International Journal of Agriculture, Environment and Bioresearch

Vol. 2, No. 06; 2017

ISSN: 2456-8643

ANALYSIS OF SPONTANEOUSLY VOIDED SALIVA AND URINE UNDER DETOMIDINESEDATION IN SOKOTO RED GOATS.

Onifade K. I.

Department of Veterinary Pharmacology And Toxicology.

Faculty of Veterinary Medicine, Usmanudanfodiyo University, Sokoto, Nigeria.

ABSTRACT

The influence of sedation with detomidine on spontaneously voided urine and saliva under different climate-induced ambient temperatures was investigated in Sokoto red goats. Twelve goats of both sexes weighing 20□6.5 and aged between 2 and 3 years were used for this study. Two sedative doses 20 µg/kg and 40 µg/kg were administered IM to six goats (n=6) in each of four treatment groups of each experiment. The experiments were carried out in two phases under low ambient temperatures (LAT), (≤ 150C) and high ambient temperatures (HAT), (≥ 39 0C) respectively. Spontaneously voided urine and saliva samples were measured from time of detomidine administration until full recovery. The frequency, total volume, pH, specific gravity of the samples were recorded. The results indicated that significantly higher ($p<0.05$) frequency and volume of urine was voided in LAT compared to HAT following detomidine sedation. Salivation of significantly higher ($p<0.05$) volume and frequency was voided under HAT compared to LAT. The pH and specific gravity of urine and saliva samples also vary with time throughout each experiment. Possible mechanisms responsible for our observations were discussed. This study provides justification for consideration of the ambient temperature as an important factor in clinical use of detomidine. Following detomidine sedation in goats, proper head positioning and placement of an indwelling catheter for free drainage of saliva and urine in HAT and LAT respectively is recommended.

Keywords: detomidine, sedation, goats, saliva, urine, ambient temperature

Introduction

The use of the α_2 - adrenoceptor agonists has become well established in veterinary anaesthesia since they possess sedative, analgesic and muscle relaxing properties which makes them good adjuncts to anesthetics. Xylazine was the first α_2-adrenoceptor agonist licensed for veterinary application, can provide sedation or immobilization depending on the dose (Greene and Thurmon 1988, Taylor 1991 Carroll et al 1998). Detomidine is a potent, selective and specific antagonist of centrally or peripherally located α_2–adrenoceptors (Virtanen 1986).Detomidine is however more specific on α_2- adrenoceptors when compared with xylazine and has been

Vol. 2, No. 06; 2017

ISSN: 2456-8643

evaluated in a number of species, but found to be particularly effective in the horses (Clarke and Taylor 1988).

The evaluation of detomidine has been undertaken in small ruminants and mild to moderate salivation and frequent urinationwerereported (Tunio et al., 2003, 2016, Moolchand et al., 2014). However previous studies did not consider the influence of ambient air temperatures. The influence of ambient temperature on the physiology and response of animals to chemical agents has been established (Gordon 1996, Malberg and Seiden 1998). In cattle it has been reported that xylazine, anα_2-adrenoceptor agonist like detomidine, causes a pronounced and prolonged response when used in high ambient temperature (Fayed *et al* 1989). Onifade and Arowolo (2015) reported that detomidine induced sedation in low ambient temperatures is qualitative different from that under high ambient temperatures.

The aim of this study was to investigate the influence of detomidine on spontaneously voided urine and saliva by Sokoto red goats under different ambient air temperatures.

MATERIALS AND METHODS

Animals.

Twelve healthy adult Sokoto red goats of either sex weighing 20±6.5 (mean ± 50) and aged between 2 and 3 years were used for this study. The goats were housed in groups according to sex and bean offal, cowpea and groundnut hay and fresh water was provided free choice. The goats were fasted overnight, but allowed only water prior to each drug treatment.

Drugs.

Detomidine (Domosedan®), (Orion Pharma Corporation, Turkur, Finland) was used for this study.

