EVALUATION OF CARDIOPULMONARY, HAEMATOLOGICAL AND BIOCHEMICAL RESPONSES OF CHLORPROMAZINE OR CHLORPROMAZINE-PENTAZOCINE SEDATED WEST AFRICAN DWARF GOATS

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ABSTRACT

Goats respond to pain and often require chemical restraints for veterinary procedures. Information regarding the cardiopulmonary, haematological and biochemical effects of chlorpromazine (CPZ) or chlorpromazine-pentazocine (CPZ-PTZ) in West African Dwarf (WAD) goats has not been fully established. The study aimed to evaluate the cardiopulmonary, haematological and biochemical responses of WAD goats following sedation with either CPZ alone or a combination of CPZ-PTZ. Six healthy adult WAD bucks were randomly selected for two separate experiments using CPZ or CPZ-PTZ in a prospective crossover trial. Anaesthetic indices were taken. Blood samples were collected before the experiment (0 minutes), 45 minutes, 90 minutes and 24 hours for haematology and serum biochemistry assay. Heart rate (HR), respiratory rate (RR) and rectal temperature (°C) were measured at intervals of 10 minutes for 90 minutes. In between clinical trials, the bucks were given a 14-day break. The duration of recumbency for CPZ (43.00 ± 12.95 minutes) was significantly lower compared to the CPZ-PTZ protocol (46.50 ± 27.32 minutes). Analgesia was recorded in only the CPZ-PTZ group for 41.67 ± 1.75 minutes. The HR was significantly higher ($p<0.05$) in the CPZ-PTZ group than in the CPZ group from 0 to 70 minutes. The CPZ-PTZ protocol was a better one as it did not exert a negative effect on the red blood cells or serum protein compared with CPZ alone in the goats. Haematological, biochemical and cardiopulmonary changes were also evident in the goats. Further research may determine the risk-benefit profile of this anaesthetic regimen.

Keywords: Goats, Sedation, Chlorpromazine, Pentazocine, Anaesthetic, Cardiopulmonary

INTRODUCTION

West African Dwarf (WAD) goats are the most popular small ruminants in West Africa; they are raised exclusively for meat and milk, are a source of flexible financial income and play important socio-cultural roles (Daramola *et al.*, 2005; Abu *et al.,* 2013). They are generally stubborn and the most popular ruminants presented for various clinical procedures (diagnostic, medical and surgical) at veterinary clinics in Nigeria (Eze and Idowu, 2002). Generally, goats are responsive to pain and often vocalise loudly even before being handled. Most goat owners, especially the ones that keep them as pets, prefer paying for tranquilisation or anaesthesia rather than observing them in pain (Abrahamsen, 2012). The goat population is currently increasing and the need for veterinarians to have more suitable drug protocols for restraining and handling goats during various clinical or surgical procedures is imperative for goat health maintenance.

Physical restraint provides a more relaxed patient with better operating conditions. The art and science of proper handling of ruminants can be achieved in the goatery to increase animal comfort and veterinarian/handler safety but also the overall productivity of the farm through proper handling and restraining (Mridha, 2023). General anaesthesia in ruminants is often associated with many side effects, hence the preference for mild sedatives, tranquillizers and analgesics (Clarke *et al*., 2014). Sedation reduces the stress associated with physical restraint and provides a more relaxed patient with better operating conditions.

Sedative classes commonly employed in small ruminants include phenothiazine, benzodiazepine and alpha-2 agonists (Clarke *et al*., 2014; Seddighi and Doherty, 2016). These injectable sedatives can be applied in both field and clinical conditions. Phenothiazine drugs in use are chlorpromazine (CPZ) and acepromazine; they are usually combined with opioids to augment their sedative effects (Nishimura *et al*., 2017). CPZ is a typical neuroleptic and antiemetic drug that produces its effect by post-synaptic blockade at D2, H1 and muscarinic receptors in the mesolimbic pathway (López-Muñoz *et al*., 2005). One of the most common opioids in Nigeria is pentazocine (PTZ). It is the first synthesised mixed agonist-antagonist opioid analgesic introduced into clinical practice and is still commonly used in humans in poor resource environments, though rarely used in veterinary medicine (Kukanich and Wiese, 2015). It has partial agonist activity on mu and delta-opioid receptors and full agonist activity on kappa and sigma-opioid receptors (Tripathi *et al*., 2008). Also, it has minimal side effects at analgesic dose rates and toxic effects only at very high doses (López-Muñoz *et al*., 2005; Riley *et al*., 2010). Both drugs selected for this study are easily available and affordable to veterinarians.

Cardiopulmonary, haematological and biochemical effects of CPZ or chlorpromazine-pentazocine (CPZ-PTZ) combinations in West African Dwarf (WAD) goats have not been fully established. The safe and efficient administration of sedative protocols in veterinary practice involving this breed of goat requires an understanding of these extensive physiological responses. The goal of the current study was to assess and contrast the haemorrhagic, biochemical and cardiopulmonary reactions of West African dwarf goats that were sedated with either PTZ and/or CPZ alone.

