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Serum Cortisol and Glucose Indices Following Rumenotomy in West African Dwarf Goats Premedicated with Xylazine or Diazepam and Inducted with Propofol

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Abstract

Purpose: Anaesthesia was induced in West African Dwarf (WAD) goats using Propofol and a combination of different sedatives, propofol (P), xylazine (X), Propofol (P), and Diazepam (D) and control Propofol (P) and the effects of rumenotomy on cortisol and glucose of West African dwarf goats were determined.

Methodology: Twelve (WAD) goats were randomly assigned to three treatment groups tagged A, B, and C. Rumenotomy was carried out on these animals, premedicated with Xylazine or Diazepam and anaesthetized with Propofol, and data was presented in charts and as (Mean ± SEM).

Findings: Cortisol concentration showed no statistical ($P > 0.05$) difference in group C pre-surgery (14.55 ± 1.34 mg/dL) and up to 96 hours post-rumenotomy (13.45 ± 0.68 mg/dL). In groups A and B, cortisol concentration significantly ($P < 0.05$) increased from pre-surgical value (14.40 ± 1.27; 13.68 ± 1.22 mg/dL) reaching a peak at 24 hours post-rumenotomy (68.85 ± 3.41; 46.63 ± 5.86mg/dL) followed by a significant ($P < 0.05$) decrease at 96 hours post-rumenotomy (33.46 ± 3.58; 13.80 ± 2.65 mg/dL), but these were statistically ($P < 0.05$) higher in group A compared to group B. The glucose concentration was statistically ($P < 0.05$) increased in group A (72.50 ± 3.30; 75.25 ± 5.02 g/dL) compared to groups B (65.50 ± 4.50; 65.50 ± 1.71 g/dL) and C (55.50 ± 2.87; 62.25 ± 8.84 g/dL) at intra-surgery and immediate post-surgery. From 24 and up to 96 hours post-rumenotomy, no statistical difference existed for the glucose concentration in all groups of goats.

Conclusion: The Cortisol and glucose indices increased across the groups which showed that the animals experienced stress during the procedure.

Recommendations: The Cortisol and Glucose indices following rumenotomy showed that the Diazepam-Propofol combination (group B) is preferred because it caused less stress and gave a good plane of anaesthesia in West African Dwarf goats.

Keywords: *Cortisol, Glucose, Xylazine, Diazepam, Propofol*

1.0 INTRODUCTION

The effects of anaesthesia and tissue trauma on bodily activities have long been recognized, perioperative stress arises from the effects of physical and psychological stimuli encountered by a patient undergoing anaesthesia and surgical intervention (Hall 2001). While partly representing perturbations induced to ensure survival, the perioperative stress responses can also adversely affect the host. Detailed knowledge of patients' perioperative statuses is of importance when evaluating the different interventions and when aiming at optimum patient care. The widespread alterations induced in physiological activities and in behavioural and emotional states have collectively been referred to as stress responses to surgery (Desborough, 2000).

Stress is a disruptive event accompanied by predictable biochemical, physiological, cognitive, and behavioral changes that are directed either toward altering the stressful event or accommodating its effects. Surgical stress is "the biological response to factors that alter or threaten homeostasis (Horta *et al*.,2007) The main stressors associated with surgical procedures are physical (e.g., tissue damage, impingement, and perception of pain) and chemical (application of antiseptics to the affected area) factors that promote specific reactions as a compensatory mechanism to prevent secondary damage and increase the availability of the substrates that essential organs require (Yuki *et al*.,2017). This process generates physiological changes that correlate with a stressful state in an animal.

