Effect of Ivermectin on semen characteristics of Iraqi Awassi ram U. D. Naoman College of Veterinary Medicine\ University of Mosul

Abstract

The objective of this study was evaluation the effect of ivermcetin on semen quality and serum testosterone levels of Iraqi Awassi ram. Ten mature Awassi rams (aged 2.5-4 years and weighing 37-44 \pm 0.3 kg) were used in this study. Rams were divided randomly into 2 groups each group contain 5 animals; the first one consider as treatment which was sub cautiously injected with ivermcetin at dose 0.2 mg/ kg bw, the second group left as control group injected with physiological normal saline. Semen samples collected by using artificial vagina at 1 day prior to ivermcetin injection and after 1, 3, 5, 7, 14 days following semen volume, mass motility, individual motility, sperms concentration, percentage of live sperm, percentage of abnormal sperms and blood samples were taken for estimated serum testosterone levels at each times of collection. Result of this study shows significantly (P<0.05) decrease in semen volume, sperm concentration and serum testosterone levels of treatment group while percentage of mass and individual motility show no insignificantly differences after 3 days following ivermcetin injection and Sperm abnormalities increase significantly (P<0.05) in treatment group comparing with the control group. After 5 days following ivermcetin injection, Semen parameters and serum testosterone levels demonstrate no significant differences between control and treatment groups. It could be concluded it's not prefer be use animals for breeding at least 5 days following the ivermcetin injection due to its harmful effect on semen quality and serum testosterone level.

تأثير عقار الايفرمكتين على صفات السائل المنوي للكباش العواسية العراقية عدي طلعت نعمان كلية الطب البيطري/ جامعة الموصل الخلاصة

أجريت الدراسة الحالية لغرض معرفة تأثير عقار الايفرمكتين على صفات السائل المنوي ومستوى هرمون التستيرون في الدم. عشرة أكباش عواسية بالغة (تراوحت أعمارها مابين 2.5 – 4 سنة وأوزانها مـابين 37-44± . 0 كغم) استخدمت في هذه الدراسة، قسمت عشوائيا إلى مجموعتين بواقع 5 حيوانات لكل مجموعة، اعتبرت الأولى مجموعة المعاملة وحقنت بعقار الايفرمكتين تحت الجلد بجرعة 2.0 ملغ/كغم من وزن الجسم بينما اعتبرت المجموعة المعاملة وحقنت بعقار الايفرمكتين تحت الجلد بجرعة 2.0 ملغ/كغم من وزن الجسم بينما اعتبرت المجموعة الثانية كمجموعة سيطرة وحقنت بمحلول الملح الفسيولوجي. جمع السائل المنوي مـن الحيوانات بطريقة المهبل الاصطناعي قبل حقن الايفرمكتين بيوم ثم جمع بعـد 1، 3، 5، 7، 14 يـوم تلـت عملية الحقن، قيمت صفات السائل المنوي الحجم، الحركة الجماعية، الحركة الفردية، نسـبة الحيـامن الحيـة، تركيز الحيامن، نسبة الحيامن المشوهة وتم جمع عينات الدم لغرض قياس تركيز هرمون التستيرون في الدم في تركيز الحيامن نسبة الحيامن المشوهة وتم جمع عينات الدم لغرض قياس تركيز هرمون التستيرون في الدم في تركيز الحيامن وانخات جمع السائل المنوي. أظهرت نتائج الدراسة انخفاضا معنويا (200<) لصـفات الحجم، تركيز الحيامن وانخفاض مستوى هرمون التستيرون في الدم بينما لوحظ انخفاضا غير معنوي في نسبة الحركة عد تركيز الحيامن وانخفاض مستوى هرمون التستيرون في الدم بينما لوحظ انخفاضا غير معنوي في نسبة الحركة عرين المائيل المنوي ومستوى هرمون التستيرون في الدم بينما لوحظ انخفاضا غير معنوي في نسبة الحركة ماجماعية والحركة الفردية، ازدادت نسبة الحيامن المشوهة في مجموعتين الموط انخفاضا غير معنوي في نسبة الحركة عن الإيفرمكتين لمجموعة المعاملة. بعد 5 أيام من حقن الايفرمكتين، لم يلاحظ وجود فروقـات معنويـة فـي صفات السائل المنوي ومستوى هرمون التستيرون مابين مجموعتي المعاملة والسيطرة. يمكن الاستناج انفرين عير المفضل استخدام الحيوانات لغرض التستيرون البين مجموعتي المعاملة والمورة. ومناوي المنتنجاج انه من عبر المفضل استخدام الحيوانات لغرض التناسي الا بعد 5 أيام على الأقل من استخدام الإيفرمكتين بسبب تأثيره

