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Scientific Article

Veterinary Medicine

Evaluation of the effect of intrauterine clindamycin and gentamicin antibiotic injection after insemination to improve fertility in cows with a history of endometritis

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Abstract: To evaluate the effect of intrauterine clindamycin and gentamicin antibiotic injection after insemination to improve fertility in cows with a history of endometritis, a total of 200 dairy cows from 4 farms were selected and used in two groups such as control and antibiotic groups. In the treatment group, a combination of clindamycin and gentamicin was injected once into the uterus 24 hours after artificial insemination. They were examined for pregnancy in a period of 120 days after insemination with antibiotics or, in case of infertility, for discharge, uterine consistency, and the effect of intrauterine antibiotic injection on subsequent inseminations. The degree of endometritis based on the severity of infection and milk production was assumed to be constant in both the Antibiotic and control groups. The fertility percentage and overall pregnancy rate, and the interval from insemination with antibiotics to pregnancy were compared in the two groups using the chi-square test and the T-test. According to the data, the overall pregnancy rate in the antibiotic-treated group 24 hours after insemination was increased and more than control group. Considering the first or numerous calving cows in both groups, the fertility rate in the multiparous calving cows with antibiotic injection was higher than the control group. Data revealed that fertility rates at the third and higher insemination periods were higher in both the antibiotic treatment and control groups. Additionally, the evaluation of the interval between days of parturition and insemination with antibiotics in the treatment and control groups showed that there were significant differences in the birth status of antibiotic-treated groups and better and natural birth status compared to the control. In conclusion, we may have demonstrated that intrauterine clindamycin and gentamicin antibiotic injection after insemination improved the fertility and overall pregnancy rate, and also natural birth status in cows with a history of endometritis.

Key words: Clindamycin, Gentamicin, Insemination, Fertility, Endometritis.

Resumo: Para avaliar o efeito da injeção intrauterina dos antibióticos clindamicina e gentamicina após a inseminação artificial na melhoria da fertilidade de vacas com histórico de endometrite, um total de 200 vacas leiteiras de 4 fazendas foram selecionadas e divididas em dois grupos: grupo controle e grupo tratado com antibiótico. No grupo tratado, uma combinação de

clindamicina e gentamicina foi injetada uma única vez no útero 24 horas após an inseminação artificial. As vacas foram examinadas quanto à prenhez em um período de 120 dias após a inseminação com antibióticos ou, em caso de infertilidade, quanto à presença de corrimento, consistência uterina e efeito da injeção intrauterina de antibiótico em inseminações subsequentes. O grau de endometrite, baseado na gravidade da infecção e na produção de leite, foi considerado constante em ambos os grupos (grupo tratado com antibiótico e grupo controle). A porcentagem de fertilidade, a taxa geral de prenhez e o intervalo entre a inseminação com antibióticos e a prenhez foram comparados entre os dois grupos utilizando os testes qui-quadrado e t de Student. De acordo com os dados, a taxa geral de prenhez no grupo tratado com antibióticos, 24 horas após a inseminação, foi maior do que no grupo controle. Considerando vacas primíparas ou multíparas em ambos os grupos, a tax on de fertilidade em vacas multíparas com injeção de antibiótico foi maior do que no grupo controle. Os dados revelaram que as taxas de fertilidade na terceira inseminação ou em períodos subsequentes foram maiores tanto no grupo tratado com antibióticos quanto no grupo controle. Além disso, an avaliação do intervalo entre os dias de parto e inseminação com antibióticos nos grupos de tratamento e controle mostrou que houve diferenças significativas no status de nascimento nos grupos tratados com antibióticos, com melhor status de parto natural em comparação ao grupo controle. Em conclusão, podemos demonstrar que an injeção intrauterina de clindamicina e gentamicina após an inseminação melhorou a fertilidade e a taxa geral de prenhez, bem como o status de parto natural em vacas com histórico de endometrite.

Palavras-chave: Clindamicina, Gentamicina, Inseminação, Fertilidade, Endometrite.