Stress and pain caused by surgery and the risk associated with anesthesia and analgesia are quite challenging to both clinicians and patients (Weledji, 2014). Surgical stress occurs, before, during, and after an operative procedure. It arises from psychological stress, tissue injury, alterations in circulation, anaesthetic agents, and postoperative complications including sepsis (Carey *et al*.,1999). Surgical stress response involves stimulation of the sympathoadrenal medullary and the hypothalamic-pituitary-adrenal axis (Moberg, 2000). Their activation causes endocrine and immunomodulatory changes after trauma (Desbourogh, 2000). The degree of physiological response is proportional to the magnitude of injury with increased demands on organ function (Desbourogh, 2000).

Two different signaling axes have been identified by which mammals mount an integrated physiological response to perceived danger. The response to danger is initiated at the level of the hypothalamus which releases corticotrophin-releasing hormone (CRH) and vasopressin (VP) (Giannoudis, 2006) These hormones transmit a signal to the pituitary gland to initiate the release of adrenocorticotropic hormone (ACTH) which targets the adrenal cortex. This hypothalamic-pituitary-adrenal (HPA) axis initiates one arm of the endocrine response to stress, mediated by the release of glucocorticoids from the adrenal cortex. The second arm of this response is very rapid and involves the sympathetic-adrenal-medullary (SAM) axis, which culminates in the release of catecholamines from the adrenal medulla. The SAM axis initiates the "fight or flight" response that includes an integrated behavioural response to perceived danger or acute stress as well as metabolic and immune responses (Chen *et al*.,2015). The consequences of prolonged exposure to stressors include sensitization to pain, longer post-surgical recovery, and in some cases, sepsis, or delays in healing.

Cortisol is an important steroid hormone secreted by the adrenal cortex and associated with inflammation, carbohydrate metabolism, and stress reaction. Cortisol is a biomarker commonly used for stress evaluation in animals (Beerda *et al*. 1997; Coppola *et al*. 2006; Horvat *et al*. 2007; Haverbeke *et al*. 2008). It offers the advantage of being a sensitive and universally accepted

indicator of stress, easily and inexpensively measurable by commercial kits. Animals respond differently to various kinds of stressors. Plasma cortisol is a useful indicator of stress and muscle damage and data are very limited on responses to surgical stress in veterinary medicine.

Glucose can be employed as a biomarker to assess the hypothalamic–pituitary–adrenal (HPA) axis response to stress However, this metabolite is also influenced by other factors, e.g., feeding and starvation (Mormede *et al*., 2007). Nevertheless, its use in conjunction with cortisol determination may lend additional support to the assessment of the HPA axis response to stress. There is a paucity of data on the level of stress ruminants experience undergoing rumenotomy under different sedatives and anaesthetic agents. This study was carried out to determine Serum cortisol and glucose indices following rumenotomy in West African Dwarf goats premedicated with Xylazine or Diazepam and induced with Propofol.

2.0 METHODOLOGY

Research Location

The research was carried out in the College of Veterinary Medicine, Joseph Sarwuan Tarka University, Makurdi, Benue State, Nigeria. The large animal surgery theater and the large animal pen were used for the surgery and housing of the animals respectively.

Experimental Design

Animals

A total of 12 West African Dwarf goats in the age category of 1-2 years and weighing between 12-14kg were used for the study. The animals were obtained from the international cattle market, North Bank in Makurdi. The animals were preconditioned for a period of 2 weeks, during which routine examination was carried out for any sign of ill health. The animals were fed with groundnut hay and bean husks, and water was provided *ad libitum*. The animals were randomly allocated into three groups of four animals each as A, B, and C

Group A: Rumenotomy was carried out on these animals, premedicated with Xylazine, and anaesthetized with Propofol. Animals were premedicated with xylazine at 0.05mg/kg and given Propofol at 5mg/kg

Group B: Rumenotomy was carried out on these animals which were premedicated with Diazepam and anaesthetized with Propofol. Animals were premedicated with Diazepam at 0.2mg/kg and given Propofol at 5mg/kg.