MATERIALS AND METHODS

Ethical Approval: This project was carried out following the approval of the Animal Care and Use Research Ethics Committee (ACUREC/UI), University of Ibadan, Nigeria.

Experimental Animal: Six healthy male WAD goats, aged between 1.5 and 2 years, with a mean weight of 10.5 ± 3.0 kg used for the study were purchased from a local goat market in Ibadan, Oyo State, Nigeria. The goats were housed in a communal goat pen at the Faculty of Veterinary Medicine Teaching and Research Farm, University of Ibadan, Nigeria. They were acclimatised for 2 weeks, during which they were fed forage, Guinea grass (*Panicum maximum*), dry cassava peels and cereal-based concentrate. Fresh, clean water was provided *ad libitum*. Before the start of the trials, the goats were judged to be in general healthy condition based on clinical examination and a normal haemogram.

Experimental Design: This research design consisted of prospective, randomised crossover experimental trials carried out on six WAD goats. Based on the drugs employed, two main studies were carried out, each consisting of two trials: CPZ or CPZ-PTZ. The goats were fasted for 12 hours before the commencement of the clinical trials. Each group received either CPZ 2 mg/kg IV (Nawaz, 1981) or CPZ 2 mg/kg plus PTZ 3 mg/kg IM (Mir *et al*., 2000). The goats were rested for 14 days in between clinical trials.

Anaesthetic Indices: Following the injection, the onset of drug action, onset of sedation, onset of analgesia, duration of analgesia, duration of recumbency and time to stand were determined (Ahmad *et al.,* 2013).

Cardiopulmonary and Rectal Temperature Assay: The heart rate (beat/minute), respiratory rate (breath/min) and rectal temperature (°C)

were observed at various intervals: before the injection as a baseline, right after injection (0 min) and at 10, 20, 30, 40, 50, 60, 70, 80 and 90 minutes post-injection of the anaesthetic. Heart rate was assessed with a stethoscope on the lower left side of the thoracic wall, respiratory rate was visually assessed and rectal temperature was measured using a digital thermometer inserted into the rectum.

Haematological and Biochemical Parameters Assay: Blood samples were collected via jugular venipuncture for haematology and serum biochemistry; 1 ml of each was collected into sterile lithium-heparin and plain bottles from the jugular veins before drug administration (baseline), 45 minutes, 90 minutes and 24 hours after drug administration. The blood samples were sent to the pathology laboratory for analysis.

For haematology, complete blood counts (packed cell volume - PCV, haemoglobin - Hb, red blood cell - RBC, white blood cell - WBC, mean cell volume - MCV, mean corpuscular haemoglobin concentration - MCHC and mean corpuscular haemoglobin - MCH) were assessed immediately after blood collection using a haematology analyser (IDEXX VetAutoreader QBC, Westbrook, Maine 04092 United States) (Ode *et al.,* 2017).

For serum biochemistry, blood samples kept in plain bottles were allowed to coagulate. They were then centrifuged (Rotofix 32 A Hettich, Föhrenstrabe 12, 78532 Tuttlingen, Germany) at 1200 × g and 4°C for 20 minutes and the serum was separated and stored at -20°C until biochemical analyses. Serum protein, albumin, globulin, calcium, chlorine, potassium, blood urea nitrogen and creatinine were analysed by a spectrophotometer using Randox Laboratory reagent kits obtained from Randox Laboratories Limited, Ardmore, United Kingdom (Olaogun *et al*., 2023).

Data Analysis: Analysis was carried out using SPSS Version 26 (Software Incorporated, San Diego, CA, USA). Independent t-tests were used to compare the anaesthetic indices between the CPZ and CPZ-PTZ groups, as well as to compare the heart rate, respiratory rate and rectal temperature between CPZ and CPZ-PTZ drug treatment groups. The haematological and serum biochemical data collected on the effects of CPZ and CPZ-PTZ in WAD goats were analysed using a one-way analysis of variance (ANOVA) and a post-hoc (Fisher's LSD) was used to separate significant means. For all statistical comparisons, differences were considered significant at $p<0.05$. The results were presented as means ± standard deviations (SD).

RESULTS

Anaesthetic Indices: The onset of analgesia, duration of analgesia, time of recovery and time to stand in the CPZ-PTZ group were significantly higher ($p<0.05$) than the CPZ group. There was no significant ($p>0.05$) difference between the CPZ-PTZ group and the CPZ group regarding the onset of drug action, onset of sedation, assumption of sternal posture and attempt to stand (Table 1).

