ORIGINAL ARTICLE

Bali Medical Journal (*Bali Med J*) 2017, Volume 6, Number 2: 345-348
P-ISSN.2089-1180, E-ISSN.2302-2914

Published by DiscoverSys

Studying uterogin drug effectiveness for acute experimental endometritis in rats

Faina V. Shakirova,* Olga A. Gracheva, Ilsur G. Galimzyanov, Anastasia N. Valeeva, Olga I. Shorkina, Dina M. Mukhutdinova, Zulfiya M. Zukhrabova

ABSTRACT

It is known that acute endometritis is accompanied by endogenous intoxication, which has a strong negative impact on the functional condition of vital organs and systems. The ability of drugs used for the treatment of endometritis to prevent the development of the inflammatory process, to reduce the degree of endogenous intoxication, and to promote the rapid normalization of the clinical status of animals is a valuable property when practicing pharmacotherapy of uterus inflammatory diseases. The aim of this study was to investigate the pharmacological activity of Uterogin drug as a therapeutic agent when used in the acute phase of the inflammatory process of reproductive system organs, and in particular, in experimental endometritis in rats. It has been established that formalin introduction into the cavity of uterine horns can simulate an acute form of endometritis. The development of experimental endometritis occurs in the background of the overall endogenous intoxication and is accompanied by a change in a number of general clinical indicators, namely suppression, decreased motor activity, disruption of the gastrointestinal tract function, increased erythrocyte sedimentation rate, decreased hemoglobin level, decreased red blood cell count, and an increase in the number of microxyphil neutrophils. The subcutaneous introduction of Uterogin in acute experimental endometritis in rats significantly reduces the inflammatory response, limits the spread of inflammation, and prevents the development of destructive and necrotic processes. The recovery of motor activity of animals is accelerated, and their clinical status is normalized. Changes in blood are less pronounced in animals to which Uterogin drug was applied twice. The anatomic and echographic studies confirm a pronounced therapeutic effect of the drug in question for acute endometritis in rats. We can draw a conclusion about the possibility of using Uterogin for clinically ill animals on the basis of the data obtained.

Keywords: rat, acute endometritis, Uterogin, treatment, efficiency
Cite This Article: Shakirova, F.V., Gracheva, O.A., Galimzyanov, I.G., Valeeva, A.N., Shorkina, O.I., Mukhutdinova, D.M., Zukhrabova, Z.M. 2017. Studying uterogin drug effectiveness for acute experimental endometritis in rats. *Bali Medical Journal* 6(2): 345-348. DOI:10.15562/bmj.v6i2.519

Faculty of Veterinary Medicine, Kazan Bauman State Academy of Veterinary Medicine, Sybirsky Tract Street 35, Kazan City, 420029, Russia

INTRODUCTION

Reproductive system diseases of small animals account for 12–20% of the total number of cases.[1] Endometritis is one of the most common obstetrical and gynecological diseases in animals. High frequency, recurrences, diagnosis and treatment difficulties, high mortality in case of a severe endometritis, and numerous complications cause urgency of this problem in modern veterinary medicine.[2–4]

To date, a sufficient number of endometritis treatment and prevention regimens have been developed; however, issues with the use of non-drug therapies have not been studied sufficiently and point to the urgency of finding new, effective, and safe medicines. Great opportunities for this are provided by homeopathy.[5–8] This was the basis to study a new drug called Uterogin and to conduct researches on the evaluation of its activities in the framework of pre-clinical trials in acute endometritis.

MATERIALS AND METHODS

The study analyzed Uterogin drug, which is an integrated homeopathic drug in a dosage form of a «solution for injection» and is a colorless transparent liquid. The composition of Uterogin includes vegetable and mineral components (per 1000 ml): Atropabelladonna 0.2 ml; Cimicifuga racemose 45 µl; Echinacea purpura 45 µl; Hamamelis virginian 0.45 µl; Matricariarecutita 30 µl; Secalecornutum 0.1 µl; HeparsulfurD4 trit. 1 g; CalciumcarbonicumHahn. Trit.D4 1.5 µg; sodium chloride 9 g; and water for injection up to 1000 ml.

