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Effects of Diazepam, Lidocaine and Their Combination on Clinical Parameters, Haematological Indices and Electrolytes Profile in the Red Sokoto Goat

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***Target Audience:** Clinicians, handlers, animal health technologists, Animal scientists.*

Abstract

The risks of cardiopulmonary depression, regurgitation, excessive salivation and bloat are the commonest complications associated with general anaesthesia in ruminants. The use of a safer technique of achieving anaesthesia as an alternative must be explored. The safety and effectiveness of epidural anaesthesia make it one of the most frequently used regional anaesthesia techniques for surgical procedures caudal to the umbilicus in ruminant's practice. This study was aimed to evaluate the effects of single intramuscular administration of 0.88mg/kg of diazepam alone and lumbo-sacral epidural injection of a mixture of 7.5mg/kg of lignocaine solution and 0.88mg/kg of diazepam solution in 12 apparently healthy Red Sokoto goats. Changes observed in the Pulse rate (PR), Respiratory rate (RR) and Rectal temperature (RT) were recorded before and after 1 hour of drug administrations. There were no significant effects (P>0.05) on the rectal temperature, although group injected with diazepam alone showed slight increase in temperature. There was slight depression of the respiratory rate with the administrations of diazepam without significant difference. Single administrations of diazepam in combination with lidocaine achieved analgesia lasting for 71±0.3 minutes, as compared with lidocaine alone with analgesia lasting for 58±0.5. The changes observed in the haematological indices and some selected serum electrolytes were statistically insignificant (P>0.05). when baseline values were compared with the treatment group. In conclusion, that epidurally administered lignocaine-diazepam mixture at 7.5mg/kg and 0.88mg/kg respectively had a fast onset of neural blockade, adequate and long duration of analgesia without profound effects on haematological and serum biochemical indices.

***Keywords:** Epidural, Analgesia; Serum electrolyte; Haematological indices Red Sokoto Goat.*

Description of Problem

Diazepam is a popular benzodiazepine derivative for use in different species of animals (1). The drug has a dose-dependent effect (2) and depending on the dose, the drug is a potent tranquillizer in humans and many animal species (3). The drug was reported to have minimal effect on the respiratory system, heart rate, and rectal temperature (4, 5), the drug has good muscle relaxation (6). Two drugs (Diazepam and Chlordiazepam) are popular in this group and extensively used in veterinary medicine. The principal site of central nervous system (CNS) depression produced by diazepam is in the brain stem reticular formation (3).

Clinically, diazepam has been used especially in dogs and cats and sometimes ruminants as an anti-anxiolytic agent and for sedative purposes (7). Diazepam alone at a dosage of 5mg/kg will produce only mild sedation and analgesia in ruminants. It is therefore limited and cannot be relied on for procedures that require prolonged analgesia (9). Diazepam had been combined in previous studies with ketamine and medetomidine and the result was excellent and prolonged anaesthesia and analgesia with good muscle relaxation (9).

Epidural anaesthesia is commonly employed in a wide range of species in Veterinary medicine for a variety of clinical indications that may include diagnostic, obstetrical and surgical interventions (10). The most frequently used epidural anaesthetic is lidocaine which comes in different concentrations, Mepivacaine, Bupivacaine, Butacaine and Procaine are other agents used (11). These agents with the notable exception of bupivacaine, provide analgesia of relatively short duration and may necessitate re-administration to maintain the resultant anaesthesia and analgesia for completion of most procedures. It has been reported too that these agents block motor, sensory and sympathetic fibres (11) resulting in motor dysfunction seen as severe ataxia and recumbency, this is particularly a major disadvantage for surgery (11). It is therefore imperative to explore ways of achieving anaesthesia and analgesia of appreciable duration with combination of drugs with minimal or tolerable effects on vital parameters (Pulse rate (PR), Respiratory rate (RR) and Rectal temperature (RT)), haematological indices (Packed cell volume (PCV),Red blood cells (RBC), White blood cells (WBC), Neutrophils, Lymphocytes, Basophils, Eosinophils, Monocytes, Heamoglobin concentration (Hb), Mean capsular volume (MCV)**)** and serum profile (Sodium **(Na^+)**, Potassium**(K^+)**, Chloride **(Cl^-)**, Bicarbonate **(HCO_3)**) in goats. This study was designed to investigate the compatibility of lidocaine combine with diazepam for anaesthesia and analgesia in Red Sokoto Goat (RSG) and the potential hemodynamical changes such combination will elicit.

Materials and Methods

Experimental animals

Twelve apparently healthy adult Red Sokoto Goats of both sexes (7 bucks and 5 does) were acquired from the Kara Market Sokoto State and used for the experiment. They were divided into three groups of four animals each. The mean age ranges of the purchased goats was 3.00±0.2 years (by their dentition at point of purchase) and average body weight of 18.00±0.3 kg, these goats were housed in the small ruminant pen (4 goats per pen) of the Faculty of Veterinary Medicine, they were allowed to acclimatize to their new environment for two weeks during which Deworming was done with Ivermectin against endo and ectoparasites at 400 μg/kg subcutaneously and 3mIs of multivitamin intramuscularly each. The mean (±SD) baseline values of vital parameters, haematological parameters and selected serum electrolytes were obtained and recorded for each group to serve as the baseline data (control).