Table 1: Anaesthetic indices in the chlorpromazine and chlorpromazine-pentazocine in WAD goats

Anaesthetic index (minutes)	Chlorpromazine	Chlorpromazine-pentazocine
Onset of drug action	3.17 ± 3.37	1.83 ± 2.04
Onset of sedation	3.67 ± 3.20	3.50 ± 2.81
Onset of analgesia	0.00 ± 0.00	18.33 ± 4.97*
Duration of analgesia	0.00 ± 0.00	41.67 ± 1.75*
Assumption of sternal posture	46.67 ± 12.26	50.17 ± 25.43*
Time of recumbency	43.00 ± 12.95	46.50 ± 27.32*
Attempt to stand	28.67 ± 36.05	30.67 ± 22.36
Time to stand	34.67 ± 15.85	44.50 ± 25.74*

** = statistically significant mean at p<0.05 using t-test pairwise comparison, n = 6, tabulated data are Mean ± SD*

Cardiopulmonary Profile: The heart rate at 50 minutes (71.5 ± 3.8 beats/minute) in the CPZ group was significantly lower ($p<0.05$) than the baseline value (90.0 ± 19.7 beats/minute). Also, the heart rate from 0 to 60 minutes in the CPZ group was significantly lower ($p<0.05$) than in the CPZ-PTZ group.

The respiratory rates at 10 minutes (37.5 ± 11.5 breaths/minute) and 50 minutes (36.0 ±

9.9 breaths/minute) in the CPZ group were significantly higher ($p<0.05$) than the baseline value (27.0 ± 3.3 breaths/minute). Also, the respiratory rate at 80 minutes in the CPZ group (28.5 ± 8.2 breaths/minute) was significantly lower ($p<0.05$) than the CPZ-PTZ group (33.0 ± 9.9 breaths/minute), while at 90 minutes, the respiratory rate in the CPZ group (36.0 ± 3.3 breaths/minute) was significantly higher ($p<0.05$) than the CPZ-PTZ group (33.0 ± 9.9 breaths/minute).

Regarding rectal temperature, there was no significant difference ($p>0.05$) within or between the two groups (Table 2).

Haematological and Biochemical Parameters: Concerning haematological responses, the RBC counts at 45 minutes (11.08 ± 1.91 x 10^6 µL) in the CPZ group were significantly lower ($p<0.05$) than the baseline value (11.88 ± 1.8 x 10^6 µL). The MCHC at 45 minutes for both the CPZ group and the CPZ-PTZ group was significantly lower ($p<0.05$) than their baseline values. There was no significant difference ($p>0.05$) between the duration values in the remaining haematological parameters (PCV, Hb, WBC count, platelet count, lymphocytes, neutrophils, monocytes, eosinophils, MCV, MCH and MCHC). There was no significant difference ($p>0.05$) between the groups in all the duration for all the haematological parameters (Table 3).

In terms of biochemical responses, serum protein at 45 minutes (7.38 ± 0.79 g/dL) in the CPZ group was significantly lower ($p<0.05$) than the baseline value (7.85 ± 0.93 g/dL). Albumin at 45 minutes (3.07 ± 0.33 g/dL) in the CPZ group was significantly lower ($p<0.05$) than the baseline value (3.37 ± 0.55 g/dL). Calcium at 45 minutes (9.98 ± 1.30 mmol/L) in the CPZ group was significantly lower ($p<0.05$) than the baseline value (10.6 ± 1.39 mmol/L). Chlorine at 45 minutes (103.07 ± 9.62 mmol/L) in the CPZ group was significantly lower ($p<0.05$) than the baseline value (108.87 ± 7.82 mmol/L). Blood urea nitrogen at 45 minutes (15.63 ± 6.25 mg/dL) in the CPZ group was significantly lower ($p<0.05$) than the baseline value (16.65 ± 7.11 mg/dL). There was no significant difference ($p>0.05$) between the duration values in the remaining biochemical parameters (globulin, albumin/globulin ratio, potassium and creatinine). There was no significant difference ($p>0.05$) between the groups in all the duration for all the haematological parameters (Table 4).

DISCUSSION

The use of sedatives in goats is imperative for chemical restraints to facilitate humane handling during most clinical procedures (Seddighi and Doherty, 2016). However, some of these sedatives have been reported to be associated with untoward systemic effects in ruminants (Clarke *et al.*, 2014). This work was designed to compare the cardiopulmonary, haematological and biochemical effects of CPZ or the CPZ-PTZ combination in WAD goats. Handling and restraining are crucial parts of overall health maintenance and successful goat farming (Mridha, 2023). This study prompted several reasons for restraining goats, including physical or clinical examination for diagnosis, medical and surgical procedures and transportation (Fabini and Ducharme, 2016). The results of this investigation showed that CPZ alone and CPZ-PTZ administration elicited decreased spontaneous motor activities accompanied by ataxia; this corroborates with similar observation in a previous study by Nawaz (1981) and Bruss (1982) after administering CPZ to goats. In this study, goats were fasted before the administration of CPZ and PTZ to avoid the possibility of ruminal content regurgitation and aspiration of stomach contents into the lungs (Hendrickson, 2013). No side effects, such as hypersalivation, were recorded in goats during this research.

