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Effect of Xylazine Sedation on Some Haematological Indices after Chloramphenicol Pre-Treatment in Sokoto Red Goats

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Abstract: The effect of a single dose pre-treatment with chloramphenicol at 50 mg kg^{-1} given intramuscularly on xylazine sedation was evaluated on 6 Sokoto Red goats weighing 11-14 kg. The duration of xylazine sedation after xylazine administration at 0.2 mg kg^{-1} IM alone was 83.16±10.95 min (control), as against 129±1.78 and 157.83±4.99 min for the other two pre-treatments with chloramphenicol, respectively. There was a significant ($p<0.05$) decrease in the haemoglobin concentration for all treatments while a significant increase in the white blood cells count was observed for all treatments. Irrespective of weight variation, the goats in all exhibited the same clinical signs. It can be deduced from this research that chloramphenicol pre-treatment may prolong the duration of action of xylazine sedation.

Key words: Xylazine, chloramphenicol, Sokoto Red goats, sedation

INTRODUCTION

Xylazine hydrochloride (Xylazin® injection, 2% solution contains xylazine hydrochloride 23.33 mg kg^{-1}, Indian Immunologicals Ltd., India) is chemically, 2(2,6-dimethylphenylamino)-4H-5,6-dihydro-1,3-thiamine hydrochloride (Adams, 2001). It is a potent sedative/hypnotic agent (Hall and Clarke, 1983). Pharmacologically, xylazine is classified as an effective sedative, analgesic, muscle relaxant, immobilizing and hypnotic agent in domestic animals (DeRossi *et al*., 2003; Adams, 2001; Ewing, 1990; Torre and Erausquine, 1988; Bush *et al*., 1978; Kreeger *et al*., 1986). As anaesthesia, xylazine hydrochloride has been satisfactorily used with other drugs (Brock and Hildebrand, 1990) and as pre-anaesthetic for capture and restraining of domestic and wild species (Omamegbe, 1985). Xylazine is also known to significantly ameliorate the effects induced by stress stimuli (Ali *et al*., 2006).

Chloramphenicol is a stable, lipid-soluble, neutral compound. It has a broad-spectrum of activity exerting a bacteriostatic effect against most gram-positive and gram-negative bacteria (Prescott, 1993). It inhibits microsomal enzyme activity, hepatic metabolism of drugs when given concurrently and may prolong the activity of phenylbutazone, as well as xylazine and ketamine in some species (Prescott *et al*., 2000).

Sokoto Red goat is a well-defined breed in Africa and its most important characteristics is production of quality skin, which is in high demand for leather product (Devendra and McLeroy, 1988). Nigeria is the fifth principal goat-producing country in the world with 10.2 million (Gracey *et al*., 1999) andthe population of goats in Sokoto state is estimated to be 2.46 million. Sokoto red goats are found virtually in every compound within the state and are managed semi-intensively. This semi-intensive system of management predisposes to dystocia and ruminal impaction resulting from the ingestion of polythene and other indigestible materials which may require surgical intervention.

In Nigeria, due to the broad spectrum of activity and availability of chloramphenicol it is widely used by veterinarians and non-veterinarians alike. Thus, the objective of this study is to evaluate the effect of xylazine sedation on the haematological indices, onset of action as well as its duration and physiological parameters in Sokoto Red goats after chloramphenicol pretreatment.

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MATERIALS AND METHODS

The study area Sokoto, is in the Northwestern part of Nigeria located on Latitude 13° 03/ N and Longitude 5° 14/ E. This study was conducted between November and December, 2005.

Six Sokoto red goats (Boar) weighing 11-14 kg were purchased from a local market and stabilized for 2 weeks. They were kept in the faculty experimental animal house on concrete floor, fed with beans offal and bran and water was provided *ad libitum*. Blood and fecal analyses were conducted for haemoparasites and helminthes during stabilization.

Three series of treatments were conducted two weeks apart. The first series excluded chloramphenicol pretreatment hence served as control. In the treatment chloramphenicol was administered 15 min prior to xylazine administration; while in the third treatment chloramphenicol was administered for 5 days (once daily) and xylazine administered on the 6th day. Prior to each treatment, the goats were starved of food but not water for about 18 h.

In all the series of treatments rectal temperature, heart rate, respiratory rate and blood samples from the jugular vein were taken before administration of xylazine and at 30, 60, 120, 180 and 240 min after xylazine administration using 5 mL syringe 21-gauge needle. The blood samples were collected in EDTA bottles and used to determine the packed cell volume, haemoglobin concentration, white blood cells and differential counts as described by McCurnin and Bassert (2002). Onset and duration of action were taken and the sedative and recovery qualities were recorded for xylazine sedation (Ko *et al*., 1996).

