	92.3
Experimental II (Prozon), n = 30	5.4* ± 0.11	29	1	96.7
Subclinical mastitis during the lactation period				
Control (Mastilex), n = 17	6.2 ± 0.49	14	3	82.4
Experimental I (OCO), n = 27	6.0* ± 0.75	24	3	88.9
Experimental II (Prozon), n = 33	5.4* ± 0.24	32	1	97.0

Note: * $p < 0.05$.

Table 3 – Efficacy of ozone therapy in males with nonspecific balanoposthitis

Group of animals	Period from the beginning of treatment to recovery, days (M ± m)	Therapy effectiveness	
		number of recovered animals	%
Boars			
Control (gentamicin), n = 5	7.6 ± 0.25	5	100
Experimental I (OCO), n = 7	6.7 ± 0.18*	7	100
Experimental II (Prozon), n = 11	6.1 ± 0.21**	11	100
Bulls			
Control (gentamicin), n = 5	7.8 ± 0.37	5	100
Experimental I (OCO), n = 6	6.7 ± 0.33*	6	100
Experimental II (Prozon), n = 7	5.1 ± 0.26**	7	100
Rams			
Control (gentamicin), n = 6	7.7 ± 0.31	6	100
Experimental I (OCO), n = 5	6.9 ± 0.25*	5	100
Experimental II (Prozon), n = 5	5.5 ± 0.23***	5	100

Note: * $p < 0.05$; *** $p < 0.001$

some drugs are toxic to the animal or expensive. Therefore, we tested ozone-containing drugs OCO and Prozon. The results are shown in Table 3.

Proposed treatment protocol for male pigs and rams with nonspecific balanoposthitis was used in the training and production center of plant and animal husbandry of the State Biotechnological University (Kharkiv), LLC «Mayak», Chuguivsky and LLC «AF» Pishchanska «Krasnograd districts of Kharkiv region, JFE «Dzherelo», Dnipropetrovsk region, LLC «40 years-Agro», Bilmatsky and farm «Yastrebo», Kamyansko-Dniprovsky districts of Zaporizhzhia region, PE «Agromash», Karlovsky district of Poltava region.

Our data demonstrate that compared to the use of gentamicin, the nonspecific balanoposthitis treatment by ozone-containing drugs reduced the recovery duration by 0.9 days (OCO) and 1.5 days (Prozon) in boars, for 1.1 and 2.7 days – in bulls, and for 0.8 and 2.2 days in rams, respectively.

Discussion

An effective remedy for treating cows with catarrhal or purulent metritis can be ozonated double-distilled water (Ablondi, 2005), saline (Chastikov, 2008; Irimia et al., 2014; González-Aguado et al., 2021; Mazzuchini et al., 2022). Pearls (Kumar et al., 2017), foam (Zobel et al., 2014; Constantin & Birtoiu, 2016; Imhof et al., 2019; Koseman et al., 2019), and gas (Kwon et al., 2005; Mali et al., 2020).

Ozone therapy can be an essential tool in preventing and treating various forms of bovine mastitis (Ablondi, 2004; Argudo & Soria, 2017; Arévalo et al., 2021). Ozone is effective for the bacteriological and clinical recovery of cows and may be an alternative to antibiotic treatment in acute clinical and subclinical mastitis (Sertkol et al., 2018; Torrico et al., 2018; Quintana et al., 2019).

New strategies were developed for postpartum dairy cows to improve their reproductive capacity. As a result, 35 days-intrauterine ozone therapy just after calving reduced the subclinical endometritis incidence and improved the reproductive features of the cows. In particular, intrauterine ozone treatment reduced the content of uterine polymorphonuclear (3.7% vs 7.6%), subclinical endometritis (5.0 vs 50.0%), the number of inseminations per conception (2.1 vs 3.1) and the interval from calving to conception (126.2 vs 149.0), while the first service conception rate increased (50.0%) (Escandón et al., 2020).

Ozone therapy was used to treat cows with subclinical endometritis as an alternative to antibiotics. Compared with rifaximin, intrauterine

ozone administration reduced the intervals between treatment and fertilization (46.4 vs. 40.0) as well as from calving to fertilization (129.4 vs. 125.0) with a similar number of inseminations (3.2 vs. 3.1) (Polat et al., 2015).

Zobel & Tkalčić (2013) used ozone for the treatment of cows with placental abruption was recognized as the most effective method. It resulted in the shortest period of open days, the smallest number of artificial inseminations for pregnancy, the smallest number of animals diagnosed with fever within ten post-calving days, the highest percentage of pregnant animals within 200 days after calving, and the smallest number of animals culled because of infertility, when compared to the other treatment groups.