Although the phenothiazine class of drugs lacks analgesic properties, they have been reported to be potent sedatives and best used with other drugs such as opioids to achieve a clinically significant effect (Simon *et al.*, 2014; Seddighi and Doherty, 2016; Nishimura *et al.*, 2017). CPZ and PTZ have also been reported to be popular neuroleptanalgesia used for chemical restraint in veterinary practice (Kukanich and Wiese, 2015). In this study, administration of CPZ and PTZ was able to achieve 41.67 ± 1.75 minutes of sedation and analgesia.

Table 2: Physiological parameters of six WAD goats sedated with chlorpromazine (CPZ) or chlorpromazine-pentazocine (CPZ-PTZ) at different time intervals

Time (minutes)	Heart rate (beats/min)		Respiratory rate (breaths/min)		Rectal temperature (°C)	
	CPZ	CPZ-PTZ	CPZ	CPZ-PTZ	CPZ	CPZ-PTZ
Baseline	90.0 ± 19.7	85.5 ± 11.5	27.0 ± 3.3	39.0 ± 13.2	39.8 ± 0.2	38.8 ± 0.6
0	61.5 ± 11.5	87.0 ± 13.2*	36.0 ± 13.1	34.5 ± 4.9	39.9 ± 0.1	38.9 ± 0.5
10	85.5 ± 4.9	105.0 ± 9.9*	37.5 ± 11.5*	42.0 ± 0.0	39.8 ± 0.1	38.8 ± 0.5
20	94.5 ± 11.5	103.5 ± 1.6*	34.5 ± 14.8	39.0 ± 0.0	39.7 ± 0.1	38.8 ± 0.5
30	85.5 ± 1.6	103.5 ± 4.9*	34.5 ± 11.5	37.5 ± 8.2	39.6 ± 0.1	38.7 ± 0.4
40	81.0 ± 6.6	100.5 ± 4.9*	36.0 ± 13.1	39.0 ± 3.3	39.5 ± 0.2	38.7 ± 0.5
50	71.5 ± 3.8	96.0 ± 3.3*	36.0 ± 9.9*	36.0 ± 13.2	39.5 ± 0.2	38.5 ± 0.5
60	75.0 ± 16.4	97.5 ± 4.9*	30.5 ± 10.4	37.5 ± 11.5	39.4 ± 0.3	38.6 ± 0.5
70	78.0 ± 3.3	88.5 ± 8.2*	33.5 ± 7.1	33.0 ± 9.9	39.3 ± 0.3	38.4 ± 0.6
80	82.5 ± 4.9	84.0 ± 9.9	28.5 ± 8.2	33.0 ± 9.9*	39.2 ± 0.4	38.4 ± 0.6
90	82.5 ± 4.9	82.5 ± 8.2	36.0 ± 3.3	33.0 ± 9.9*	39.2 ± 0.4	38.4 ± 0.6

*C = chlorpromazine, CPZ-PTZ = chlorpromazine-pentazocine, * = statistically significant mean at p<0.05 using t-test pairwise comparison, n = 6, tabulated data are Mean ± SD*

Table 3: Haematological parameters of six WAD goats sedated with chlorpromazine (CPZ) or chlorpromazine-pentazocine (CPZ-PTZ) at different time intervals