Introduction

Awassi sheep are one of the most economically important skin, milk and meatbreed of sheep reared in Iraq (1). The reproductive activity of the ram appears to be influenced, in certain breeds and regions, by the season of the year (2) with photoperiod being the key environmental signal timing the reproductive cycle (3,4). ivermcetin is abroad spectrum anti-parasitic agent belonging to the avermactine family, It is highly acceptable anti-nematode and ecto-parasite drug because of its broad range of activity and widely rage of safety (5). The veterinarian are use ivermcetin as a routine treatment against nematode and ecto-parasite before and within the breeding seasons of Awassi sheep which start in Iraq from June(Summer) until terminate in November (Autumn) (1), this period is represent period of some parasitic invasion (7). Previous studies were refers to deleterious effect of ivermectin on semen characteristics and hyaluronidase enzyme in ram (10,11), buck (12). Other report refers to no action of ivermectin on semen quality or animal sexual desire (13). Other studies (14),(15) were reported the improvement of semen quality after long term effect of ivermcetin in stallions. The objective of this study was evaluation the effect of ivermcetin on semen quality and serum testosterone levels of Iraqi Awassi ram.

Material and Methods

Ten mature Iraqi Awassi ram aged between 2.5-4 years, weighting 37-44±0.3 Kg were used in this study, animals were housed in the animal house, Collage of Veterinary Medicine, University of Mosul. This study was carried out from 1-6-2011 to 15-6-2011. Rams were divided randomly into 2 groups each group contain 5 animals; the first one consider as treatment which was sub cautiously injected with ivermcetin¹ at dose 0.2 mg/ kg bw, the second group left as control group injected with physiological normal saline. Semen samples collected by using artificial vagina at 1 day prior to ivermcetin injection and after 1, 3, 5, 7, 14 days following semen volume, light microscope was used to evaluated mass motility, individual motility, percentage of live sperm, percentage of abnormal sperms (18). Sperms concentration calculated by using spectrophotometer (2), and blood samples were taken for estimated serum testosterone levels at each times of collection. Serum testosterone levels were determined in lap by using ELISA TEST (Enzyme linked immuno sorbent assay) (Hollandsr. 17, D-53881 Euskirchen, Germany) (13). Statistical analysis: the results were expressed as means \pm SE data analyzed statistically using one way analysis of variance Data were analyzed using Simastat (Jandel Scientific Softwaer V3.1) and tested by using Duncan's multiple rang test to show differences between groups and the differences within groups and (P<0.05) was consider as statistically significant.

Results

Effect of ivermcetin on semen parameters and serum testosterone levels in both treatment and control groups were summarized in Table 1. Ejaculated semen volume in treated group were show significantly decrease (P<0.05) after 3 days followed ivermcetin injection in comparing either with control group or its levels before injection, at the end of study (14 days) there were significant increase of semen volume in both treatment and control groups (1.44 ± 0.8 , 1.42 ± 0.8 respectively) in comparing with its parameters in same groups (treatment and control groups) before the injection (1.27 ± 0.1 , 1.2 ± 0.6 respectively). There is no significant changes in semen mass motility and semen individual motility during the studies between treated or control groups. Sperm concentration show significant decrease in treated group after 3 days followed ivermcetin injection in comparing with its mean in both control or treatment

¹(IVERMECTIN (%1), production of Saudi Pharmaceutical industries, Riyadh- KSA (SPI))

group, sperm concentration in both treatment and control groups show highly significant (p<0.05) increase after 14 days of study. The percentage of live sperm show no significant changes. Percentage of morphologically abnormal sperms show significant (p<0.05) decrease after 5 days followed ivermcetin injection in treatment group $(8.8 \pm 0.5)\%$ in comparing with its values in same group or with in control group $(3.8\pm0.1)\%$. Testosterone level show sharply significant (p<0.05) decrease $(0.31 \pm 3.5 \text{ ng/ml})$ after 3 days.