Study design.

The goats were divided into two groups of six each (n = 6). Six goats in each group received six different drug treatments at the rate of one treatment per week in a randomized order. The treatments comprised 20 or 40μg/kg detomidine during high ambient temperature (HAT) or low ambient temperature (LAT). The HAT experiments were carried out at ambient temperature range 39 - 43^{o}C. While the LAT experiments were carried out at ambient temperature range 10 - 15^{o}C.

Collection and evaluation of urine and saliva.

Vol. 2, No. 06; 2017

ISSN: 2456-8643

Specially designed receptacles were placed on each goat as soon as it is laterally recumbent for continuous sampling of spontaneously voided urine and saliva. The volume, pH and specific gravity of each spontaneously voided urine and saliva samples were measured using a graduated pipette, pH meter and a reflect meter (Yellow Springs Instruments Co. NY) respectively and the frequency noted. The samples collected were numbered 1 to 6 where applicable throughout the experiments.

Statistics - Data were analyzed, using ANOVA, and pair wise comparisons were made, using least-significant difference multiple comparison test. All data are presented as mean ±SD and $P<0.05$ was considered significant.

RESULTS

The frequency of urine spontaneously voided (number of samples) under detomidine sedation in LAT was significantly higher ($P < 0.05$) than in HAT at the two dose levels (Table 1). Times following detomidine when urination commenced also differ significantly ($P < 0.05$) from that of HAT. The volume of spontaneously voided urine exhibited two peaks in LAT, one during deep sedation (usually sample 2) and one in the recovery phase. The volume of urine samples at these two points was significantly ($P < 0.05$) higher than at other times before or post drug administration.

The pH of urine samples decreased significantly ($P < 0.05$) following drug administration beginning from sample 2 up to sample 4 in LAT. In HAT the pH of sample 2 was lower than that of sample 1 but the difference was not significant. With increasing time elapsing post drug administration and number of urine samples collected the pH tends to decrease, such that the values for sample 5 and 6 were not significantly ($P >0.05$) different from the reference value for untreated goats.

The specific gravity of the spontaneously voided urine following detomidine, decreased significantly ($P >0.05$) compared with untreated goat urine. The urine sample collected in the recovery phase some minutes after the goats regain the ‘on-feet’ posture consistently had the lowest specific gravity.

The administration of detomidine at both doses in HAT resulted in profuse salivation, which was evident before recumbency in most cases. The volume of saliva collected during sedation in HAT was significantly higher ($P < 0.05$) than in LAT. The pH of voided saliva in HAT was higher than that of LAT but the difference was not statistically significant ($P > 0.05$) (Table 2).

Vol. 2, No. 06; 2017

ISSN: 2456-8643

DISCUSSIONS

A constant observation in all the goats following detomidine administration, under LAT and HAT, was an increased spontaneously voided urine production. It has been reported that xylazine inchreased urine output in treated cows (Greene and Thurmon, 1988) and goats (Adetunji and Ogunyemi, 1998). Our result is in line with previous reports in this species following the administration of other α_2- adrenoceptor agonists (Mohammed et al., 1991, Clark et al., 1993, Mohammed and Yelwa 2001). The increased frequency and total volume of spontaneously voided urine in LAT following detomidine administration, as observed in this study, has not to the best of our knowledge, been previously reported in goats. The frequent urination induced in Sokoto red goats in this study is in agreement with a previous report following detomidine in goats (El-Kammar et al., 2014b, Tunio et al 2003, 2016, Moolchand 2014). The high correlation between the depth of sedation and the volume of urine spontaneously voided in this study indicates that the effect is dependent on sedation. Other α_2 – adrenoceptor agonists (e.g. clonidine, guanabenz and rilmenidine) also produce diuretic and natriuretic responses in anaesthetized (and conscious) animals and human (Hayashi and Maze, 1993, Evans et al., 1997).