Indices	Group	Duration (minutes and hours)			
		0 min	45 mins	90 mins	24 hours
PCV (%)	CPZ	26.50 ± 5.09^{ab}	23.67 ± 5.20^{a}	24.17 ± 4.96^{a}	28.50 ± 8.26^{b}
	CPZ-PTZ	26.17 ± 5.98^{ab}	24.83 ± 5.78^{a}	24.67 ± 6.41^{a}	29.8 ± 2.23^{b}
Hb (g/dL)	CPZ	8.68 ± 1.79^{ab}	7.40 ± 1.93^{a}	7.97 ± 1.77^{a}	9.10 ± 2.78^{b}
	CPZ-PTZ	8.57 ± 2.00^{ab}	7.95 ± 1.94^{a}	8.10 ± 2.18^{a}	9.77 ± 0.91^{b}
RBC (x10^{6}µL)	CPZ	11.88 ± 1.80^{b}	11.08 ± 1.91^{a}	11.30 ± 2.11^{a}	12.09 ± 2.36^{b}
	CPZ-PTZ	11.72 ± 2.17^{ab}	11.55 ± 2.60^{a}	11.41 ± 2.59^{a}	12.91 ± 0.41^{b}
WBC (x10^{3}µL)	CPZ	7616.7 ± 5812.9^{c}	5500.0 ± 2159.6^{b}	4641.7 ± 1916.9^{a}	5216.7 ± 1225.4^{b}
	CPZ-PTZ	6600.0 ± 1823.5^{b}	5733.3 ± 1118.8^{a}	5100.0 ± 1224.3^{a}	6475.0 ± 2908.6^{b}
Platelets (µL)	CPZ	127666.7 ± 57922.9^{b}	109666.7 ± 23303.8^{a}	119666.7 ± 34737.1^{ab}	120833.3 ± 38112.6^{ab}
	CPZ-PTZ	127833.3 ± 17826.0^{b}	125666.7 ± 30480.6^{ab}	122000.0 ± 39253.0^{ab}	115000.0 ± 59011.9^{a}
Lymphocytes (%)	CPZ	58.33 ± 7.39^{a}	61.83 ± 8.93^{ab}	61.17 ± 5.98^{ab}	63.17 ± 3.37^{b}
	CPZ-PTZ	63.50 ± 6.32^{b}	62.00 ± 4.34^{ab}	62.17 ± 6.82^{ab}	61.83 ± 4.02^{a}
Neutrophil (%)	CPZ	35.33 ± 6.38^{b}	33.50 ± 7.94^{ab}	33.67 ± 6.31^{ab}	31.17 ± 4.31^{a}
	CPZ-PTZ	32.67 ± 5.75^{a}	33.83 ± 3.66^{b}	33.00 ± 7.45^{ab}	32.67 ± 4.23^{a}
Monocyte (%)	CPZ	2.33 ± 1.03^{ab}	1.67 ± 0.82^{a}	1.67 ± 0.82^{a}	2.50 ± 1.05^{b}
	CPZ-PTZ	2.00 ± 0.89^{a}	2.00 ± 0.89^{a}	2.33 ± 0.82^{a}	2.83 ± 0.41^{a}
Eosinophil (%)	CPZ	4.00 ± 1.67^{a}	3.00 ± 1.79^{a}	3.50 ± 1.64^{a}	3.17 ± 0.98^{a}
	CPZ-PTZ	2.00 ± 1.27^{a}	2.17 ± 1.17^{a}	2.50 ± 1.38^{a}	2.67 ± 1.51^{a}
MCV (fl)	CPZ	22.25 ± 1.85^{a}	21.23 ± 1.44^{a}	21.36 ± 1.15^{a}	22.61 ± 3.41^{a}
	CPZ-PTZ	22.19 ± 1.88^{a}	21.55 ± 1.62^{a}	21.51 ± 1.41^{a}	23.09 ± 1.18^{a}
MCHC (%)	CPZ	32.67 ± 1.36^{a}	31.00 ± 1.47^{b}	32.84 ± 1.34^{a}	31.78 ± 1.19^{ab}
	CPZ-PTZ	32.67 ± 1.18^{b}	31.91 ± 0.82^{a}	32.69 ± 1.05^{b}	32.71 ± 0.67^{b}
MCH (pg)	CPZ	7.26 ± 0.60^{ab}	6.59 ± 0.74^{a}	7.01 ± 0.36^{ab}	7.36 ± 1.17^{b}
	CPZ-PTZ	7.25 ± 0.62^{ab}	6.87 ± 0.49^{a}	7.03 ± 0.48^{ab}	7.56 ± 0.52^{b}

*CPZ = chlorpromazine, CPZ-PTZ = chlorpromazine-pentazocine, PCV = packed cell volume, Hb = haemoglobin, RBC = red blood cell, WBC = white blood cell, MCV = mean cell volume, MCHC = mean corpuscular haemoglobin concentration, MCH = mean corpuscular haemoglobin, mins = minutes, ^{abc} = mean values with different letter superscript on a row (duration) are significantly different (p<0.05), * = statistically significant mean at p<0.05 using t-test pairwise comparison (CPZ vs CPZ-PTZ), tabulated data are Mean ± SD*

Table 4: Metabolic parameters of six WAD goats sedated with chlorpromazine (CPZ) or chlorpromazine-pentazocine (CPZ-PTZ) at different time intervals