Group C: Animals served as control and were subjected to rumenotomy under Propofol anaesthesia only. These animals were administered Propofol at 6mg/kg

Surgical Procedure

The goats were fasted for 12 hours for feed and 6 hours for water. The left paralumbar fossa was shaved and the area was prepared aseptically with 0.2% chlorhexidine gluconate (Savlon, Vervaadingdeur, Johnson and Johnson Ltd London), A standard laparotomy incising was made on the upper paralumbar fossa of the flank. The rumen was gently exteriorized out of the incision and firmly anchored to the skin. A ten-centimeter (10cm) incision was made over a less vascularized portion of the rumen with greater curvature and the rumen was explored and foreign materials mostly plastic bags were seen in some of the animals. The edges of the rumen incision were cleaned with 0.9% saline solution, and a double-layer Cushing suture pattern was used to invert the rumen

edges with a number 2 chromic catgut (Lifecare, Anhui Kangning Industries Group Co, Ltd Tianchang City, Anhui, China) The skin was closed using size 2 nylon suture (Lifecare, Anhui Kangning industries group Co, Ltd Tianchang City, Anhui, China) using ford interlocking suture pattern.

Sampling Procedures

Blood

Blood sample (5 mL) was collected through the jugular vein before rumenotomy was carried out to establish preliminary data for all groups. This was accompanied by sampling during the procedure and immediately after the procedures at 0 hr 24 hr, 72 hr, and 96 hr, post-surgery. Furthermore, the blood was emptied into a plain vacutainer tube for serology and kept at room temperature for two hours before centrifuging. After the centrifuging, harvested serum was emptied into a micro vial and stored at -20˚C until it was used for serum cortisol and glucose analysis.

Glucose was determined using a glucometer (Accucheck) while cortisol (Accu Bind) code no 3625-300, Monobind Inc USA was carried out according to the manufacturer's specification.

Assay procedure

i. After the standard was prepared all the standards and samples were added in duplicate to the microplate.
ii. 0.025 ml of the specimen was pipette into the assigned well.
iii. 0.050 ml of the cortisol enzyme reagent was added to all wells.
iv. The microplate was swirled gently for 20-30 seconds to mix
v. 0.050 ml of cortisol biotin reagent was added to all wells
vi. The microplate was swirled gently for 20-30 seconds to mix
vii. The microplate was covered and incubated for 60 minutes at room temperature
viii. The content of the microplate was discarded by decantation.
ix. 0.350ml of buffer was added and later decanted which was repeated two times for a total of three (3) washes.
x. 0.100ml of working substrate solution was added to all wells
xi. It was incubated at room temperature for fifteen (15) minutes
xii. 0.050ml of stop solution was added to each well and gently mixed for 15 seconds.
xiii. The absorbance in each well was read at 450 nm using a microtiter plate reader within 30 minutes of adding the stop solution

Data Analysis

Data obtained was tabulated as the mean and standard error of the mean (Mean ± SEM). One-way ANOVA was used, and the Bonferroni post-Hoc test was used. GraphPad Prism software version 5.0 was used for the analysis $P<0.05$ was statistically significant

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3.0 FINDINGS

Cortisol Concentration

The mean cortisol concentrations of goats pre-medicated with xylazine and/or diazepam and at different periods post-rumenotomy are presented in Figure 1. Cortisol concentration showed no statistical ($P > 0.05$) difference in group C pre-surgery (14.55 ± 1.34 mg/dL) and up to 96 hours post-rumenotomy (13.45 ± 0.68 mg/dL). In groups A and B, cortisol concentration significantly ($P < 0.05$) increased from pre-surgical value (14.40 ± 1.27; 13.68 ± 1.22 mg/dL) reaching a peak at 24 hours post-rumenotomy (68.85 ± 3.41; 46.63 ± 5.86mg/dL) followed by a significant ($P < 0.05$) decrease at 96 hours post-rumenotomy (33.46 ± 3.58; 13.80 ± 2.65 mg/dL), but these were statistically ($P < 0.05$) higher in group A compared to group B.