Experimental studies were carried out on clinically healthy, adult, white mongrel rats with an initial body weight of 230–250 g, which were then divided into three groups: Group 1—control animals (6): they were administered physiological saline subcutaneously at a dose of 0.2 ml once a day; Group 2—the first experimental group (6): Uterogin drug was subcutaneously administered at the dose of 0.2 ml once a day; Group 3—the second experimental group (6): they were subcutaneously administered Uterogin drug at the dose of 0.2 ml 2 times per day for 7 days after administering formalin.

An experimental model of acute endometritis was reproduced by administering 0.2 ml of 2% formalin aqueous solution[9] under ether inhalation

*Correspondence to: Faina V. Shakirova, Faculty of Veterinary Medicine, Kazan Bauman State Academy of Veterinary Medicine, Sybirsky Tract Street 35, Kazan City, 420029, Russia
trubba26@mail.ru

Received: 2017-03-04
Accepted: 2017-04-30
Published: 2017-05-1

anesthesia.[10] Formalin was injected through a urethral catheter with the mandrin into the cavity of the uterus horn under ultrasound monitoring. On the next day after the introduction of formalin (the initiation of a pathological process), the administration of the drug was started.

Every day, during a period of 8 days, thermometry was carried out, as well as the examination of the general condition of the animals, paying attention to the preservation of the food excitability, separation of feces and urine, and the nature of secretions from the genitals.

The registration of body weight was conducted before the start of the experiment and before withdrawing the animal from the experiment.

Taking blood was performed before the start of the experiment, on the third and the eighth day after formalin administration. The erythrocyte sedimentation rate (ESR), hemoglobin concentration, erythrocytes and leukocytes count, and leucocytes morphological composition were determined by the universally accepted technique.[11]

Ultrasonography (US) was performed with an ultrasound scanner Ultrascan PY 2200 equipped with a dual-frequency sector sensor with scanning frequencies of 5 and 7.5 MHz.[12] The ultrasonographic examination determined the dorsal-ventral size (diameter) of the uterine horns,[13,14] the state of its cavity, the echogenicity and echostructure of its walls[15] in healthy animals, as well as the horns under study and intact ones on the third and the eighth days of the experiment.

A postmortem examination was conducted on animals euthanized on the third and the eighth days of the experiment. Morphological changes were studied in an isolated organ complex of a reproductive system in 2 healthy rats and 18 rats after they received an inflammation model in the process of conservative treatment.

The weighting factor was determined by the ratio of the weight of the organ (the uterus) to the weight of the animal's body in grams.

For a histological research longitudinal and transverse histological sections of the organ 5–7 microns thick were made, which were then stained with hematoxylin and eosin and also by van Gieson.

A statistical analysis of the data was performed using SPSS v.13 package.

RESULTS AND DISCUSSION

At a clinical examination on the first day after the introduction of formalin the animals of all three groups demonstrated the following signs: the general condition was somewhat depressed, the motor activity was decreased, and the food anxiety was normal. Only one rat had hemorrhagic excretions from the external genitalia in volume 0.1–0.2 ml.

On the second day, the rats of all the three groups demonstrated identical signs, which were accompanied by pronounced depression, a decrease in the motor activity (the animals were mainly lying), and the food anxiety was normal. Visible vaginal secretions were absent.

On the third day, the general condition of the experimental animals was satisfactory, and the food excitability was expressed. Group 3 animals exhibited improved motor activity. The animals of Groups 1 and 2 showed liquefaction of feces.

By the fourth day in all of the animals groups, the motor activity was recovered. Rats of Group 3 were the most active. The general condition of the animals was satisfactory. However, rats of Group 1 still demonstrated a slight depression, and liquefaction of feces remained; food excitability was found in all of the animals preserved.

By the fifth day and further on, before the withdrawal of animals from the experiment (the eighth day), the general condition of animals of all the groups was satisfactory and clinical manifestations of the disease were absent.

