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Original Article

Onset and duration of ejaculatory suppression effect of tamsulosin in goat

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ABSTRACT

The duration of ejaculatory suppression of alpha adrenoceptor antagonist (tamsulosin, TAM) was investigated in goats. Five males were injected intramuscularly with TAM 80 μg/kg (179.8 nmol/kg). Semen was collected using an artificial vagina with estrous female goats and the semen quality and libido score were evaluated at 1, 3, 6 and 9 h post TAM injection. Two replicates were carried out in the study. Heart rates were also measured before the injection and at 30 min before semen collection. The results showed that the libido score was not affected by TAM. At 1 h post injection, the highest percentage of suppressed ejaculation (80%) was recorded and this effect was maintained for up to 3 h post injection (60%). Thereafter the percentage of suppressed ejaculation was significantly decreased ($p < 0.05$) at 6 h (20%) and ejaculation was completely recovered at 9 h post injection. The semen characteristics of the collectable semen, semen volume and number of spermatozoa were lowest at 1 h and 3 h, thereafter they suddenly increased at 6 h and the significantly highest peak was noted at 9 h post injection. TAM injection suppressed goat ejaculation within 1 h and the duration was maintained up to 3 h post injection.

Introduction

Male temporary contraception during a specific period is occasionally required in some animal species, especially in some species of wildlife or feral animals that can multiply rapidly (Malik et al., 1984; Hughes and Macdonald, 2013; Bassi et al., 2015). Male permanent contraception is difficult and expensive (Murray et al., 2015; Zapata-Rios and Branch, 2016). Moreover, this procedure must be performed on the dominant male of the herd and so the best genetic information may be eliminated from the population and maintaining the sexual desire in the dominant male has benefit in preventing repeat copulation from other males in some species (Hynes et al., 2005; Surbeck et al., 2011).

The inhibition of the ejaculation process would be useful for this purpose. Alpha adrenoceptor antagonist is used as a treatment for lower tract symptoms caused by benign prostatic hyperplasia and one of the drugs in this group, tamsulosin (TAM) has been reported to have a side effect on ejaculatory dysfunction or ejaculation disorder (Schulman, 2001; Giuliano et al., 2006; Hellstrom and Sikka, 2006b, Hellstrom et al., 2009; Hisasue et al., 2006). Oral administration of TAM (0.8 mg) significantly reduced the semen volume compared to a placebo in human volunteers (Hellstrom and Sikka, 2006b). A negative role in the expulsion phase of ejaculation has been observed after intravenous injection of TAM (1 μg/kg) in rats (Giuliano et al., 2006). The effects of TAM on the temporary suppression of goat ejaculation without changing sexual desire and physiological characteristics have been reported by the current researchers (Kimsakulvech et al., 2014).

To facilitate contraception usage of alpha1 adrenoceptor antagonist, knowledge of its onset and duration effects are necessary. In humans, some previous studies obtained ejaculatory dysfunction only once after some consecutive days of TAM administration (0.4 mg) while the ejaculatory volume recovered at 3 d following TAM withdrawal (Giuliano et al., 2006; Hisasue et al., 2006; Hellstrom et al., 2009). Previously, TAM has been shown to

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suppress ejaculation in goats at 3 h and 6 h and the effect was eliminated within 24 h (Kimsakulvech et al., 2014). Interestingly, TAM has been reported to decrease the blood pressure from a baseline in humans with oral administration of 0.4 mg TAM decreasing the systolic and diastolic blood pressure from a baseline during 2–10 h and causing an increased pulse rate from a baseline during 2–6 h after administration (Michel et al., 2005b). In dogs, intravenous administration of TAM at 3 μg/kg had a maximal effect on decreasing the mean arterial blood pressure within 30 min (Ohtake et al., 2004).

However, effective duration of suppressed ejaculation still remains unavailable. Therefore, the present study aimed to clarify the ejaculatory suppression effect of TAM in goats, in terms of the onset and effective duration. Male goats have distinct characteristic of a high libido which may suit testing for suppression of the sexual process. Very little information on the effects of TAM in this species is currently available. This study thus investigated the effect of TAM on the sexual interest, characteristics of ejaculation and semen quality in goats.