Experimental Design and Animal Grouping

Animals were divided into three treatment groups, containing of four goats per group. Group 1 received diazepam intramuscularly administered at 0.8mg/kg. Goats in group 2 were treated with 2% lidocaine at 0.02mg/kg (14) epidurally between the last lumbar and the first sacral vertebrae (L6-S1) as described by (Bigham and Shafiet). Animals were physically restrained on the surgical table while the induction was carried out. While goats in group 3 received diazepam intramuscularly administered at 0.8mg/kg and immediately followed by epidural administration of 2% lidocaine at 0.2mg/kg.

Evaluation of Quality of Analgesia

The quality of analgesia was evaluated using needle prick and loss of pedal reflex (achieved by observing absence of pedal reflex at interdigital space of hind legs) as described by William and Wyatt. The reflex was observed before and after diazepam and diazepam-lidocaine epidural administration.

Hemato-biochemical Parameters

The hematological parameters considered for the analysis included leukocyte count (WBC), mean corpuscular volume (MCV), and differential leucocyte count (neutrophil, lymphocyte, eosinophil, monocyte and basophil).

The calorimetric analysis without deprotenization was used to determine the Sodium, Bicarbonate, Potassium and chloride ions concentration, Biomerieux reagents and methylene blue were used as an indicator as described by (12).

Table 1: The effect of diazeparn, lidocaine and the combination of both drugs on mean serum electrolyte levels and vital parameters in red sokoto goat

Parameters	Control	Diazaepam	Lidocaine	Diazepam+Lidocaine
Sodium (Mmol/L)	146±2.0	140.4±1.3*	142±2.7*	141±2.5*
Potassium (Mmol/L)	4.5±1.8	5.02±0.9	4.41±2.1	4.6±0.3
Chloride (Mmol/L)	102.6±2.3	104±2.6	94±1.6*	98±2.6*
Bicarbonate (Mmol/L)	23.6±2.3	21.2±1.4*	24.4±1.9	21.7±2.5
RT (^{0}C)	38.6±1.3	36.4±0.8*	37.7±1.3	36.2±2.5*
PR (beats/mm)	71±1.5	61±1.5*	63±1.8*	68.6±2.3*
RR(Cycles/min)	23±2.5	17±1.8*	19±2.3*	20±2.1*

*Denotes significant differences between baseline values and the treatment groups (One way Anova; P<0.05). data were reported as mean ±SD

Table 2: Effect of diazepam, lidocaine and the combination of both drugs on hematology in red sokoto goat

Parameters	Control	Diazaepam	Lidocaine	Diazepam+Lidocaine
PCV (%)	28.4±1.3	25±5.5*	26.0±2.3	23.0±0.2*
RBC (x10^{6}/µL)	10.2+0.9	9.7±1.6	9.37±0.5	9.1±1.8
WBC (x10^{3}/µL)	5.8±3.1	8.12±1.6	8.6±2.3	8.23±3.1
Neutrophils (%)	25±2.5	27.6±3.1	38.8±4.8*	34±2.9*
Lymphocytes(%)	66±4.3	63±6.1	56±4.4*	60.4±3.1*
Basophils (%)	01±1.2	0.4±0.8	0.4±0.2	0.2±0.5
Eosinophils (%)	4.6±1.8	3.2±1.2	2.6±1.3*	3.2±2.1
Monocytes (%)	3.2±0.8	3.8+2.8	1.8±1.9	2.2±2.1
Hb (g/dL)	9.4±1.7	8.3±1.3	8.6±0.6	7.6±1.6*
MCV (x10^{-6}/µL)	5.5±4.1	3.3±1.2	27.7±0.4*	25.2±2.7*

***Denotes significant differences between baseline values and the treatment groups (One way Anova; P<0.05). data were reported as mean ±SD**

Baseline Data

Rectal temperature, Respiratory rate, Pulse rate were measured and recorded. A total of 6mls of blood was collected from the left jugular vein and divided into equal parts, one part was stored in a plain bijou bottle and the other part in an EDTA bottle for haematological and serum biochemical analysis before drug administration to form the baseline values.

Data Analysis

Baseline values (Controls) were compared with measured (Test) values by the one-way analysis of variance, treatment means were separated for significance of variation at $P<0.05$ using the least significant difference (LSD) method of mean comparison as contained in Minitab statistical software (13).

Results

Evaluation of Quality of Analgesia

There was complete loss of measured pedal reflex (21) and sensitivity to needle prick. Analgesia of 71±0.3 minutes with lidocaine-diazepam combination and 58±0.5 minute with lidocaine alone were recorded.

Effects on Biochemical Indices

The effects of diazepam and diazepam-lignocaine combination are as presented in table 1.

There was decrease level of serum sodium in all the treatments groups when compared with the baseline values. Significant differences between the baseline serum sodium level with the lignocaine alone and with diazepam-lignocaine combination were observed. There were no significant differences ($P>0.05$) between baseline serum potassium level with any other treatment group. A significant difference in serum chloride level between baseline with lignocaine alone and the combination of diazepam-lignocaine was observed. Whereas a significant difference in baseline serum bicarbonate level with diazepam alone treated groups was also observed (Table 1).