Thus, the data of the clinical observations evidence that the animals of the third group were restored to their general condition and their level of motor activity got quicker.

The temperature indicator in healthy animals before the introduction of formalin into the uterine cavity averaged 38.5–39°C. The dynamics of fluctuations in this indicator during the experiment corresponded to physiological norms for this type of animals.

Analyzing the results obtained from the hematological studies we can conclude that the nature of changes in hemoglobin concentration, quantitative indicators of leukocytes, erythrocytes, and formed elements of leukocytes in the control group and two experimental ones are similar. However, an insignificant increase in leukocyte number, segmentonuclear neutrophils, is probably related to the more pronounced toxic effect of the pathological process on the body. The course of the disease is accompanied by a shift of the leukocyte formula to the left in the animals of Groups 1 and 2, which is typical of an acute inflammatory process. The eosinophilia in the animals of Group 1 indicates some degree of sensibilization of the body. It should be noted that all these changes are only slightly higher than the permissible accepted physiological norms.

The ultrasonography showed that the pathology of rats of all the three groups was accompanied by an increase in the diameter of the uterine body and its horns (Table 1).

Table 1 The diameter change dynamics in the US-studied horn

Rat groups	Before formalin introduction	On the third day	On the eighth day
1	2.26 ± 0.20	3.61 ± 0.22	3.00 ± 0.43
2	2.30 ± 0.20	3.61 ± 0.16	3.45 ± 0.41
3	2.14 ± 0.25	3.6 ± 0.09	2.93 ± 0.26

Table 2 The ratio of rat body weight and the uterus weight

Rat groups	On the third day	On the eighth day
1	0.59	0.58
2	0.57	0.55
3	0.65	0.46

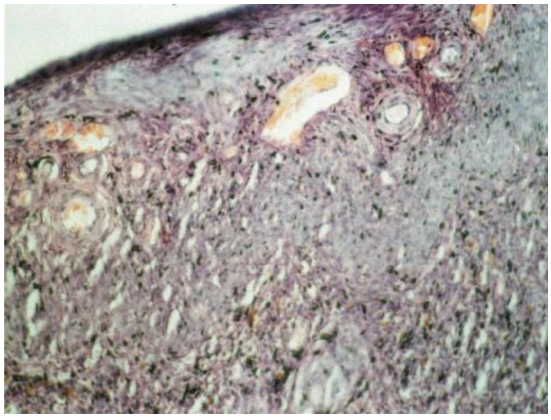

Figure 1 Endometrium lumen and vessels expansion. Stain with hematoxylin and eosin × 200

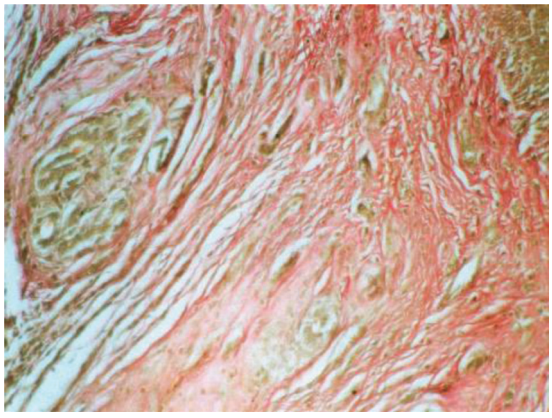

Figure 2 Interstitial edema in the myometrium. Van Gieson stain × 200

As a result of the research conducted we discovered that irrespective of the pathological condition of the reproductive system, its differentiation in anatomic sections is well expressed: the cervix, the body, and the horns. The pathologically changed uterine horn was macroscopically characterized by an increase in the length and diameter, pronounced vascular pattern, the expansion of the cavity, and the accumulation of mucous and hemorrhagic exudate in there.

The ratio of the animal's body weight to the weight of the extracted organ in the comparison of all the three groups allows us to conclude that the lowest uterine weight was in the third group of rats (Table 2).