Materials and methods

Animals and treatment

Experiment procedures was approved by the Animal Usage and Ethics Committee, Kasetsart University (ID no. ACKU 02156). Five mixed-breed, male goats aged 1–3 yr and weighing 27–65 kg were selected from a private farm. On the farm, the male goats had been kept together in a pen separated from female goats. All male goats studied were evaluated and confirmed to have good libido, were able to serve an artificial vagina (AV) and had normal semen quality. Attempts at semen collection using AV with an estrous female at 1 h, 3 h, 6 h and 9 h post intramuscular injection of TAM (80 μg/kg) were carried out. Two replicates, a week apart, were carried out in the study.

Soluble preparation

Tamsulosin hydrochloride and dimethyl sulfoxide (DMSO) were purchased from Sigma–Aldrich Pte Ltd. For ease of injection, TAM was diluted with DMSO to gain the amount required for each goat.

Libido scoring and semen collection

Each goat had chances to serve the AV at least once within 10–20 min in the designated periods. In the first attempt, if no ejaculated semen was found in the AV collecting tube after thrusting, the anejaculate male was allowed to have a second attempt within 10 min. Sexual interest was recorded using the method of Frydrychova et al. (2011) and recorded for libido.

Ejaculatory characteristics

The ejaculation response in this study was classified as complete ejaculation or suppressed ejaculation. Ejaculation with spermatozoa having a volume of 0.1 mL or more was classified as complete ejaculation and no ejaculated semen or a volume less than 0.1 mL was classified as suppressed ejaculation.

Semen quality assessment

The semen attributes in this study were: the semen volume, mass spermatozoa movement score, percentage of motile and live spermatozoa, sperm concentration, number of spermatozoa per ejaculate and seminal alkaline phosphatase (ALP). Semen on the AV cone and collecting tube was collected and included in the semen volume measurement. The semen volume was measured with the aid of automatic pipettes. The mass spermatozoa movement score ranging from 0 (immotile) to 5 (high) and the percentage of motile spermatozoa were evaluated under a light microscope. The sperm concentration was estimated using a hemocytometer. Semen was diluted 400 fold with hypo-osmotic swelling solution and the percentage of live spermatozoa was evaluated (Revell and Mrode, 1994). Seminal alkaline phosphatase (ALP) was analyzed using the Reflotron® dry chemistry method (Roche Boehringer; Mannheim, Germany).

Heart rate measurement

The heart rate was measured in beats per minute (bpm) at 30 min before the treatment injection and before collecting semen for all time periods in the study.

Statistical analysis

The numbers of suppressed ejaculations in each time period were compared using Pearson's χ^2 test. Libido scores were examined using the Friedman test and Wilcoxon test. Mean values were considered statistically different at $p < 0.05$ ANOVA using the repeated measurement model procedure was applied for continuous complete ejaculation, semen volume, percentages of motile and live spermatozoa, sperm concentration, number of spermatozoa and ALP between times. Heart rate data were analyzed using ANOVA and the general linear model procedure. All values except the numbers of ejaculation were presented as the mean and standard error of mean (SEM). Statistical analysis was performed using the SPSS package (SPSS Inc.; Chicago, IL, USA).

Results

Effect on libido

In total, 10 attempts at semen collection were carried out for each designated period. There were no differences in the libido scores among the periods as shown in Table 1.

Effect on ejaculation

The number of suppressed ejaculations after TAM injection is shown in Table 1. It was found that number of suppressed ejaculations at 1 h (8, 80%) was not significantly different from that at 3 h (6, 60%) but that at 1 h was significantly higher ($p < 0.05$) than those of 6 h and 9 h. At 3 h, the number of suppressed ejaculations was significantly higher than at 9 h. It then significantly decreased at 6 h (2, 20%) and all goats had complete ejaculation at 9 h post injection.