Đuričić et al. (2014) applied an ozone spray that has the potential to alleviate metritis and endometritis as an impactful and cost-effective treatment option with an overall positive effect on fertility and the host regarding tissues in Holstein cows. The relevant studies were conducted on goats with delayed litter, which were mated successfully and became pregnant during the next kidding season, regardless of the treatment applied (Djuricic et al., 2015). In addition, Đuričić et al. (2016) outlined a new approach to ewe reproductive tract treatment using ozone foam spray for some obstetrical issues.

Nikolaev (2016) used ozonated emulsion in cows with acute postpartum endometritis, which increases the therapeutic efficacy by 35.2%, reduces the number of drug injections, saves about 182.8 ml of the drug, has a positive effect on the recovery of the reproductive system, reduces the manifestations of the first stage of sexual arousal after calving by 25.8 days, the period from delivery to the subsequent pregnancy – by 82.2 days, and fertilization index – to 1.3 on average.

Nikolaev & Konopelcev (2019) reported that using an emulsion with ozonides prevented the risk of inflammation in the endometrium by 36.7% and reduced the period from birth to pregnancy by 25.6–48.1 days. The same authors also used the ozonated emulsion to treat first-born cows with manure retention and acute postpartum endometritis. It reduced the number of livestock with acute endometritis by 30.0% (Nikolaev & Konopelcev, 2016).

Naumenko et al. (2019) reported that the use of ozone-air mixture in the complex pharmaco- and ozone therapy of acute postpartum endometritis of cats increased the effectiveness of treatment by 29.4%, reduced the duration of treatment by an average of 3 days and prevented recurrence of this disease.

Ozonated solution of furacilin has a pronounced antimicrobial and antimycotic effect on pathogens isolated from the secrets of the male preputial cavity of breeding boar. The mechanism of its

action is pronounced in a disturbance of submicroscopic systems and selective permeability of microbial cells and fungal spores that activates autolytic enzymes, which caused the lysis of intracellular and intraspore structures. It does not irritate the mucous membrane and does not adversely affect the lymphoid tissue of the foreskin. The use of the ozonated solution of furacilin (1 : 5000) provides a high rate of remediation, changes the microbial community of the male foreskin space, reduces the total number of microorganisms in semen by 23%, and increases coli-titer by 0.017. Using ejaculates of the boar treated in such a way helps to increase the fertility of sows by 6.7% and reduces the number of underdeveloped and stillborn piglets by 29.2% and 55%, respectively (Filatov et al., 2001).

In some research (Osipova, 2004), the combined use of the ozonated solution of furacilin and colostrum in treating cow postpartum endometritis helped to reduce the treatment duration by 8.2 days, the service period – by 17.5 days, and increase fertility by 4.2%.

Ozonated fish oil has a high antimicrobial activity against gram-positive and gram-negative microorganisms. The remedy destructs the bacterial cell wall and cytoplasmic membrane and activates microbial enzymatic systems of the cell, which leads to its lysis. It can stimulate tissue regeneration and activate the contractility of the muscular structures of the uterus (Konopelcev et al., 2000). The use of ozonated fish oil in treating the «metritis–mastitis–agalactia» (MMA) syndrome in sows provides their 100% recovery, fertility restoration in 70.0% of animals and successful surveillance of 78% of piglets. In the case of acute postpartum endometritis, it provides 100%, 77.7%, and 84.8%, respectively. Moreover, the treatment of chronic endometritis with ozonated fish oil increases the fertility of recovered animals by 8.6% (Filatov & Konopelcev, 2005).

The therapeutic efficacy of ozonated fish oil in the complex therapy of acute catarrhal mastitis provides recovery of 86.7% of cows in 4.1 days, reducing the treatment duration by 1.2 days. For chronic catarrhal mastitis, such treatment is effective in 63.6% of cases with a treatment duration of 8.8 days (Antipina & Konopelcev, 2010).

Konopelcev (2017) proposed a comprehensive treatment protocol for cow chronic catarrhal-purulent endometritis including the ozonated fish oil and isotonic sodium chloride solution. The effect was the decrease in clinical recovery term for 88.7% of animals and the restoration of reproductive function in a shorter time (87.5% of cows) with a fertilization index of 1.8.

Ozonated refined vegetable oil has a wide range of antimicrobial action against potential pathogens of acute postpartum endometritis and MMA. Therefore, it entails positive changes in the endometrium morphological structure and myometrium contractility. Compared to a 10% suspension of furazolidone in a vegetable oil can, its use increases the effectiveness of therapy of acute postpartum endometritis in sows by 4.7%, reduces the frequency of drug administration by 30%, and increases the safety of young animals by 9.5%. In the case of MMA, these improvements are 20%, 15%, and 2.9%, respectively (Filatov et al., 2003).