Histologically, inflammatory response developed in the uterine horns, which were administered with formalin, with varying severity. The inflammation in many cases grasped not only endometrium but also the muscular layer (metroendometritis). Some observations showed all layers of the uterus were totally affected by the involvement of its body and the parametrium and the presence of leukocytes in the lumen of a uterine horn (Fig.1, Fig.2).

Inflammatory infiltrates of focal or diffuse nature were represented mainly by neutrophils with an admixture of lymphocytes, macrophages, individual eosinophils, and plasma cells. Sometimes we encountered microabscesses as well as more extensive leukocyte and necrotic aggregates with tissue melted.

In rats treated with Uterogin, the intensity of the inflammatory response from the uterus part was significantly lower. There were virtually no cases of diffuse inflammatory infiltration, and separate clusters of cells were kept in the endometrium around the vessels and the submucosal layer. There was a redistribution of the inflammatory infiltrate composition toward macrophages and lymphocytes with neutrophils decrease. The inflammation was most often limited to the endometrium, without involving the muscle layer. The endometrial and glandular epithelium were in the state of a moderate hyperplasia without affecting the normal histological structure.

We were unable to identify any differences in the uterine response to single or double administration of Uterogin. Reactive changes in the two groups were similar, and the level of reduction of the inflammatory process was practically similar.

CONCLUSION

The introduction of formalin into the cavity of the uterine horns can simulate an acute inflammatory reaction from endometritis up to the total destruction of all the layers, involving the surrounding tissue (pelvic cellulitis). The application of Uterogin is highly efficient in the early stages of the inflammatory process in animal reproductive organs system. It significantly reduces the inflammatory response, restricts the spread of inflammation beyond the mucosa, and prevents the development of destructive and necrotic processes. The drug has a pronounced stimulatory action on smooth muscles.

Uterogin has no effect on the overall condition of the animal; it does not cause significant changes in blood morphological composition.

Based on the obtained data of the drug-specific activity we can draw a conclusion about the possibility of Uterogin application for clinically sick animals.

REFERENCES

1. Shafikova A.V. (2006) The etiology, diagnosis, and treatment of endometritis in dogs. thesis abstract.
2. Jones D.E. (1984) Reproductive clinical problems in the dog. London. Wright.
3. McEntee K. (1990) Reproductive pathology of domestic animals. California. Academic Press.
4. Chandler E.A. (1995) Canine Medicine and Therapeutics. London. Blackwell Science Ltd.
5. Rogers A. (1992) Europe: Homeopathic medicine. Lancet. 340: 167-168.
6. Lokken P. (1995) Effect of homeopathy on pain and other events after acute trauma: placebo controlled trial with bilateral oral surgery. BMJ. 310: 1439-1442.
7. Kikos J. (1999) Homeopathy and Community Nursing. Aust. Nurs. 6: 33.
8. Foxman E. (1999) Homeopathy Better Nutrition. Aust. Nurs. 12: 44-47.
9. Botoeva E.A. (2011) Pharmacotherapy experimental endometritis of vegetable origin. Bulletin of Medical Sciences 1: 247-248.
10. Hilbery A.D. (1989) Manual of Anaesthesia for Small Animal Practice. London. BS AVA.
11. Kondrahin I.P. (1985) Clinical laboratory diagnostics in veterinary medicine. Moscow. Agropromizdat.
12. Plambeck K. (2004) Practical Musculoskeletal Ultrasound. Elsevier Science 23: 350-354.
13. Gallarbo E., Barder I., Serrano A. (2001) Correlation between high-resolution ultrasound and microscopic anatomy in the evaluation of the biceps tendon disorders. European Congress of radiology 11: 210.
14. Bartel-Friedrich S., Friedrich R.E., Plambeck K. (1996) B-scan ultrasonography for diagnosis of midfacial fractures. European Radiology 4: 567.
15. Meuwly J., Rossier P., Schnyder P. High-resolution sonography of small parts: evaluation of real-time compound imaging. European Congress of radiology.