Semen attributes	Groups	Days of semen collection					
		-1	1	3	5	7	14
Volume (ml)	Treatment	A,a	B,b	B,b	A,a	A,a	C,b
		1.27±0.1	1.12 ± 0.1	1.12±0.7	1.24±0.1	1.38 ± 0.1	$1.44{\pm}0.8$
	Control	A,a	A,a	A,a	A,a	A,a	A,a
		1.2±0.6	1.25 ± 0.1	1.22±0.8	1.26±0.5	1.30±0.2	1.42 ± 0.8
Mass motility (%)	Treatment	A,a	A,a	A,a	A,a	A,a	A,a
		89.0±1.8	84.0±1.0	89.0±1.0	91.0±1.0	89.0±3.5	91.0±2.2
	Control	A,a	A,a	A,a	A,a	A,a	A,a
		89.0±0.7	90.6±1.5	90.2±1.2	90.0±1.0	90.0±3.5	90.0±0.1
Individual motility (%)	Treatment	A,a	A,a	A,a	A,a	A,a	A,a
		90.0±0.1	90.0±0.1	86.6±0.8	87.6±1.2	88.6±2.1	88.0±03.6
	Control	A,a	A,a	A,a	A,a	A,a	A,a
		88.0±0.9	88.0±1.0	89.0±1.0	98.0±1.0	89.1±6.1	89.0±01
Sperms concentration (×10 ⁹)	Treatment	A,a	A,a	B,b	A,a	A,a	C,a
		1.83±0.3	1.75 ± 0.4	1.69 ± 0.8	1.80 ± 0.3	1.81±0.7	2.02±0.1
	Control	A,a	A,a	A,a	A,a	A,a	B,a
		1.79±0.2	1.82 ± 0.6	1.81±0.1	1.83 ± 0.7	1.91±0.4	1.97±0.9
Live sperms (%)	Treatment	A,a	A,a	A,a	A,a	A,a	A,a
		85.8±1.5	86.6±0.6	80.6±0.1	90.6±1.4	91.0±0.4	92.6±1.2
	Control	A,a	A,a	A,a	A,a	A,a	A,a
		887.6±1.0	87.2±0.2	88.2±3.5	88.2±1.4	88.9±1.4	90.8±0.8
Abnormal sperms (%)	Treatment	A,a	A,a	B,b	A,a	A,a	A,a
		3.2±0.7	4.1±0.4	8.8±0.5	4.4±0.6	4.0 ± 0.4	3.6±0.7
	Control	A,a	A,a	A,a	A,a	A,a	A,a
		3.8±0.1	4.2 ± 0.2	3.8±0.1	3.9±1.1	4.1±0.4	3.3±2.4
Testosterone levels (ng)	Treatment	A,a	A,a	B,b	A,a	A,a	A,a
		0.43±0.1	0.37 ± 0.2	0.31±3.5	0.41±2.5	0.42 ± 3.1	0.45±0.9
	Control	A,a	A,a	A,a	A,a	A,a	A,a
		0.39 ± 2.1	0.39 ± 2.1	0.38±3.7	0.40 ± 2.5	$0.44{\pm}2.0$	0.43±1.0

Table (1) Effect ivermcetin on Iraqi Awassi semen parameters and serun	n							
testosterone levels before and after injection								

A, B Different letters within same rows means significantly different at (P<0.05).

a, b Different letters within same columns for each properties means significantly different at (P<0.05).