Several mechanisms have been suggested to be responsible for diuresis following α_2-adrenoceptor agonists in various mammalian species. α_2-adrenoceptor agonists reportedly inhibit release of antidiuretic hormone from the pituitary in dogs and some other species (Kimura et al., 1981). An osmotic diuresis resulting from elevated blood glucose concentrations following α_2-adrenoceptor agonists have also been suggested to be a contributing factor in the polyuria (Reid et al., 1979).

A number of studies have also established that activation of central α_2 -adrenoceptors, inhibits the release of vasopressin in conscious and anaesthetized animals (Kimura et al., 1984, Brooks et al., 1986). Inhibition of CNS secretion and/or renal tubular action(s) of vasopressin is a possible mechanism of α_2-adrenoceptor-induced diuresis (Cabral et al., 1997). Considerable evidence also indicates that the activation of renal α_2-adrenoceptors is a predominant mechanism by which selective α_2-adrenoceptor agonists produce diuretic and natriuretic responses in several mammalian species, (Standhoyet al., 1982, Stanton et al., 1987, Gellai and Edwards, 1988, Gellai, 1990). It has been demonstrated that xylazine activate α_2–adrenoceptors in the paraventricular nucleus of the hypothalamus to contribute to the increase in urine flow rate, but not urinary sodium excretion (Cabral et al., 1997).

The diuretic effects of detomidine in goats and other species need to be taken into consideration when this drug is indicated. Urination during surgical procedures could result in contamination of the operating field. The placement of an indwelling urethral catheter to direct urine away and

Vol. 2, No. 06; 2017

ISSN: 2456-8643

maintain the sterility of the surgical field as previously suggested, (Adetunji and Ogunyemi, 1998), would be desirable.

Drug-induced diuresis in goats with pre-existing hypovolaemia or urethra obstruction may respectively lead to shock or urinary bladder rupture (Knight, 1980). Animals with such pre-existing conditions are poor-risk patients for α_2-adrenoceptor agonists administration. Allowing the goats free access to fresh water and salt-lick post- detomidine administration would be helpful especially in prolonged sedation / anaesthesia.

Salivation was among the earliest signs of drug effect following detomidine. This observation concurred with previous reports that profuse salivation is one of the prominent effects observed in goats following administration of α_2 – adrenoceptor agonists including detomidine (Ndeereh et al., 2000, Mpanduji et al., 2000, Tunio et al 2003). The quantification of the volume and pH of spontaneously voided saliva following detomidine administration in goats has not been previously reported. Adetunji and Ogunyemi (1998), quantified the volume of saliva produced during the anaesthesia induced with xylazine / ketamine combinations in West African dwarf goats. In this study salivation (total volume) was more profuse during HAT than in LAT experiments unlike urination. The reason for the significantly higher volume of saliva produced in HAT with detomidine remains unclear. Profuse salivation in goats has been reported in many studies following detomidine or medetomidine (Singh et al., 1991b, Kumar et al., 1997b, Dilipkumar et al., 1998, Kinjavdekar et al., 1999, Mahmood and Mohammed 2000, Mpanduji et al., 2000)

Vomiting caused by xylazine in cats has been shown to follow stimulation of receptors in the chemoreceptor trigger zone (CTZ) in the brain (Colby et al., 1981). Since the stimulation of the CTZ also induces salivation in most species this could be the mechanism of detomidine-induced salivation in goats observed in this study.

Since profuse salivation is a constant feature of the use of α_2-adrenoceptor agonists in this species, possibility of hypovolaemia is high (Taylor 1991). In well-hydrated and healthy goats, the highest volume of saliva voided in HAT in this study may not induce hypovolaemia but could interfere with pulmonary gas exchange leading to serious hypoxemia if aspirated by the sedated goat. The possibility of saliva aspiration is higher if the pharyngeal or swallowing reflex is lost consequent upon the CNS depressant effect of these drugs.

In this study the risk of saliva aspiration was reduced by the positioning of the goat on the right lateral recumbency with the head supported on a pillow at the poll, which allows free drainage of saliva into the collecting device.