The data obtained were summarized as means with standard deviations or errors of means and comparison of means was done by one-way ANOVA with Least Significant Difference (LSD) at the probability of 5% (Petrie and Watson, 2002).

RESULTS AND DISCUSSION

The blood and fecal analyses conducted were negative for haemoparasites and helminthes ova. The duration of action was prolonged for T_2 and T_3 as compared to T_1 and it was significantly different using one-way ANOVA while the onset of action decrease slightly between T_1 and T_3 as shown in Table 1.

The mean of respiratory rate decreased between the T_1 and T_2 though not significant ($p<0.05$) and the heart rate also changed between all the treatments while the mean temperature rate has no significant difference as shown in Table 2.

Table 3 shows the mean haemoglobin concentration, packed cell volume and white blood cell count. The haemoglobin concentration decreased significantly between 120 and 240 min for T_1 and at 30 and 240 min for T_2 while at all intervals for T_3 except at 120 min.

Table 1: Onset and duration of action of xylazine sedation

Statistical analysis	T_1		T_2		T_3	
	OA	DA	OA	DA	OA	DA
X	3.33	83.16[a]	3.10	129.00[a]	2.66	157.83[a]
SD	0.51	10.95	0.54	1.78	0.51	4.99
SEM	0.21	4.47	0.22	0.73	0.21	2.04
LSD	NS	12.26	NS	12.26	NS	22.00

OA: Onset of action (min), DA: Duration of action (min), T_1: Xylazine 0.2 mg kg^{-1} I.M, T_2: Xylazine 0.2 mg kg^{-1} I.M.15 min after chloramphenicol 50 mg kg^{-1} I.M, T_3: Xylazine 0.2 mg kg^{-1} I.M. after 5 days chloramphenicol 50 mg kg^{-1} I.M. pretreatment daily, X: Mean, SD: Standard Deviation, SEM: Standard mean of error, LSD: Least significant difference of 5%, [a]Superscript [a]signifies significant difference, NS: Not significant

Table 2: Respiratory rate, heart rate, and rectal temperature changes after xylazine singly or with chloramphenicol pretreatment

Time after injection (min)	T_1			T_2			T_3		
	RR	HR	RT	RR	HR	RT	RR	HR	RT
0	27.16±2.56	80.50±1.87	39.55±0.28	22.00±3.09	81.00±2.89	39.48±0.27	27.50±1.97	79.83±2.04	39.45±0.10
30	14.16±5.30	64.83±8.54	39.50±0.27	17.33±5.46	62.33±6.74	39.30±0.22	16.83±5.60	57.33±8.64	38.85±0.50
60	16.00±4.38	68.00±5.05	39.13±0.51	13.50±2.94	63.00±7.12	38.75±0.43	14.66±3.26	62.66±9.68	38.55±0.60
120	18.33±1.96	74.00±3.34	38.30±0.68	16.33±2.65	64.66±5.88	38.00±0.27	16.66±3.93	64.00±9.12	38.36±0.59
180	22.00±2.19	77.50±3.20	38.18±0.72	19.00±1.67	70.00±5.51	37.71±0.49	18.66±4.13	66.66±9.00	38.41±0.54
240	24.33±0.81	78.66±3.01	38.65±0.45	23.66±1.96	74.33±5.12	37.68±0.76	20.00±2.53	68.66±5.88	38.35±0.65
X	20.33	73.91	38.89	19.47	69.22	38.49	19.05	66.52	38.66
SD	5.02	6.26	0.60	4.99	7.38	0.80	4.52	7.58	0.43
SEM	2.05	2.56	0.24	2.04	3.01	0.33	1.85	3.09	0.17
LSD	NS	NS	NS	NS	NS	NS	NS	NS	NS

RR: Respiratory rate (cycles min^{-1}), HR: Heart rate (beats min^{-1}), RT: Rectal temperature (°C), NS: Non significant

Table 3: Haemoglobin concentration, packed cell volume and white blood cells changes after xylazine singly or with chloramphenicol pretreatment