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Introduction

Endometritis is defined as an inflammatory disease that affects the endometrium, leading to the accumulation of purulent contents or sometimes just polymorphonuclear cells (Bondurant, 1999). In cows, the disease is classified as clinical endometritis or subclinical endometritis (RICHARDSON, 1993). It occurs when vaginal organisms invade the endometrial cavity during the labor process and cause infection (FARO, 2005). Clinically, endometritis occurs after calving and leads to delayed uterine involution and late return to estrus, thereby reducing conception rates and increasing the number of inseminations required. Subclinical forms of endometritis are equally negative, as they affect the service period and the viability and quality of the embryo (ARTHUR, 1989). The pathogenesis of endometritis in cows is not fully understood yet, but it is becoming increasingly clear that postpartum uterine diseases, particularly in high-producing dairy cows, are mediated by an impaired immune response, probably related to negative energy balance (AMIRIDIS et al., 2003). The main role in the etiology of endometritis in cows in the postpartum period is assigned to bacterial opportunistic microflora. In the etiology of endometritis, the basic role is played by Staphylococcus spp., Streptococcus spp., and Escherichia coli. Other bacteria can cause endometritis in cows, such as Actinomyces pyogenes, Fusobacterium necrophorum, Proteus mirabilis, Proteus vulgaris, Pseudomonas aeruginosa, Prevotella spp., and Bacteroides spp. In many cases, acute postpartum endometritis in cows is caused by the association of microorganisms, especially Escherichia coli with streptococci and staphylococci (BATEMAN et al., 2002). Some research results showed that the dominant organism linked to endometritis is Trueperella pyogenes, but cows developing endometritis may delay differentiation between the microbiome of the vagina and the uterus (BRETZLAFF, 1986). Opportunistic pathogens from the normal vaginal flora or the environment may invade the uterus from time to time (Dohmen et al., 1995). Disrupting several factors such as balance between microbes, host immunity, and other environmental or animal factors may lead to endometritis (BARRAGRY, 1994). A cow with adequate immunologic response can eliminate transient infections, but cows with inadequate immunologic status may develop chronic endometritis. Some epidemiological data indicate that the prevalence of postpartum uterine infections can occur in herds where calving hygiene,

nutritional balance, and reproductive management are suboptimal (HAJURKA et al.,2003).

Some scientific literature showed that the administration of PGF2-alpha is not effective for the treatment of clinical endometritis or subclinical endometritis in dairy cows. Many antibiotic treatment protocols have such as intrauterine application of clindamycin, gentamicin, penicillin, tetracycline, cefapirin, and systemic administration of ceftiofur been used to treat clinical endometritis (HAIMERL et al., 2016; KHAN AND KHAN, 1989). Clindamycin is a semi-synthetic derivative of lincomycin in clinical use. In veterinary medicine, it has been widely administered to dairy cattle for the prevention and treatment of mastitis (KIM AND KANG, 2003). Gentamicin belongs to aminoglycoside antibiotics and is used to treat serious bacterial infections in many different parts of the animal's body (LIVINGSTON et al., 2003). It is very effective in treating repeat breeding due to subclinical infections and has been tried in different treatment regimens by different workers (SINHA, 1994).

Some studies carried out to find out the effectiveness of low doses of gentamicin administered as intrauterine infusion for the treatment of repeat breeding in cows, and result showed that beneficial effect of single infusion with small dose of gentamicin can be attributed to elimination of sub clinical infection making the uterine environment congenial for embryonic development and establishment of pregnancy (SINHA et al., 1994). Some researchers showed that the combination of clindamycin and gentamicin would be effective in most cases of endometritis (SINGH, 1994). Until now, many methods have been used in the treatment of endometritis; in most of them, animals are inseminated in the next estrus, which causes an increase in calving to conception interval and calving to first service interval and high economic loss (KHAIR et al., 2018).

Therefore, recently, some studies administered intrauterine antibiotics after insemination to solve this problem, so the aim of this study was to determine the effect of intrauterine clindamycin and gentamicin antibiotic injection after insemination to improve fertility in cows with a history of endometritis.

Material and Methods

The current study was done in four dairy farms in Isfahan province. The experimental cows were examined approximately 30 days after calving via rectal

examination and ovaries and uterine secretions condition, the diagnosis of inflammation of the uterine horns and asymmetry between the two horns were examined, and the history of the animal in terms of the number of births, cases of retained placenta, dystocia, stillbirth, endometritis or possibly recorded estrus before this time was taken into account. Items such as uterine size, uterine wall thickness, content, and volume of uterine fluids, with the number of days since parturition, were also used to diagnose postpartum endometritis. Only healthy cows were studied, and if they had abnormal discharge, they were not selected for insemination and removed from the study. In the present study, the cows selected either had clinical endometritis after calving or were calving cows with a history of uterine infections. For choosing healthy cows, factors such as calving time, insemination time, calving status, discharge status, examination of peripartum diseases, season of the year, and the interval between calving and insemination were considered, along with antibiotics for the cows in the treatment group, and finally, 200 cows with the same characteristics were selected for the control group.

In the treatment group, a combination of clindamycin and gentamicin was injected once into the uterus after mixing with 20 ml of distilled water and reaching a certain volume and constant temperature, 24 hours after artificial insemination. In terms of the range of days from calving to insemination with antibiotics, cows in the treatment group were in the range of 50 to 345 days after calving, while this range was 50 to 275 days after calving in the control group.

Dairy cows were examined for pregnancy in a period of 120 days after insemination with antibiotics or, in case of infertility, for discharge, uterine consistency, and the effect of intrauterine antibiotic injection on subsequent inseminations. Therefore, the degree of endometritis based on the severity of infection and milk production in this study was assumed to be constant in both groups. The specific characteristics of each cow were evaluated using cattle identification cards and recorded in designed tables.