Vol. 2, No. 06; 2017

ISSN: 2456-8643

To prevent possible saliva aspiration by the sedated goats following detomidinepremedication with atropine has been employed (Dilipkumar et al., 1998, Tunio et al., 2003). It has been suggested that atropinization could make the saliva more viscous and more difficult to drain and compound detomidine-induced ruminal stasis, (Taylor, 1991). Postural drainage of saliva could thus be used in dealing with profuse salivation in comparison to atropinization in sedated goats (Adetunji A. and Ogunyemi T.R. 1998)

ACKNOWLEDGEMENTS

We thank MirjaHuhtinen of Orion Pharma Corporation, Finland for the generous donation of the generic product, detomidine used in this study.

REFERENCES

Adetunji A. and Ogunyemi T.R. (1998) An evaluation of Xylazine/Ketamine anaesthesiain West African Dwarf goats. *Trop. Vet.* 16:115-117.

Carroll G.I. Hooper R.N. Slater M.R. Harfield S.M. Matthews N.S. (1998) Detomidine butorphanolpropofol for carotid artery translocation and castration or ovariectomy in goats. *Vet. Surg*.27(1) 75-82.

Brooks, D.P.; L. Share, and Crofton J.T. (1986) Central adrenergic control of vasopressin release. Neuroendocrinology 42: 416-420.

Cabral, A.M.; Verner K.J., and Kapusta D.R. (1997). Renal excretory responses produced by central administration of opioid agonists in ketamine and xylazine- anesthetized rats. *J.Pharmacol. Exp. Ther.* 282:609-616.

Clarke, K.W. and Taylor P.M. (1988) Detomidine: A new sedative for horses. *Equine. Vet. J.* 18: 366-370.

Clarke T.P.PurohitR.C.and Wilson R.C.(1993). Evaluation of sedative and analgesic properties of detomidine in goats.*Agri. Pract* 14(4)29-33.

Vol. 2, No. 06; 2017

ISSN: 2456-8643

Colby E.D., McCarthy L.E., and Borison H.L. (1981) Emetic action of xylazine on the chemoreceptor trigger zone for vomiting in cats. *J. Vet. Pharmacol. Therap*.4:93-96.

Dilipkumar D. Sharma A.K and Gupta O.P. (1998) Comparative cardiopulmonary effects of xylazine and detomidine in goats.*Indian Vet.J* 75 (10) 899-900.

El-Kammar M.H., Gad S.B. and Korittum A.S.(2014) Evaluation of sedative, analgesic, physiological and haematological effects of intravenous detomidine, detomidine-butorphanol, romifidine and romifidine-butorphanol in baladi goats. Global Veterinaria 12,(1);36-44.

Evans, R.G, Shweta, A,;Malpas S.C., Fitzgerald, S.M.; and Anderson W.P. (1997). Renal effects of rimenidine in volume- loaded anesthetized dogs. *Clin. Exp. Pharmacol. Physiol*. 24: 64-67.

Fayed A.H., Abdalla E.B. and Anderson R.R. (1989) Efferts of xylazine in heifers under thermoneutral or heat stress conditions. *Am. J. Vet. Res*. 50: 151-153.

Gellai, M. (1990). Modulation of vasopressin antidiuretic action by renal $\alpha_2$adrenoceptors.*Am.J.Physiol.*259 (Renal Fluid Electrolyte Physiol. 28): F1-F8.

Gellai, M.; and Edwards R.M. (1988) Mechanism of α_2-adrenoceptors agonist-induced diuresis.*Am. J Physiol.* 255 (Renal Fluid electrolyte Physiol.24): F317-F323.

Gordon C.J (1996) Thermoregulatory aspects of environmental exposure to anticholinestrase agents.*Rev. Environ. Health* 11;101 –107.

Greene S.A and Thurmon J.C (1988) Xylazine – a review of its pharmacology and use in Veterinary medicine. *J. Vet. Pharmacol.Ther* 11:295-313.