Time after	T_1			T_2			T_3		
injection (min)	HG	PCV	WBC	HG	PCV	WBC	HG	PCV	WBC
0	12.53±1.37	32.96±3.73	15.55±1.72	12.36±0.32	32.76±3.43	15.63±0.89	12.23±0.46	32.70±2.97	15.68±1.02
30	12.28±1.90	31.20±1.75	15.90±1.52[a]	9.96±1.39[a`]	30.58±3.30	16.78±1.52[a]	9.46±0.41[a]	30.91±1.25	17.18±1.60[a]
60	11.76±2.26	28.60±3.76	16.78±1.07[a]	10.48±2.13	31.63±4.82	16.45±0.78[a]	9.23±0.28[a]	29.81±10.98	17.61±1.39[a]
120	11.63±1.60[a]	30.41±2.03	15.90±1.17	10.73±1.59	31.85±1.72	16.85±0.85[a]	9.20±0.46	29.38±0.91	17.72±0.99[a`]
180	12.66±1.60	34.11±3.71	16.35±1.81[a]	10.36±1.69	30.75±3.08	16.75±0.98[a]	9.03±0.52[a]	29.30±1.81	18.06±0.82[a]
240	12.08±1.41[a]	32.15±1.95	16.90±1.32[a]	9.35±1.11[a]	29.38±3.20	17.41±0.48[a]	8.91±0.64[a]	28.80±1.11	18.11±0.58[a]
X	12.16	31.57	16.23	10.54	31.16`	16.64	9.69	30.15	17.39
SD	0.41	1.95	0.54	1.01	1.18	0.59	1.30	1.44	0.90
SEM	0.17	0.80	0.22	0.41	0.48	0.24	0.53	0.59	0.37
LSD	6.75	NS	7.7	6.75	NS	5.8	6.86	NS	5.8

HG: Haemoglobin concentration (g dL^{-1}), PCV: Packed cell volume (%), WBC: White blood cells (μL^{-1})

Table 4: Granulocytes, agranulocytes and platelets changes after xylazine singly or with chloramphenicol pretreatment

Time after	T_1			T_2			T_3		
injection (min^{-1})	GR	AGR	PLT	GR	AGR	PLT	GR	AGR	PLT
0	57.33±12.22	42.66±12.22	235.83±82.33	58.33±6.53	42.50±8.00	237.66±67.60	57.16±6.30	42.83±8.93	238.00±67.70
30	49.50±8.04	50.50±8.04	244.83±119.54	44.50±12.17	53.83±8.88	278.66±89.54	52.66±15.26	47.33±15.72	332.83±62.77
60	47.66±16.03	50.66±13.23	288.83±89.21	50.00±12.26	5.00±12.16	302.16±98.26	55.16±16.60	48.16±12.26	321.16±64.87
120	45.30±12.61	53.00±9.29	286.83±42.36	44.66±18.08	56.33±12.12	315.50±77.13	52.16±13.16	47.83±13.16	321.66±46.65
180	58.50±8.78	41.50±8.78	330.66±77.01	53.16±13.74	46.83±13.74	263.83±66.48	51.33±11.82	48.66±11.82	302.66±60.02
240	52.50±11.50	47.50±11.50	306.00±76.30	60.00±19.33	40.33±19.19	233.33±82.81	53.50±15.56	48.16±11.87	294.16±59.86
X	51.80	47.64	282.16	51.77	48.30	271.86	53.66	47.16	301.74
SD	5.30	4.66	36.13	6.62	6.28	33.43	2.15	2.17	34.24
SEM	2.16	1.90	14.75	2.70	2.56	13.64	0.88	0.88	13.97
LSD	NS	NS	NS	NS	NS	NS	NS	NS	NS

R: Granulocytes (%), AGR: Agranulocytes (%), PLT: Platelets (μL^{-1}), NS: Not significant

Table 5: Sedative quality and recovery quality changes after xylazine singly or with chloramphenicol pretreatment

Time after	T_1		T_2		T_3	
injection (min^{-1})	SQ	RQ	SQ	RQ	SQ	RQ
0	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00
30	3.00±0.00	0.00±0.00	3.00±0.00	0.00±0.00	3.00±0.00	0.00±0.00
60	2.50±0.54	0.00±0.00	2.50±0.54	0.00±0.00	2.66±0.51	0.00±0.00
120	1.00±0.00	3.00±0.00	1.00±0.00	2.33±0.51	1.83±0.40	1.66±0.51
180	0.00±0.00	3.00±0.00	0.00±0.00	3.00±0.00	0.00±0.00	3.00±0.00
240	0.00±0.00	3.00±0.00	0.00±0.00	3.00±0.00	0.00±0.00	3.00±0.00
X	1.08	1.50	1.08	1.39	1.25	1.28
SD	1.36	1.64	1.36	1.54	1.42	1.48
SEM	0.55	0.67	0.55	0.63	0.58	0.60
LSD	NS	NS	NS	NS	NS	NS