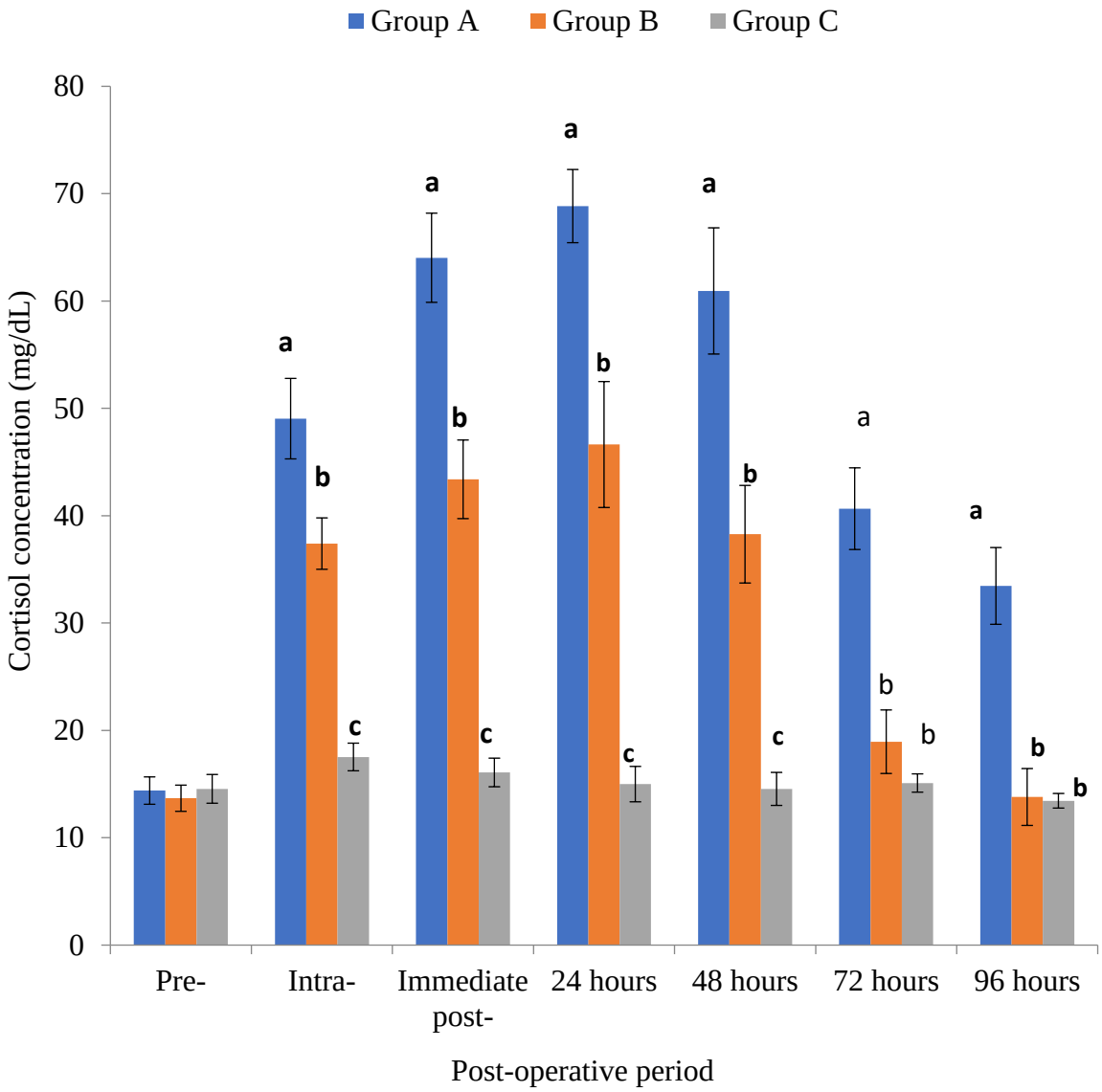

Figure 1: Cortisol concentrations of goats pre-medicated with xylazine and/or diazepam and at different periods post-rumenotomy. Values with different superscript alphabet in the same time differ significantly at $P < 0.05$.