Indices	Group	Duration (minutes and hours)			
		0 min	45 mins	90 mins	24 hours
Serum protein (g/dL)	CPZ	7.85 ± 0.93^{b}	7.38 ± 0.79^{a}	7.53 ± 1.03^{ab}	7.92 ± 0.64^{b}
	CPZ-PTZ	7.55 ± 0.76^{ab}	7.32 ± 0.92^{a}	7.22 ± 0.76^{a}	8.02 ± 0.39^{b}
Albumin (g/dL)	CPZ	3.37 ± 0.55^{b}	3.07 ± 0.33^{a}	3.15 ± 0.43^{ab}	3.18 ± 0.32^{b}
	CPZ-PTZ	3.13 ± 0.34^{ab}	3.07 ± 0.36^{ab}	2.93 ± 0.23^{a}	3.18 ± 0.19^{b}
Globulin (g/dL)	CPZ	4.48 ± 0.46^{ab}	4.32 ± 0.47^{a}	4.38 ± 0.61^{a}	4.73 ± 0.43^{b}
	CPZ-PTZ	4.42 ± 0.55^{ab}	4.25 ± 0.61^{a}	4.28 ± 0.56^{a}	4.83 ± 0.44^{b}
A-G ratio	CPZ	0.75 ± 0.09^{ab}	0.71 ± 0.02^{a}	0.72 ± 0.03^{a}	0.67 ± 0.07^{a}
	CPZ-PTZ	0.72 ± 0.08^{ab}	0.73 ± 0.06^{a}	0.69 ± 0.05^{b}	0.67 ± 0.09^{b}
Calcium (mmol/L)	CPZ	10.6 ± 1.39^{b}	9.98 ± 1.30^{a}	10.50 ± 1.49^{b}	11.33 ± 1.28^{b}
	CPZ-PTZ	10.88 ± 0.89^{a}	10.38 ± 1.21^{a}	10.18 ± 0.93^{a}	11.42 ± 0.83^{a}
Chlorine (mmol/L)	CPZ	108.87 ± 7.82^{bc}	103.07 ± 9.62^{a}	105.30 ± 14.22^{ac}	110.87 ± 6.77^{b}
	CPZ-PTZ	109.00 ± 9.32^{ab}	104.50 ± 12.87^{a}	103.83 ± 9.95^{a}	112.50 ± 6.15^{b}
Potassium (mmol/L)	CPZ	5.88 ± 2.00^{ab}	4.97 ± 1.38^{a}	5.43 ± 1.81^{a}	6.48 ± 1.47^{b}
	CPZ-PTZ	6.15 ± 1.55^{ab}	5.72 ± 1.83^{a}	5.07 ± 1.62^{a}	7.22 ± 0.55^{b}
BUN (mg/dL)	CPZ	16.65 ± 7.11^{b}	15.63 ± 6.25^{a}	16.42 ± 6.86^{b}	17.15 ± 3.36^{b}
	CPZ-PTZ	17.32 ± 1.39^{ab}	16.33 ± 2.61^{a}	16.17 ± 1.70^{a}	16.90 ± 1.78^{a}
Creatinine(mg/dL)	CPZ	1.95 ± 0.99^{ab}	1.55 ± 0.59a	1.73 ± 0.75^{a}	2.55 ± 0.86^{b}
	CPZ-PTZ	1.85 ± 0.86^{ab}	1.60 ± 0.97^{a}	1.68 ± 0.98^{a}	1.95 ± 0.56^{b}

*CPZ = chlorpromazine, CPZ-*PTZ *= chlorpromazine-pentazocine, BUN = blood urea nitrogen, A-G ratio = albumin-globulin ratio, mins = minutes, ^{abc} = mean values with different letter superscript on a row (duration) are significantly different (p<0.05), * = statistically significant mean at p<0.05 using t-test pairwise comparison (CPZ vs CPZ-PTZ), tabulated data are Mean ± SD*

This period should be sufficient for proper handling and restraining needed for various routine procedures carried out on farm animals, especially goats (Mridha, 2023). The reported half-life of CPZ was 1.51 hours in goats, which is shorter than the half-life values of the drug in other species (Nawaz, 1981). In this study, the total duration of recumbency in goats administered with CPZ alone was 43.00 ± 12.95 minutes and 46.50 ± 27.32 minutes in the CPZ-PTZ protocol, respectively. Also, the time to stand in the CPZ alone group was significantly shorter (p<0.05) compared to the CPZ-PTZ group; this implies that procedures with longer duration should consider using the CPZ-PTZ protocol.

The physiological parameters in this study surprisingly recorded significantly elevated (p<0.05) heart rate in the CPZ-PTZ protocol compared with CPZ alone. The mechanism of action of this drug combination effect on the heart rate was not well understood, as very limited work has been done in goats, but this may probably be the effect of PTZ, which is an agonist-antagonist opioid (Brogden *et al*., 1973). In a previous study in animals administered PTZ, there were elevated plasma catecholamine levels, indicating that PTZ-induced circulatory alterations may be caused by an increase in sympathetic activity, thus a slightly increased heart rate (Brogden *et al*., 1973; Kukanich and Wiese, 2015). Also in this study, the respiratory rate was significantly higher (p<0.05) at 10 minutes in the CPZ-PTZ trial compared with the CPZ-only trial. This corroborates a previous report by Mortola and Lanthier (2005) which established the unique breathing frequency of ruminants in the resting phase which exceeds the value expected for their body weight. This report concluded that high breathing frequency in ruminants especially cattle is a result of response to the elastic load imposed on the respiratory system by the rumen. In this study, there can be no reason to assume that PTZ causes less respiratory depression than an equianalgesic dose of morphine when this is compared with estimations of relative analgesic properties (Brogden *et al.,* 1973; Zaig *et al.,* 2021). Consequently, with deep sedation, any alteration in the respiratory rate of tidal volume will have a major effect on the respiratory system (Clarke *et al*., 2014). The rectal temperature recorded throughout both clinical trials did not show any significant difference and at no point was hypothermia recorded.