Discussion

The current findings in this study showed that all semen parameters and testosterone levels show a dramatic changes represented by sharp decrease after 3 days followed ivermcetin injection, but its return to its values after 7 days followed the injection. The significant (P<0.05) decrease in volume of semen observed in the ivermcetin treated group is in agreement with a similar study on rams which reported that ivermcetin caused significant decrease in semen volume (12), the decrease of semen volume may be due to effect of the drug on animal sexual behavior, ivermcetin is irritant subcutaneous drug and cause pain to animal at site of injection (5), (8) pain may be leading to produce short ram amounting time until ejaculation, with a low semen volume, another causes of this state is diminish of testosterone level (which also recorded in this study) may lead to decrease production of accessory sex gland which responsible for formation 70% of semen volume (19), another explaining of these case is that related to action paralytic of ivermcetin action on parasite muscles, ivermcetin

may be make animal undergo in same effect (16), leading to decrease sperm volume and sexual desire which effected by reaction time and number of animal amount during semen collection (21). Other study (9) reported that the levels of semen volume increased significantly after 73 hours followed the treatment, and then sharp decrease of semen volume after 120 hours following ivermcetin injection, these data disagreement with this study, the discrepancy may be due to breed variation of animals and differences of semen collection time which play important role for determine semen volume (22). Semen mass motility and individual motility decrease after 3 days followed ivermcetin injection, but it's not significant when comparing with control groups, these data agreement with other reports study effect of ivermcetin effect on semen motility (10), (12), sperm movement did not effected by action of ivermcetin, this may due to sperms protection by blood testes barrier which prevent entrance of any foreign chemical material in to site of spermatogenesis (14). A decrease in sperm concentration, serum testosterone levels and increase sperm abnormalities were observed in the ivermeetin treated groups, the results of this study is in agreement with the findings of other studies (10), indicating that low levels of testosterone was always associated with low values of semen characteristics (17). In a similar study with ivermcetin (12), reported decrease of testosterone level with Spermatogenesis stimulating hormone SSH after ivermcetin treatment, the lack of these hormones leading to deleterious effect in semen values in sheep, SSH is known to increase the yield of spermatogonia by preventing atrasia of differentiating type of spermatogonia and increase the level of the androgen binding protein production by sertoli cells, Therefore, lack of SSH which leading to the decreased sperm concentration and lack of active testosterone so increase sperm abnormalities (10), (12), these explanations are explain the effect of ivermcetin on testosterone and FSH levels but do not explain the effect on spermatogenesis which needs about 60 days to full complete and need continues injection of ivermcetin to see if there is any affected sperms, however ivermcetin may be effected substance interfere with spermatogenesis like testosterone or accessory sex glands. Low levels of sperms concentration and increase abnormal sperms after ivermcetin injection may due to effected muscle fiber in whole male reproduction system leading to decrease of total force of ejaculation or muscle paralysis in same manner that ivermcetin effected parasite muscle (8). In another studies in the stallions Janett et al., 2001 (14) finding that long term effect of ivermcetin leading to improve semen quality and quantities, these reports disagreement with data of this study, this may be due to be attributed to the species variation of animals. In conclusion, it's not prefer be use animals for breeding at least 5 days following the ivermcetin injection due to its harmful effect on semen quality and serum testosterone level.

References

- 1. Azawi, O. I. & Ismaeel, M. A. 2012. Effect of seasons on some semen parameters and bacterial contamination of Awassi ram semen. Reprod. Dom. Anim., 47: 403-406.
- Karagiannidis, A.; Varsakeli, S.; Alexopoulos, C. & Amarantidid, I. 2000. Seasonal variation in semen characteristics of Chios and Friesian rams in Greece. Small Rumin. Res. 37: 125-130.
- 3. Lincoln, G. A. & Short, R. V. 1980. Seasonal breeding: nature's contraceptive. Prog. Horm. Res. 36: 1-52.
- 4. Kofi, M.; Safdarian, M. & Hashemi, M. 2004. Seasonal variation in semen characteristics, scrotal circumference and libido of Persian Karakul rams. Small Rum. Res., 53:133-139.