Glucose Concentration

The mean glucose concentrations of goats pre-medicated with xylazine and/or diazepam and at different periods post-rumenotomy are presented in Figure 2. The glucose concentration was statistically ($P < 0.05$) increased in group A (72.50 ± 3.30; 75.25 ± 5.02 g/dL) compared to groups B (65.50 ± 4.50; 65.50 ± 1.71 g/dL) and C (55.50 ± 2.87; 62.25 ± 8.84 g/dL) at intra-surgery and immediate post-surgery. From 24 and up to 96 hours post-rumenotomy, no statistical difference existed for the glucose concentration in all groups of goats.

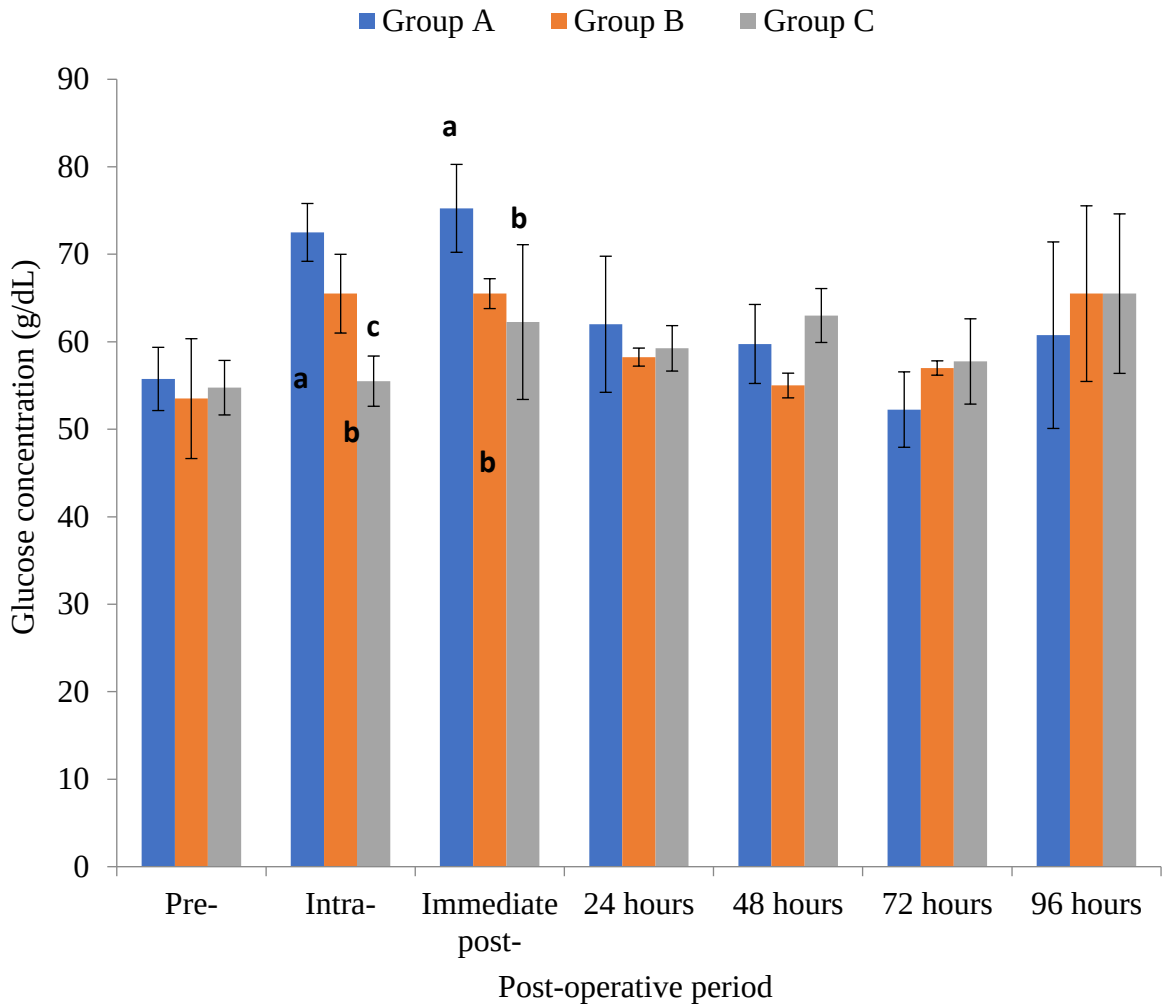

Figure 2: Glucose concentrations of goats pre-medicated with xylazine and/or diazepam and at different periods post-rumenotomy. Values with different superscript alphabet at the same time differ significantly at $P < 0.05$.

Discussion

Stress in an animal can occur because of adverse effects in the environment or management system which forces changes in the animal's physiologic or behavior to avoid physiological malfunctioning and assist the animal in coping with its environment. Stress can also be viewed from the perspective that it is a major aspect of animal welfare and can be assessed using many quantitative physiological variables (Broom,2000).

In groups A and B, cortisol concentration significantly ($P < 0.05$) showed increased value reaching a peak at 24 hours after rumenotomy followed by a significant ($P < 0.05$) decrease at 96 hours post-rumenotomy. This finding agrees with the report of Saidu *et al*., (2016) in Sahel goats who got an increase in cortisol levels after administration of Diazepam-Bupivacaine The possible reason for the increase is that stressors influence the activation of the hypothalamic-pituitary-adrenal axis followed by synthesis of corticotrophin or adrenocorticotrophic hormone (ACTH) by the anterior pituitary. This stimulates adrenal cortical secretion of glucocorticoids leading to increased circulating concentration of cortisol.