Effect on semen quality

The semen volume increased with time, being the lowest at 1 h and 3 h; thereafter, it suddenly increased at 6 h and was highest at 9 h (Table 2). The numbers of spermatozoa were lowest at 1 h and 3 h; thereafter, they increased and were highest at 9 h. On the other hand, the mean percentage of live spermatozoa was highest at 1 h, after which, it abruptly decreased at 3 h and was lowest at 6 h and 9 h.

The continuity of complete ejaculation for each goat was calculated each time. Only three goats had complete ejaculation at 3 h, 6 h and 9 h post injection and the semen quality of these goats is shown in Table 2. The semen volume at 3 h showed significantly lower values ($p < 0.05$) than those at 6 h and 9 h. The number of

Table 1
Libido score (mean ± SE), percentage of suppressed ejaculation and heart rate (mean ± SE) at 0–9 h of tamsulosin injection (80 μg/kg).

Time (h)	*n*	Libido score	Suppressed ejaculations (%)	Heart rate (beats/min)
0	10	–	–	85.80 ± 6.40
1	10	4.80 ± 0.20	8 (80)[a*]	109.40 ± 10.74
3	10	4.80 ± 0.20	6 (60)[ab]	104.40 ± 9.13
6	10	5.00	2 (20)[b]	103.80 ± 8.76
9	10	5.00	0 (0)[c]	105.0 ± 5.94

*Values with different lowercase superscripts in the same column are significantly different at $p < 0.05$.

spermatozoa at 3 h was significantly lower ($p < 0.05$) than at 6 h. There was no time effect on motile spermatozoa, mass spermatozoa movement, sperm concentration, percentage of live spermatozoa and ALP.

Effect on heart rate

The heart rate prior to TAM injection was 85.80 ± 6.40 bpm before injection and suddenly increased at 1 h (109.40 ± 10.74 bpm); thereafter, it slightly decreased but sustained a high rate until 9 h post injection (Table 1).

Discussion

This study demonstrated that TAM can suppress goat ejaculation at 1 h post injection and the duration of ejaculatory suppression was maintained for up to 3 h post injection. TAM may also have affected the semen quality in terms of the semen volume and number of spermatozoa.

Sexual desire after TAM treatment was not diminished even though each goat had several copulations per day post TAM injection. These results confirmed evidence that TAM at a dosage of 80 μg/kg did not affect sexual desire in goats (Kimsakulvech et al., 2014).

Previous studies had shown an ejaculatory dysfunction effect of alpha1 adrenoceptor antagonist. However, the onset and period of this chemical were not determined (Kedia and Persky, 1981; Schulman, 2001; Andersson and Wyllie, 2003; Hisasue et al., 2006; Hellstrom and Sikka, 2006a, 2006b). The present study demonstrated that TAM at 80 μg/kg resulted in a high percentage of suppressed ejaculations at 1 h post injection and the effect was maintained for 3 h post injection. Therefore, this study clarified the temporary ejaculatory suppression effect of TAM in goats.

The mechanism of TAM-induced ejaculatory suppress action is not well documented in goat. A possible mechanism has been proposed previously in humans, where it has been suggested that TAM may suppress ejaculation through an affinity of 5-hydroxytryptamine 1A (5HT1A) and Dopamine2 (D2)-like receptors in the central command of ejaculation (Andersson and Wyllie, 2003; Giuliano et al., 2006). This may result in relaxation of the urethral smooth muscle, decreasing the seminal vesicle, reducing bulbospongiosus muscle contraction and resulting in ejaculatory suppression (Giuliano et al., 2004, 2006; Ohtake et al., 2006; Kobayashi et al., 2009) This mechanism might also be involved in the suppression of goat ejaculation.

In humans, TAM at 0.4 mg once a day for 3 d resulted in ejaculatory disorder at the third day. The semen volume recovered at 3 d following TAM withdrawal (Hisasue et al., 2006). In comparison with this reported result, all goats in the current study returned to normal ejaculation at 9 h post injection and the semen volume was restored to approximately normal (Ritar et al., 1992) within 6 h post injection. This suggested that the goats had partially recovered from suppressed ejaculation at 6 h after TAM injection and this effect had not persisted for more than 9 h post injection.