Hayashi Y and Maze M. (1993), Alpha$_2$adrenoceptor agonists and anaesthesia. *Brit. J. Anaesth.*81: 108 – 118.

Kimura T. Share L., Wang B.C., and Crofton J.T.(1981) The role of central adrenoceptors in the control of vasopression release and blood pressure. *Endocrinology*.108, 1829-1836.

Kimura, T., Shoji T.M, Litake, K, Ota K.; Matsui K.; and Yoshinaga K. (1984) The role of Central α_1- and α_2- adrenoceptor in the regulations of vasopressin release and the cardiovascular system. *Endocrinology* 114: 1556-1562.

Kinjavdekar P.; Singh, G.R.; Amarpal; Pawde, A.M.; and Aithal H.P. (1999) Effects of

Vol. 2, No. 06; 2017

ISSN: 2456-8643

Subarachroid xylazine and medetomidine in haemodynamics and ECG.In goats.*J.Vet. Med.*

46 (5) 271-275.

Knight, A.P. (1980) Xylazine *J. Am. Vet. Med. Assoc*. 176:454-455.

Kumar D.D., Sharma A.K. and Gupta O.P.(1997b) Comparative studies on effect of detomidine (Domosedan®) an Xylazine (Rompun®) premedication on cardiopulmonary system in ketamine anaesthetized goats. *Indian Vet. J*. 74(10): 880-881.

Mahmood M.B and Mohammed F.K. (2000) Medetomidine analgesia and sedation in goats. *Iraqi J.Vet. Sci.* 13 (2) 409-413.

Malberg J.E and Seiden L.S. (1998) Small changes in ambient temperature cause large changes in 3,

4methylenedioxmethamphetamine (MDMA)- induced serotonin neurotoxicity and core body

temperature in the rat. *J. Neurosci.* 18: (13) 5086-5094

Mohammad A. and Yelwa H.A. (1993).Effect of xylazine hydrochloride (Rompun®) on Sokoto Red Goats.*Small Rum. Res*. 12:107-113.

Mohammad A. and Yelwa H.A. (1993) Effect of xylazine hydrochloride (Rompun) on

Sokoto Red Goats.*Small Rum. Res*. 12:107-113.

Mohammad F.K. Zangana I.K. and Al-Kassim N.A. (1991) Clinical observations in Shami

goat kids sedated with medetomidine. *Small Rum. Res.* 5:149-153.

Moolchand M., Kachiwal A.B, Soomro, S.A. and Bhutto Z.A.(2014) Comparison ofsedative and analgesic effects of xylazine, detomidine and medetomidine in sheep. Egyptian J. Sheep and Goat Sci. 9 (2) P:43-48.

Mpanduji D.G Bittegeto S.B.P Mgasa M.N and Batamuzi E.K (2000).analgesic, behavioural and, cardiopulmonary effects of epidurally injected medetomidine. (Domitor®) in goats.J. Vet Med. series A. 47 (2) 65-72.

Ndeereh D.R., Mbith; P.M.F and Kihurani D.O. (2000). The evaluation of 4 aminopyridine for the reversal of xylazine sedation in goats *J. Israel Vet. Med. Assoc* 55 (1).1-6.

Onifade K.I. and Arowolo R.O.A. (2015) Detomidine sedation of Sokoto red goats under

differentambient temperatures. Vet. Res. Int. 3(4) 109-114

Vol. 2, No. 06; 2017

ISSN: 2456-8643

Reid, J.A; Nolan P.L; Wolf J.A and Keh I.C. (1979). Suppression of vasopressin secretion by clonidine: effect of alpha-adrenoceptor antagonists. *Endocrinology* 104,1403 – 1406.

Singh, A.P. Singh J. Peshin P.K. Sharif D., and Patil D.B (1991b). Evaluation of detomidine as a sedative in goats. *Acta Vet. Hung.* 13(3-4) 109-114.