Beloborodenko et al. (2017) reported positive changes in the blood morphological and immunological indices of the lactating cows recovered clinically after treatment with ozonated refined sunflower oil and blue clay.

It is believed that ozone therapy (ozonated oil) can have a therapeutic effect in the case of chronic mastitis (Jo et al., 2005). Konopelcev & Shuljat'ev (2007) developed a method of subclinical and acute purulent-catarrhal chronic mastitis treatment in lactating cows with a combination of ozonated sunflower oil and isotonic sodium chloride solution. The authors demonstrated that such systemic ozone therapy contributes to normalizing the chemical composition and physicochemical properties of the udder secrete.

Effective treatment of first-born cows having acute postpartum endometritis used ozonated olive oil. It provided the clinical recovery

of 96.3% of animals, 100% fertilization, a fertilization rate of 2.25 and a duration of infertility of 89.8 days. (Chuchalin & Konopel'cev, 2003).

The treatment of cows and goats having both hypoluteoidism and subclinical endometritis with ozone-containing drugs OCO and Prozon allows for eliminating not only the clinical signs of the disease (reducing the therapy duration and estrus and increasing fertility) but also complete recovery. In particular, the duration of treatment periods was reduced by 1.6–6.1 days and estrus manifestations – by 4.5–12.6, while fertility was increased by 21.4–47.1% (Fedorenko et al., 2018).

According to Skliarov et al. (2021), the using ozone-containing drug Prozon in the treatment of goats with mastitis reduces the duration of the treatment alone and in a combination with phonophoresis with higher efficiency by 6.6%.

Skopin & Konopelcev (2018) used ozonated autologous blood in the complex treatment of cows' chronic endometritis. It increased the effectiveness by 12.1% and reduced the recovery-pregnancy period by 24.2 days. The proposed treatment protocol reduced the number of intrauterine injections of antimicrobial drugs by 0.5 and the use of sperm doses by 0.9. Using ozonated blood restores the animal reproductive capacity in 86.4% of cases at a fertilization rate of 1.7 and reduces the period of infertility down to 23 days.

Ozonated autologous blood increases the cure effectiveness by 17.3% and fertility by 31.6% if treating a cow's acute uterine subinvolution. It reduces the term of therapy by six days and the infertility period by 23.6 days. In the event of chronic subinvolution of the uterus, this method of treatment increases effectiveness and fertility by 9.3%, reduces the period of therapy by 4.1 days and the period of infertility – by 18.3 days (Skopin & Konopelcev, 2019).

Skliarov & Koshevoj (2015) developed a method to increase the viability of newborn lambs using ozonated material (OCO), which allows having 10% fewer neonatal newborns with bad clinical conditions with low development potential.

As a remedy for highly productive cows with inflammatory diseases of bacterial etiology, the ozonated linseed oil does not cause antibiotic resistance but does not reduce the quality of dairy products (Nikolaev & Konopelcev, 2021). The authors claim that it does not provoke the occurrence of inhibitory substances in milk. Moreover, the subsequent one-time artificial insemination guarantees a pregnancy in 63.3% of cows (Konopelcev & Nikolaev, 2019).

Our data testify high therapeutic effectiveness of ozone-containing drugs for reproductive pathologies treatment in livestock. The developed protocols propose using ozone corn oil (OCO) or binary preparation of ozonated corn oil and alcohol solution of propolis (Prozon) instead of antibiotics. Obtained data demonstrate that ozone-containing drugs successfully cure mastitis, postpartum catarrhal-purulent endometritis, and nonspecific balanoposthitis in domestic animals. We found a decrease in treatment duration and recovery efficacy but an increase in the reproductive potential of livestock.

Conclusion

Thus, ozone therapy is effective in the treatment of animals with reproductive pathology:

- the treatment of cows and goats with postpartum catarrhal-purulent endometritis reduces the term of cure by 0.7–4.8 days, the period from birth to estrus by 1.8–11.1 days and increases the fertility by 8.5–41.9%;

- the treatment of cows with subclinical mastitis during the dry and lactation periods reduces the period from the beginning of treatment to recovery by 0.2–2.0 days and raises the effectiveness of cure by 5.6–14.6%;

- the treatment of males with nonspecific balanoposthitis lessens the duration of the period from the beginning of treatment to recovery by 0.8–2.7 days.

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