Regarding semen quality, the semen volume and number of spermatozoa increased with time after TAM treatment. This result related to the gradual recovery from the TAM ejaculatory suppression effect. Noteworthy, was that the number of live spermatozoa at 9 h was more varied than at 1 h post injection. This may have been due to the effect of alpha1 adrenoceptor antagonist on changing the epididymal environment which requires testing in further studies.

The heart rate suddenly increased and was highest at 1 h post TAM injection. According to previous study, the heart rate at 3 h post TAM injection tended to be higher than before injection in goats (Kimsakulvech et al., 2014). In dogs, TAM at 3 μg/kg intravenous administration could decrease the mean arterial blood pressure within 30 min by about 10 mmHg (Ohtake et al., 2004). Alpha1 adrenoceptor antagonist has been reported to decrease blood pressure through relaxing smooth muscle. However, TAM has been developed to further improve the efficacy:safety ratio with a lower incidence of cardiovascular system problems through the use of a vasodilator (Ohtake et al., 2004; Michel et al., 2005a; Michel and Chapple, 2006; Kobayashi et al., 2009). In the present study, TAM 80 μg/kg show no distinct evidence of a decrease in blood pressure or heart rate; nevertheless, this may depend on the dosage, effect duration or animal species.

The present study clearly showed that TAM could suppress ejaculation within 1 h post injection in goat and the effect was maintained for up to 3 h post injection. Recovery occurred within 9 h post injection without changing sexual desire and copulation. Tamsulosin may have different effects on different animal species. This study in goats is a model of the use of alpha1 adrenoceptor antagonist on the suppression of ejaculation and can be applied to other species. Many types of alpha1 adrenoceptor antagonists may possess more advantages for the suppression of ejaculation. In further studies, other types of alpha1 adrenoceptor antagonist should be compared and examined.

Table 2
Semen quality and seminal alkaline phosphatase (mean ± SE) at 1–9 h post tamsulosin injection.

Time (h)	*n*	Semen volume (mL)	Motile spermatozoa (%)	Mass spermatozoa movement score	Spermatozoa concentration ($\times 10^9$ cells)	Numbers of spermatozoa ($\times 10^9$ cells)	Live spermatozoa (%)	ALP ($\times 10^4$ IU*)
0	2	0.24 ± 0.04	97.50 ± 2.50	5.00	5.90 ± 0.78	1.45 ± 0.45	65.50 ± 17.00	5.24 ± 3.57
1	4	0.21 ± 0.06	82.50 ± 10.89	4.50 ± 0.50	3.77 ± 0.39	0.80 ± 0.22	40.75 ± 17.01	6.51 ± 1.70
3	8	0.60 ± 0.12	85.63 ± 3.05	4.63 ± 0.18	3.79 ± 0.58	1.88 ± 0.21	25.68 ± 8.35	5.12 ± 1.11
6	10	0.73 ± 0.11	81.00 ± 3.71	4.40 ± 0.26	4.15 ± 0.64	2.89 ± 0.50	26.85 ± 4.07	5.44 ± 0.94
Continuous complete ejaculation at 3, 6 and 9 h post tamsulosin injection								
3	3	0.25 ± 0.08[a†]	78.33 ± 14.24	4.33 ± 0.66	3.51 ± 0.41	0.88 ± 0.29[a]	41.83 ± 24.00	4.96 ± 1.25
6	3	0.67 ± 0.16[b]	80.00 ± 5.77	4.33 ± 0.33	3.46 ± 0.83	2.05 ± 0.12[b]	17.00 ± 3.50	6.83 ± 2.18
9	3	0.73 ± 0.06[b]	75.00 ± 10.41	4.10 ± 0.60	3.20 ± 0.60	2.29 ± 0.32[ab]	29.00 ± 5.85	5.37 ± 1.77

*International units.
†Values with different lowercase superscripts in the same column are significantly different at $p < 0.05$.

Conflict of interest

No conflicts of interest influenced this research.

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