Strandhoy J.N., Morris M. and Buckalew V. M.Jr (1982). Renal effects of the antihypertensisveguanabenz, in the dog. *J Pharmacology.Exp.Ther*221: 347 352.

Stanton, B., Puglisi E., and Gellai M. (1987). Localization and mechanical of α_2- adrenoceptor-mediated increase in renal Na^+, K^+, and water excretion. *Am. J. Physiol*. 252 (*Renal Fluid Electrolyte Physiol*. 21): F1016-F1021.

Taylor P.M. 1991. Anaesthesia in sheep and goats *Practice* 13:31 –36.

Tunio A., Bughio S., Sahito K.J., Shah G.M., Ebrahimi M., Tunio P.Z. (2016) Observation of physiological changes after detomidine administration in Pateri goat. Mac. Vet. Rev.; 39 (1): 77-81.

Tunio A.N., Kalhoro A.B., and Kathio I.H.(2003) Sedative and analgesic effects of detomidine hydrochloride in goats. Pakistani Vet. J.23(3) 143-149

Virtanen R.H. (1986) Pharmacology of detomidine and other α_2-adrenoceptor agonist in the brain. *Acta Vet.Scand Suppl.* 82, 35-45.

Vol. 2, No. 06; 2017

ISSN: 2456-8643

Table 1:- Some urine values (mean ± SD) in Sokoto red goat following detomidine sedation during low and high ambient temperatures.

Samples		Treatment groups			
		20µg/kg		40µg/kg	
No	*Variables*	**LAT**	*HAT*	**LAT**	**HAT**
1.	TV (min)	38.6±9.4	50.5±9.4*	28.5±6.2	66.5±7.38*
Vol (ml)		67.5±6.1	5.8±14.3*	52.5±3.8	8.5±5.6*
	pH	10.7±0.4	9.8±0.5	10.1±0.5	9.6±0.5*
	SG	1.041±0.005	1.046±0.003	1.036±0.005	1.036±0.003
2	TV	142.8±10.7	197.2±10.4*	57.2±5.9	152.4±9.7*
Vol		125.3±5.5	12.6±4.8*	76.4±8.4	12.6±4.5*
	pH	10.6±0.4	9.6±0.4	8.2±0.5	9.2±0.5
	SG	1.040±0.004	1.044±0.003	1.021±0.002	1.030±0.003
3	TV	216.8±151.1	NS	93.7±8.2	NS
Vol		30.2±6.3		68.5±9.1	
	pH	10.8±0.5		8.6±0.5	
	SG	1.038±0.005		1.016±0.003	
4	TV	271.3±12.6	NS	142.0±16.8	NS
Vol		23.0±7.4		86.4±15.6	

Vol. 2, No. 06; 2017

ISSN: 2456-8643

	pH	10.6±0.5		9.2±0.5	
	SG	1.039±0.005		1.013±0.003	
5	TV	NS	NS	205.4±22.7	NS
Vol		-		65.3±12.2	
	pH	-		9.6±0.4	
	SG	-		1.012±0.002	
6	TV	NS	NS	243.8±10.9	NS
Vol		-		26.5±6.2	
	pH	-		10.2±0.5	
	SG	-		1.018±0.005	

TV- Time voided Vol- Volume SG- Specific gravity NS- No sample* Difference between LAT and HAT (P<0.05)

Vol. 2, No. 06; 2017

ISSN: 2456-8643

Table 2:- Volume and pH of secreted saliva (mean ±SD) in Sokoto red goats following detomidine sedation in low and high ambient temperatures.

Saliva sample	Treatment groups			
	20µg/kg		40µg/kg	
Variables	**LAT**	*HAT*	**LAT**	**HAT**
Total volume(ml)	3.5±1.2	12.4±2.1*	5.8±1.2	20.3±3.8*
pH	10.0±0.1	10.1±0.3	1.0±0.2	10.3±0.2