- Egerton, J. R.; Ostlind, D. A.; Blair, L. S.; Eary, D. H.; Suhayda, D.; Cifeili, S.; Riek, R. F. & Campell, W. C. 1979. Avermeetins, a new family of potent antihelmintic agent: efficacy on the B1A component. Antimicrob Agents Chemother., 15:372-378.
- 6. Aitken, I. D. 2007. Diseases of sheep. 4th ed. Blackwell publishing. Edinburgh. England. PP. 321-322.
- Pony, S. S.; Wang, C. C. & Frita, I. C. 1980. Studies on the mechanism of action of avermectin B1a, stimulating of release of gamma amino butyric acid from brian synatosomes. Neurochem., 34: 351-358.
- Burg, R.W.; Miller, B. M.; Baker, E. E.; Bimbaum, J.; Currie, J. A.; Harman, R.; Kong, V. L.; Monaghan, R. I.; Olson, G.; Putter, I.; Tunac, J. P.; Wallick, H.; Stapley, E. O.; Oiwa, R. & Omura, S. 1979. The action of avermectin on identified central neurons from helix and its interaction with acetylcholine and gamma-aminobutyric acid response. Antimicrob Agents Chemother. 15: 361-367.
- 9. Tanyildizi, S. & Bozkurt, T. 2002. An investigation of the effects of ivermectin on blood serum, semen hyaluroidase activities and spermatological characteristics in sheep. Turk J. Vet. Anim. Sci., 26:353-357.
- 10. Schroder, J.; Swan, G. E. & Barrick, R. A. 1986. Effects of ivermectin on the reproductive potential of breeding rams. J. S. Afr. Vet. Assoc., 57: 211-213.
- Onakpa, M. M.; Ajagbonna, O. P.; Onifade, K. I. & Akande, M. 2010. Effects of Diminazene aceturate and ivermectin on Semen and Serum Sokoto buck. Int. J. Chem. Tech. Res., 2(1): 738-743.
- 12.Leaning, W. H. D.; Roncalli, R. A. & Brokken, E. S. 1983. The efficacy and safety evaluation of ivermectin: A new injectible antiparasitic agent for cattle. Proc MSD AGVET Symposium on Recent Developments in the Control of Animal Parasites, XXII World Veterinary Congress, Perth, Australia. PP. 25-41.
- Janett, F.; Thun, R.; Ryhiner, A.; burger, D.; Hossig, M. & Hertzberg, H. 2001. Influence of Eqvalan (Ivermectin) on quality and freeze ability of stallion semen. Theriogenology. 55: 785-792.
- 14. Wrona, Z. & Krzyzanowski, J. 1995. Influence of Ivomec ® on some indexes of the boar semen results of sow insemination. Medycyna Weterynaryjna. 51:7.
- Bearden, J. H.; Fuquay, J. W. & Willard, S. T. 2004. Applied Animal reproduction. 6th ed. New jersey: Pearson Education, Inc., Upper Saddle River., PP. 47-48, 56-57, 170.
- Abdulhakeem, A.; Al-Majed, A. A.; Al-Yahya, A. M.; Al-Bakairi, O.; Alshabanah, A. & Qureshi, S. 2006. Reproductive, cytological and biochemical toxicity of yohimbe in male swiss albino mice. Asian J. Androl., 8 (4): 469-467.
- 17. Schurmeyer, T. & Nieschlag, E. 1984. Effect of ketoconazole and other imidazole fungicides on testosterone biosynthesis. Acta. Endocrinol., 105(2):275-280.
- 18.Naoman, U. T. & Taha, M. B. 2010. Effect of hemi-castration on testicular growth and seminal characteristics of Iraqi male goats. Iraqi J. Vet. Sci., 24 (2):71-74.
- 19. Noakes, D. E.; Parkinson, T. J.; England, G. C. W. & Arthur, G. H. 2001. Arthur's veterinary reproduction and obstetrics. 8th ed, Elsevier Sci. Ltd. P.686.
- Shamsuddin, M.; Amiri, Y. & Bhuiyan, M. 2001. characteristics of buck semen with regarded to ejaculation number, collection interval, diluents and preservation period. 53-57.
- Lezama, V.; Orihuela, A. & Angulo, R. 2003. Effect of restraining rams or change of the stimulus ewe on the libido and semen quality of rams. Small Rum. Res., 49: 219-222.