Considering the PCV, there was a slight difference between the two treatment protocols, due to the significant decrease in RBC with CPZ at 45 minutes. It has been reported that RBC in

goats is smaller in size compared to those of other species and when determined using automatic apparatus, they are known to produce false values (Adili *et al.,* 2016; Arfuso *et al*., 2016). The findings from this study suggest that the goats should be closely monitored, especially at 45 minutes, as this may probably have an impact on gas exchange, leading to hypoxia. It has been reported in previous studies in goats, that determination of haematological indices is very important for monitoring metabolism and health status. Hence, CPZ-PTZ administration tends to be a better protocol as it does not impact the RBC when compared with CPZ alone in the goats. This agrees with Shimada and Yamagata (2018) where PTZ administration induced kindling in mouse models. Also, both treatment protocols influenced the MCHC, although this may not be too risky in clinically healthy goats, morbid goat patients may be closely monitored (Rai *et al*., 2020).

The reduction in serum protein and albumin for CPZ suggests that the drug may probably suppress liver activities, but these changes were not seen with the CPZ-PTZ treatment protocol. Thus, it suggests that CPZ-PTZ is better adapted to goats (Nawaz, 1979). The significant decrease in calcium and chlorine further suggests that there may be a disruption of metabolism involving calcium and chlorine (metabolic disorder) with CPZ alone administration, whereas there was no such metabolic disorder recorded with CPZ-PTZ administration (Tinawi, 2021).

Conclusion: This study was able to establish that both drug protocols used for this study produced an appreciable duration of analgesia in goats, which is highly desirable for handling and restraining various procedures. Although CPZ and PTZ produced analgesic effects, which can be used for handling painful procedures, this combination was associated with an unusually elevated heart rate and respiratory rate. Goats with cardiovascular diseases may be exempted from this protocol in clinical practice. The duration of recumbency recorded in both protocols was less than an hour; hence, procedures that require a long duration of action may consider sedatives with a longer duration of action. Also in this study, the CPZ-PTZ protocol was better as it did not exert a negative effect on the RBC or TP compared with CPZ alone in the goats. Both protocols influenced the MCHC; this may require monitoring in clinically morbid goats. It might be necessary to do further research to determine the full risk-benefit profile of this anaesthetic regimen.

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REFERENCES

ABRAHAMSEN, E. J. (2012). Chemical restraint and injectable anesthesia of ruminants. *The Veterinary Clinics of North America: Food Animal Practice*, 29(1): 209 – 227.

ABU, A. H., MHOMHA, L. I. and AKOGWU, E. I. (2013). Assessment of udder characteristics of West African Dwarf (WAD) goats reared under different management systems in Makurdi, Benue State, Nigeria. *African Journal of Agricultural Research*, 8(25): 3255 – 3258.

ADILI, N., MELIZI, M. and BELABBAS, H. (2016). Species determination using the red blood cell morphometry in domestic animals. *Veterinary World*, 9(9): 960 – 963.

AHMAD, R. A., KINJAVDEKAR, P., AITHAL, H. P., PAWDE, A. M. and KUMAR, D. (2013). Potential use of dexmedetomidine for different levels of sedation, analgesia and anaesthesia in dogs. *Veterinarni Medicina*, 58(2): 87 – 95.

ARFUSO, F., FAZIO, F., RIZZO, M., MARAFIOTI, S., ZANGHÌ, E. and PICCIONE, G. (2016). Factors affecting the hematological parameters in different goat breeds from Italy. *Annals of Animal Science*, 16(3): 743 – 757.

BROGDEN, R. N., SPEIGHT, T. M. and AVERY, G. S. (1973). Pentazocine: a review of its pharmacological properties, therapeutic efficacy and dependence liability. *Drugs*, 5(1): 6 – 91.

BRUSS, M. L. (1982). Effects of chlorpromazine on plasma glucose kinetics and concentration of long chain fatty acids in sheep. *General Pharmacology*, 13(5): 421 – 426.

CLARKE, K. W., TRIM, C. M. and HALL, L. W. (2014). Anaesthesia of sheep, goats and other herbivores. Pages 345 – 383. *In:* CLARKE, K. W., TRIM, C. M. and HALL, L. W. (Eds.). *Veterinary Anaesthesia*. 11th Edition, Saunders Elsevier, Philadelphia, United States.

DARAMOLA, J. O., ADELOYE, A. A., FATOBA, T. A. and, A. O. (2005). Haematological and biochemical parameters of West African Dwarf goats. *Livestock Research for Rural Development*, 17(8): 95. http://lrrd.cipav.org.co/lrrd17/8/daracit.htm

EZE, C. A. and IDOWU, O. S. (2002). Distribution of surgical cases at the University of Nigeria Veterinary Teaching Hospital (1985 – 1995). *Tropical Veterinarian*, 20(1): 52 – 56.

FABINI, S. L. and DUCHARME, N. G. (2016). *Farm Animal Surgery*. 2nd Edition, Saunders, St Louis, United States.

HENDRICKSON, D. A. (2013). *Techniques in Large Animal Surgery*. 3rd Edition, John Wiley and Sons, Hoboken, New Jersey, USA.