The pregnancy percentage in the first, second, and third inseminations, the overall pregnancy percentage, and the interval from insemination with antibiotics to pregnancy were compared in the two groups using the chi-square test and T-test.

Result

The effect of antibiotic injection after insemination on overall fertility and pregnancy rate is shown in Table 1.

According to the data, the overall pregnancy rate in the antibiotic-treated group 24 hours after insemination was increased and more than control group. The effect of post-inoculation antibiotic injection on fertility by the separation of the number of calving is shown in Table 2. Considering the first or numerous calving cows in both groups, the fertility rate in the multiparous calving cows with antibiotic injection was higher than the control group. The effect of post-inoculation antibiotic injection on fertility by separating inoculation times is shown in Table 3. Data revealed that fertility rates at the third and higher inseminations were higher in both the antibiotic treatment and control groups. Also, the evaluation of the interval between days of parturition and insemination with antibiotics in the treatment and control groups showed significant differences, and checking the birth status of antibiotic-treated groups showed better and natural birth status compared to the control.

Table 1. Result of antibiotic injection after insemination on overall fertility and pregnancy rate

Treatments	Number of cows	Fertility	Pregnancy rate
Control	100	25	25%
Antibiotics	100	36	36%

Table 2. The effect of post-inoculation antibiotic injection on fertility in primiparous and multiparous cows

Treatments	Primiparous	Multiparous	Fertility %	p-Value
Control	50	50	2.2^{b*}	0.001
Antibiotics	50	50	2.5^{a}	0.001

*a-b: Means within the letters have significant differences

Table 3. The interval between days of parturition and insemination with antibiotics in the treatment and control groups

Treatments	Means of the days	p-Value
Control	135	0.001
Antibiotics	162	0.001

Table 4. Calve birth status in the antibiotic treatment and control groups

Treatments	Natural	Twins	Dystocia	Incomplete birth	Placenta retain
Control	68	2	17	3	10
Antibiotics	78	6	12	1	3

Discussion

Uterine infections are one of the main causes of infertility in dairy cows and lead to less fertile cows than uninfected cows after treatment (MOHAMMED, 2024). The interval between conceptions is a valuable and more accurate criterion for confirming the adequacy of endometritis treatment, and in the present study, such a criterion and the fertility rate were considered. In the study of the interval between days of calving and insemination with antibiotics, which was significantly greater in the treatment group than in the control group, it was due to cows that had a much longer interval to calving, and these cows were generally cows with multiple pregnancies. Therefore, the passage of time can, with a small probability, increase fertility in these types of cows (MOSAFERI et al., 2013). Some researchers tested the relationship between the timing of insemination and the timing of use of antimicrobial compounds through numerous studies (HAJURKA et al., 2003, and RICHARDSON, 1993).

The Result of their study showed that cows that received intrauterine treatment 24 hours after insemination showed higher fertility rates after the first insemination than the previous two groups, and this increase in fertility rates after the second or third insemination was similar for both groups (KIM AND KANG, 2003). In another study, pregnancy rates were evaluated using intrauterine antimicrobial compounds 24 hours after insemination in cows with endometritis, and better fertility and pregnancy rates have been shown after intrauterine antimicrobial compounds. In some researchers' opinion, the reason for using antibiotic combinations 24 hours after insemination is to provide an opportunity to evaluate the ovaries for the effect of ovulation and, if ovulation does not occur, to re-inseminate, which improves fertility efficiency (KHAIR et al., 2018).

The result of the current study showed that this treatment had no significant effect on pregnancy rates in primiparous cows, but improved fertility in multiparous

cows compared to the control group.

It appears that younger cows are more successful in resolving uterine infections than older ones.

Results showed that antibiotic application was not effective or had very little effect after the first insemination but had a significant effect in the second and subsequent inseminations. The comparison of the treatment and control groups suggests that uterine infections may still play a role in preventing fertility in the short period after delivery until the first insemination, but other issues still affect fertility (OXENDER and SEGUIN, 1979).

The effectiveness of the low dose of gentamicin when administered locally can be attributed to the attainment of adequate bactericidal concentration inside the uterine lumen. Instead, systemic administration necessitates a very high dose for attainment of the same bactericidal concentration inside the uterus (SINHA et al., 1994).

Mosaferi et al (2013) showed that considering the insignificant differences between treatment and control groups in the case of conception rate and the decrement in interval between calving and the time of first insemination in the treatment group and they suggested the application of an antibiotic 24 hours after artificial insemination in cows with endometritis. Other researchers concluded that there was no advantage relative to the control on the first service conception rate (AMIRIDIS et al. 2003)

Conclusion

In conclusion, we may have demonstrated that intrauterine clindamycin and gentamicin antibiotic injection after insemination improved the fertility and overall pregnancy rate, and the natural birth status in cows with a history of endometritis.

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