SQ: Sedative quality, RQ: Recovery quality, NS: Non significant

The packed cell volume shows no significant difference for all treatments. The mean white blood cells increase significantly in all treatments except at 120 min in T_1. There were no significant changes in the mean values of granulocytes, agranulocytes and platelets in all the treatments, though there are slight changes as shown in Table 4. The mean sedative quality is about the same except for T_3 at 120 min. while the recovery quality decreased for T_2 and T_3 as compared to T_1 as shown on Table 5.

Clinical manifestations observed in all the goats were profuse salivation, bleating, flexing of the neck and polyuria.

The onset of sedation of xylazine was 3.33 min for the first treatment, 3.10 and 2.66 min for the second and third treatments, respectively. The decrease in the onset of action was not significant using the one-way ANOVA for T_2 and T_3 but slightly lower for T_3. This is in agreement with Adetunji and Adewumi (1990) who found out that chloramphenicol do not interfere with the onset of action of xylazine. The duration of action of xylazine however was prolonged and it can be deduced that chloramphenicol tends to prolong the effect of xylazine sedation.

Chloramphenicol, is known to be a cytochrome P-450 inhibitor and retard the biotransformation of several drugs in mice and man (Prescott, 1993). Interaction between chloramphenicol and other concurrently administered drugs has been recognized. It is known to prolong pentobarbital anaesthesia in dogs, cats and mice (Adams *et al.*, 1977) and recumbency time after thiamylal in horses (Burrows *et al*, 1989). These effects are through

inhibition of the metabolic activity of several isoenzymes of the cytochrome P-450 complex (Mandsager *et al*, 1995; Adetunji and Adewumi, 1990).

There was a significant decrease in the haemoglobin concentration after the administration of xylazine, which was significantly ($p<0.05$) different at 120 and 240 min, respectively for the first treatment. In the second treatment there was also decrease in haemoglobin concentration at 30 and 240 min while in the third treatment at 30, 60, 180 and 240 min post xylazine administration. Likewise, there was no significant changes in the PCV values obtained and this is contrary to Mohammed *et al*. (2001) that observed decrease in PCV values in Sahelian goats. Decrease in PCV values of animals under xylazine sedation has been attributed to increase pooling of blood into the spleen (Mohammed *et al*., 2001). Chloramphenicol is also known to suppress the bone marrow and the most common form is the dose related suppression of the bone marrow precursor erythroid series (Adams, 2001).

The white blood cells showed a significant increase ($p<0.05$) at all the intervals for all treatments except at 120 min for the first treatment. Xylazine has been reported to decrease the white blood cells count in camel (Mohammed *et al*., 2001) but there were scanty information on the effect of the sedative on the white blood cells count of small ruminants.

The ruminal motility drastically decreased 30 to 60 min post administration of xylazine in all the three treatments. The motility returns to normal at 120 min. It has been observed that the ruminal motility decreased at 20-50 min post injection of xylazine in other ruminants (Mohammed and Yelwa, 1993). Decrease in ruminal motility may interfere with eructation and cause secondary ruminal tympany and free gas bloat (Radostits *et al*., 1997).

In all the treatments, there was a loss of sensation to pin prick, pronounced salivation and polyuria. The polyuria could be as a result of the prolonged hyperglycemia due to reduction in glucose utilization and can persist for 150 min post injection (Mohammed and Yelwa, 1993).

The recovery from sedation was uncomplicated in this study, this may as a result of withholding of feed prior to administration of the sedative agent. Complications such as bloat, regurgitation of ruminal content and aspiration pneumonia are common observations in administration of xylazine in cattle (Adams, 2001).

The prolong duration of sedation may be suggestive of inhibition of the microsomal drug-metabolising enzyme system of the liver that tend to inactivate xylazine (Adams, 2001).

Antibacterial drugs are generally selected primarily on the basis of broad spectrum activity against, availability and affordability, which may lead to indiscriminate usage resulting in drug resistance and potentiating the activities of other drugs used concurrently (Prescott *et al*., 2000).

It is therefore, advisable for clinicians to find out as much as possible about the history of drugs used before xylazine administration, so as to guide in the rational use of drugs and to prevent unwarranted complications during surgical procedures.

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