

**Application Of The Sildenafil Citrate As Intravaginal Suspension
In Treatment Of The Dairy Buffalo-Cows, Suffering
From Inactive Ovaries**

Barakat, T.M.;

Dept. Theriogenology Vet. Med. Zagazig University

ABSTRACT

Ten dairy buffalo-cows which were 4 to 7 years old and gave births 1-3 times, were investigated during the period from January to March 2003, the animals belonged to private farm in Dakahlia Province. The animals gave normal births and puerperial period but suffered from anestrus for more than 8 months after delivery. Gynecological examination showed smooth inactive ovaries without any lesions in the tubular genitalia. The animals were divided into two equal groups. Each animal (gp,1) was given 400 mg. sildenafil citrate intravaginally suspension in 20 ml. distilled water. Gp, (2) each animal was given 20ml. distilled water intravaginally (control).

Gp,(1) returned to heat 10 days after treatment. Three buffalo-cows ultimately became pregnant from the 1st service and the other two buffalo-cows came in cycle and conceived from the 2nd service. While, the animals in the control group remain anestrus during the course of the experiment.

It could be concluded that the sildenafil citrate could be used intravaginally for the treatment of the buffalo-cow suffering from inactive ovaries.

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INTRODUCTION

Sildenafil citrate is a pyrazolopyrimidine which is a potent and selective inhibitor of 3, 5, phosphodiesterase. Phosphodiesterase (PDE) is a family of isoenzymes that hydrolyse adenosine cyclic monophosphate (cAMP) and guanosine cyclic monophosphate (cGMP). Specific inhibitors of PDE subtypes have been identified that can augment the effect of cyclic nucleotides on target tissue, such as spermatozoa (*Fisch, 1*). Sildenafil citrate is a newly developed type 3, 5, specific PDE inhibitor that prevents the break down of cAMP, cGMP and potentiates the effects of the nitric oxide (NO.) (*Amit, 2*) In the past few years, much interest has been focused on the role of NO as a modulator of uterine blood flow, (*Cameron, 3*). The NO release leads to the relaxation of the vascular smooth muscle through a cGMP mediated pathway (*Bailard, 4*). Inducible NO synthase isoforms have also

been identified in the vascular endothelium of human endometrium and myometrium (*Telfer, 5*). Sildenafil increased the genital blood flow and vaginal lubrication besides the intravaginal pre-and post-sexual stimulation in women (*Berman, 6*). Sildenafil citrate was shown to improve significantly both the subjective and physiologic parameters of the female sexual response (*Perelman, 7*).

The aim of this work was to try the sildenafil citrate, as a vaginal suspension, to treat the dairy buffalo-cows suffering from inactive ovaries.

MATERIAL AND METHODS

This investigation was carried out on 322 buffalo-cows which were 4 to 7 years old, and gave births 1-3 times. The animals were raised at a private farm in Dakahlia province. The study was undertaken during the period from January to March 2003. The farm was

investigated and proved to be free from brucellosis and tuberculosis at the time of the investigation as revealed by the serum agglutination and tuberculin test, periodically done by the veterinary authorities of the province. The buffalo-cows were stabled in free system within yards. Each buffalo cow was daily offered the following ration (5kg. Concentrates, 5 kg rice straw and 25 kg . Barseem during winter and 5 kg. Concentrates, 5 kg rice straw and 5kg drees during summer). These animals were naturally bred by the clinically normal and sexually proven fertile bulls. The herd was recorded average 3.18% (10/322) suffering from anestrus for 8 months from the delivery time. The course of parturition and the puerperial period of the anestrus buffalo-cows were apparently normal.

Gynecological examination of the anestrus buffalo-cows revealed smooth inactive ovaries without lesions in the tubular genitalia. The ten buffalo-cows were allotted into two equal groups. Each buffalo-cow (Gp,1) was received 400 mg. Sildenafil suspension in 20 ml. distilled water intravaginally. Gp(2), was similarly given 20 ml. distilled water intravaginally (control). These animals were observed and that showed signs of estrus was normal bred by proven fertile bull. Pregnancy diagnosis was done rectally two month later. Sildenafil suspension was prepared from the oral tablets (viagra) (Pfizer, inc., Cairo, Egypt).

RESULTS

Gp,(1) came to heat 10 days after treatment. Three buffalo cows ultimately conceived and pregnant from the 1st service and the other two buffalo cows came in cycle and conceived from the 2nd service.

Gp,(2) remained in the anestrus.

DISCUSSION

The animals with inactive ovaries of gp.(1) came in heat 10 days after the end of treatment. Three buffalo-cows ultimately

became pregnant from the 1st service and the other two buffalo cows came to estrus in the 2nd cycle and conceived. The sildenafil acted in two pathways. The 1st pathway could be attributed to the potent and selective inhibition of type 5-specific PDE inhibitor that prevents the breakdown of cGMP and potentiates the effects of the NO (Amit, 2). The nitric oxide is a mediator of uterine blood flow (Cameron,3). A definite improvement in the uterine blood flow and endometrial development were reported by Sher,(8). The 2nd pathway is through the gonadotropins, (follicular stimulating hormone and luteinizing hormone) which primarily utilize the cyclic adenosine 3, 5 monophosphate (cAMP) pathway to stimulate steroid hormone biosynthesis. It is generally established that the gonadotropins stimulate ovarian steroidogenesis via a cAMP mediated mechanism (Peter, 9).

It could be concluded that the intravaginal suspension of the sildenafil citrate can be used in the treatment of the inactive ovaries in the dairy buffalo-cows. However, before recommending its wide application, it should be evaluated in a randomized manner and we are in need for further investigation

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الملخص العربي

استخدام عقار سترات السيلدانا فيل عن طريق المهبل لعلاج الجاموس الحلاب

الذي يعاني من خمول المبايض

توفيق بركات

قسم التوليد والتاسل والتلقيح الاصطناعي - كلية الطب البيطري - جامعة الزقازيق

أجريت هذه الدراسة على ١٠ جاموسات حلابة تعاني من الخمول الجنسي لمدة ٨ أشهر بعد الولادة الطبيعية من المدة يناير الى مارس ٢٠٠٣م، تراوحت أعمارها ما بين ٤ إلى ٧ سنوات وعدد الولادات ١-٣ ولاده. في مزرعة خاصة في محافظة الدقهلية. قسمت الحيوانات الى مجموعتين المجموعة الأولى (خمس جاموسات) تلقت كل واحدة منها عقار السيلدانا فيل مستحلب في ٢٠ سم مياه مقطرة أدخلت عن طريق المهبل. والمجموعة الثانية خمس جاموسات (كمجموعة ضابطة) تلقت كل واحدة منها ٢٠ سم مياه مقطرة عن طريق المهبل.

واظهرت النتائج أن الحيوانات في المجموعة الأولى قد شاعت بعد عشرة ايام من العلاج وتم تلقيحها طبيعيا وعشرت ثلاثة منها من التلقيح الاولي. والاثان الآخران عادت إلى الشيوخ في الدورة الثانية وعشرت من التلقيح الثانية. أما المجموعة الثانية التي تركت (كضابطة) فلم تظهر الشيوخ واستمرت لمدة شهرين بعد تلقي المياه المقطرة.

ولذلك من الممكن استخدام عقار السيلدانا فيل لعلاج الحالات التي تعاني من خمول المبايض في الجاموس الحلاب.