Effects on Vital Parameters

There were significant decreases in rectal temperature, pulse and respiratory rates when treatment groups were compared with baseline data. There were significant differences between baseline vital parameters with all the vital parameters of the treatment groups (Table 1).

Effects on Haematological Indices

There was a significant decrease in PCV between the base line with diazepam alone treatment group and with diazepam and lignocaine combination. There was decrease trend of RBC without significant difference ($P>0.05$) between the baseline values and all the treatment groups. There was slight increase in WBC when baseline data was compared with the treatment group, but it was not significant ($P>0.05$). The neutrophils values significantly increased when treatment groups were compared with baseline data. There were significant differences between neutrophils baseline with lignocaine alone and with diazepam-lignocaine combination. There were significant differences in lymphocyte values between the baseline data with lignocaine alone and with the combination of diazepam-lignocaine. There was no significant difference observed in baseline basophils values when compared to all other treatment groups. There was significant difference of eosinophils values between baseline with lignocaine alone treatment group. There was no significant difference between haemoglobin concentration baseline data with any other treatment group. A significant difference was observed between the baselines of the mean corpuscular volume with the group treated with diazepam-lignocaine group (table 2).

Discussion

The purpose of anaesthesia is to provide reversible unconsciousness, amnesia, analgesia and immobility with minimal risk to the patient (16). One important requirement or advantage of any anaesthetic and analgesic is its ability to exert its effects without serious compromise of the respiratory system, haematological indices and serum electrolytes. Lidocaine has been used extensively in both small and large animals without toxicities to the cardiovascular system; in fact, the drug has been used as an antiarrhythmia (17). In order to avoid complications resulting from general anaesthesia, epidural injection of local anaesthetic agents has widely been used for surgical procedures (18, 19). Investigations also revealed that local anaesthetics when used alone have various side effects, although with excellent analgesic property (20). Most clinicians combine lidocaine and a phenothiazine (Acepromazine/chlorpromazine) or a benzodiapine (Diazepam) derivative for local anesthesia and analgesia for most surgical procedure, lidocaine has also been combined with xylazine with excellent results for surgical procedures (14). There was complete loss of measured pedal reflex (21) and sensitivity to needle prick. Analgesia of 71±0.3 minutes with lidocaine-diazepam combination and 58±0.5 minute with lidocaine alone were recorded.

It is demonstrated from this research that a combination of lidocaine and diazepam is advantageous in Red Sokoto Goats as this combination limited the disadvantages of the individual drugs when used alone (short duration of analgesia). Most importantly, the combination provided good analgesia in the Sokoto Red Goat with limited fluctuations in haematological indices and vital parameters (Pr, Rr T^0) (Table 1). Serum electrolytes were maintained at narrow limits (Table 2) consistent with homeostasis.

The combination however, resulted to a reversible non-life-threatening respiratory depression. Some studies done previously used xylazine to premedicate lidocaine anaesthesia with reported bradycardia, respiratory depression and hypothermia (23).

In our study, sedation with diazepam and epidural administration of the diazepam-lidocaine combination resulted in a significant decrease ($P<0.05$) in the mean rectal temperature, Pulse and respiratory rates which is similar to the work of Kul *et al.,* and Davidson *et.al.,*. The decrease in the rectal temperature has been previously to be attributed to the depression of the hypothalamic thermoregulatory center (26). The significant changes observed in the serum electrolytes in the present study after diazepam and diazeparm-lidocaine combination can be attributed to the depression effects of diazeparm on hypothalamic thermoregulatory center thereby causing frequent urination (26).

The statistically significant decrease observed in the values of the Packed Cell Volume (PCV), Red Blood Cells (RBC) and Haemoglobin concentration (Hb) and the mean corpuscular volume may be the result of pooling of the circulating blood cells to the spleen and other reservoirs secondary to decreased sympathetic activity; this observation has been previously reported in calves (27).

This work has studied the analgesic property of diazepam, lidocaine and advantages of diazepam-lidocaine combination in the Red Sokoto Goats. It gives better result to combine both drugs and it has been demonstrated from this study that the combination only resulted in reversible alterations in vital parameters, haematological indices and some serum electrolyte profiles analyzed, therefore this combination is recommended in this breed.

Conclusion and Applications

1. Synergistic effects of combining Lidocaine and Diazepam resulted in analgesia of 71±0.3 minutes than otherwise 58±0.5 minutes documented using Lidocaine alone. This has promise in selecting safe local anaesthesia for procedures requiring extended period of analgesia. Caesarian section anesthesia and analgesia can be improved with this combination.
2. There was non-lethal and reversible depression of the respiratory system when lidocaine is pre-medicated with diazepam for inducing anesthesia and analgesia.
3. Use of Lidocaine singly and, in combination with diazepam resulted in a statistically insignificant (P>0.05) PCV, RBC and Hb concentration, these were all reversible with complete recovery from anaesthesia.

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