Surgery, sedatives, and anaesthetic agents are included in the list of most potent activators of this process among others such as infection, tissue injury, trauma, neoplastic growth, or immunological disorder (Desborough,2000). Psychological and physical factors like anxiety and pain influence the activation of the hypothalamic–pituitary–adrenal axis (HPA) leading to cortisol release; a core mediator of stress response Burton *et al*., (2004) which in turn promotes glycogenolysis and gluconeogenesis resulting in hyperglycemia. The stress-induced cortisol secretion exists so that the body can handle and recuperate after an injury, physical activity, or physiological strain.

The glucose concentration was statistically ($P < 0.05$) increased in group A compared to groups B and C at intra-surgery and immediate post-surgery. There was a significant increase in blood glucose at 0 hours across the groups ($P < 0.05$) but from 24 and up to 96 hours post-rumenotomy, no statistical difference existed for the glucose concentration in all groups of goats. This is because acute pain occurs immediately after an injury or trauma (Kahn, 2005). The post-operative pain elicits a cellular stress response, which diminishes the autonomic, somatic, and endocrine reflexes leading to protein break down which will eventually lead to hyperglyceamia (Kehlet, 1998; Singh, 2003). Also, cortisol and catecholamines facilitate glucose production as a result of increased hepatic glycogenolysis and gluconeogenesis. However, it might have been probably caused by the hyperglyceamia effect of xylazine. Xylazine has been reported to cause temporal hyperglyceamia in cattle and goats.

4.0 CONCLUSION AND RECOMMENDATIONS

Conclusion

The Cortisol and glucose indices increased across the groups which showed that the animals experienced stress during the procedure.

Recommendation

The Cortisol and Glucose indices following rumenotomy revealed that the Diazepam-Propofol combination (group B) is preferred because it caused less stress and gave a good plane of anaesthesia in West African Dwarf goats.

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