KUKANICH, B. and WIESE, A. J. (2015). Opioids. Pages 207 – 226. *In:* TRANQUILLI, W. J., THURMON, J. C. and GRIMM, K. A. (Eds.). *Lumb and Jones' Veterinary Anesthesia and Analgesia*. John Wiley and Sons, Hoboken, New Jersey, USA.

LÓPEZ-MUÑOZ, F., ALAMO, C., CUENCA, E., SHEN, W. W., CLERVOY, P. and RUBIO, G. (2005). History of the discovery and clinical introduction of chlorpromazine. *Annals of Clinical Psychiatry*, 17(3): 113 – 135.

MIR, S. A., NASKI, A. R. and RAINA, R. (2000). Comparative electrocardiographic studies and differing effects of pentazocine on ECG, heart and respiratory rates in young sheep and goats. *Small Ruminant Research*, 37(1-2): 13 – 17.

MORTOLA, J. P. and LANTHIER, C. (2005). Breathing frequency in ruminants: a comparative analysis with non-ruminant mammals. *Respiratory Physiology and Neurobiology*, 145(2-3): 265 – 277.

MRIDHA, F. (2023). Handling and restraining of goats. Pages 21 – 32. *In:* RANA, T. (Ed.). *Principles of Goat Disease and Prevention*. John Wiley and Sons, Hoboken, New Jersey, USA.

NAWAZ M. (1979). Spectrofluorometric assay of chlorpromazine, half-life and pharmacokinetics of chlorpromazine in goats of different ages. *Nordisk Veterinaermedicin*, 31(3): 129 – 136.

NAWAZ, M. (1981). Pharmacokinetics and dosage of chlorpromazine in goats. *Journal of Veterinary Pharmacology and Therapeutics,* 4(2): 157 – 163.

NISHIMURA, L. T., VILLELA, I. O. J., CARVALHO, L. L., BORGES, L. P. B., SILVA, M. A. M. and MATTOS-JUNIOR, E. (2017). The effect of acepromazine alone or in combination with methadone, morphine, or tramadol on sedation and selected cardiopulmonary variables in sheep. *Veterinary Medicine International*, 2017: 7507616. https://doi.org/10.1155/2017/7507616

ODE, S. A., ADAMU, M. and SAROR, D. I. (2017). Determination of haematocrit using Mindray BC-2800Vet® automated haematology analyser and microhaematocrit method: a comparative study. *Sokoto Journal of Veterinary Sciences*, 15(2): 62 – 65.

OLAOGUN, S. C., AKINNIYI, O. O. and ADEDOKUN, R. A. M. (2023). Clinical, enzymatic and hormonal profile of apparently healthy polo horses in Ibadan Nigeria. *Research Journal of Veterinary Sciences*, 16(1): 01 – 09.

RAI, S., TANAKA, H., SUZUKI, M., ESPINOZA, J. L., KUMODE, T., TANIMURA, A., YOKOTA, T., ORITANI, K., WATANABE, T., KANAKURA, Y. and MATSUMURA, I. (2020). Chlorpromazine eliminates acute myeloid

leukemia cells by perturbing subcellular localization of FLT3-ITD and KIT-D816V. *Nature Communications*, 11(1): 4147. https://doi.org/10.1038/s41467-020-17666-8

RILEY, J. L., HASTIE, B. A., GLOVER, T. L., FILLINGIM, R. B., STAUD, R. and CAMPBELL, C. M. (2010). Cognitive-affective and somatic side effects of morphine and pentazocine: side-effect profiles in healthy adults. *Pain Medicine*, 11(2): 195 – 206.

SEDDIGHI, R. and DOHERTY, T. J. (2016). Field sedation and anesthesia of ruminants. *Veterinary Clinics of North America: Food Animal Practice*, 32(3): 553 – 570.

SHIMADA, T. and YAMAGATA, K. (2018). Pentylenetetrazole-induced kindling mouse model. *Journal of Visualized Experiments (JoVE)*, 136: 56573. https://doi.org/10.3791/56573

SIMON, B. T., SCALLAN, E. M., SIRACUSA, C., HENDERSON, A., SLEEPER, M. M. and MENZIES, M. P. L. (2014). Effects of acepromazine or methadone on midazolam-induced behavioral reactions in dogs. *The Canadian Veterinary Journal*, 55(9), 875 – 885.

TINAWI, M. (2021). Disorders of calcium metabolism: Hypocalcemia and hypercalcemia. *Cureus*, 13(1): e12420. https://doi.org/10.7759/cureus.12420

TRIPATHI, A., KHURSHID, N., KUMAR, P. and IYENGAR, S. (2008). Expression of δ-*and* μ-opioid receptors in the ventricular and subventricular zones of the developing human neocortex. *Neuroscience Research*, 61(3): 257 – 270.

ZAIG, S., DA SILVEIRA SCARPELLINI, C. and MONTANDON, G. (2021). Respiratory depression and analgesia by opioid drugs in freely behaving larval zebrafish. *eLife*, 10: e63407. https://doi.org/10.7554/eLife.63407