Veterinary and Animal Science 14 (2021) 100203

Contents lists available at ScienceDirect

Veterinary and Animal Science

journal homepage: www.elsevier.com/locate/vas

Effects of time on differential leucocyte counts and biochemical parameters of ovariohysterectomy, gastrotomy and intestinal resection and anastomosis in Nigerian indigenous dogs

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ARTICLE INFO

Keywords:
Electrolytes
Creatinine
Lactate
Surgery
Anaesthesia
Leucocytes
Acute kidney injury

ABSTRACT

Differential leucocytes counts and some biochemical parameters could be affected over time by surgical procedures leading to kidney failure. Hence this study evaluates the effects of ovariohysterectomy (OVH), gastrotomy (GAT) and intestinal resection and anastomosis (ITR) on differential leucocyte counts and some biochemical parameters in Nigerian dogs. Twelve dogs of both sexes weighing 10.8±0.7 kg were randomly divided into three experimental groups of four each. The dogs were pre-treated with atropine sulphate (0.04 mg/kg), Xylazine (2 mg/kg) and propofol (6 mg/kg) parenterally, for induction and maintenance of anaesthesia. Pentazocine (3 mg/kg) was injected after surgery. Pre and post-surgery blood samples were obtained at 0, 2, 24, 48, 72, 96, 120 and 144 h respectively to determine differentials in leucocyte counts, electrolytes, lactate, blood urea nitrogen (BUN) and serum creatinine. Mathematical formulas were used to calculate plasma creatinine, creatinine clearance, plasma creatinine clearance, creatinine half- life, urine creatinine and urine volume. There were significant increases ($p \leq 0.05$) in mean sodium, chloride and bicarbonate concentrations at 2, 24, 48, 72, 96 and 120 h post-surgery in group 1 and 2, while group 3 had significant decreases ($p \leq 0.05$) in sodium, chloride and bicarbonate ions. Lactate value decreased significantly ($p<0.05$) in group 1, and increased in group 2 and 3 respectively.BUN increased significantly ($p<0.05$) in group 1,2 and 3.However, there were significant increases ($p<0.05$) in lymphocyte concentrations in group 1 and 3, respectively. Monocytes decreased significantly ($p<0.05$) after surgery. Conclusion: Xylazine and propofol anaesthetics cause hyperlactatemia which can be detrimental in surgical patients with co-morbidities.

1. Introduction

Celiotomy (laparotomy) is a common surgical approach undertaken by veterinary surgeons for either elective or emergency purposes (Welsh, 2015), with consequences of neurological, hormonal, immunological and hematologic stress (Paruk & Chausse, 2019). The severity of tissue injury during surgery is determined by the type and duration of surgery, age, sex, disease comorbidities and postoperative pain (Abdelmalak et al., 2013). Stress response prevents deleterious effects of surgery and protects against disease causing organisms, by mobilizing the acute inflammatory and immune systems that begin the process of wound repair (Lay, 2014). Surgical injuries are classified as primary or secondary. Primary injuries could be direct or indirect injuries that result from decreased tissue perfusion. Secondary injury is due to inflammatory mediators (Scott & Miller, 2015). Despite the significant improvements in anaesthesia that have significantly reduced the incidence of anaesthetic induced complications and mortality in surgical patients, death still occur from organ injury that subsequently end in multiple organ failure (Bartels et al., 2013). For example, abdominal surgery is a major cause of acute kidney injury (AKI) (Cho et al., 2011), which is a leading cause of postoperative organ failure, occurring in 18.7% of cardiac surgeries and12-13.2% of thoracic surgeries (Grams et al., 2016). Complications associated with surgery results in increased death rates and treatment costs (Weiser et al., 2008). Advance evaluation of renal function ensures early recognition and treatment of renal problems (Dalton, 2010). Cardio-renal syndrome has been reported to be a leading cause of disease and death in dogs and cats (Chakrabarti et al., 2013). Renal damage is evaluated using creatinine, urea, and electrolytes in blood. Creatinine is a recognized marker for measuring glomerular filtration rate (GFR), a diagnostic parameter for measuring

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https://doi.org/10.1016/j.vas.2021.100203
Received 8 June 2021; Received in revised form 28 August 2021; Accepted 29 August 2021
Available online 30 August 2021

and evaluating renal function (Kashani et al., 2019). Measurement of electrolytes is important in assessment of homeostasis and acid-base imbalance (Kristopher, 2013). Electrolyte imbalance can potentiate adverse effects of anaesthetic drugs and lead to increased risk of arrhythmias, hypotension (Fantoni and Shih, 2017) and multiple organ dysfunction (Hosana and Elasbali, 2016). Lactate is a biomarker of patient outcome and is a valuable weapon in the emergency and critical care diagnostic toolbox (Rosentein et al., 2018). Increased lactate concentrations are associated with increased disease severity, morbidity, and mortality in sick and injured human and animals (Rosenstein and Hughes, 2015).

Leucocytes function in host defence, control of inflammation and immunity (Blackwood, 2016). Determination of leucocyte count helps identify patients at risk of infection and complications after surgery (Li et al., 2012). The aim of the present study is to evaluate the comparative effects of ovariohysterectomy (OVH), gastrotomy (GAT) and intestinal resection and anastomosis (IRT) on differential leucocyte counts and biochemical parameters of Nigerian dogs under a xylazine-propofol-atropine anaesthetic combination.

2. Materials and methods

2.1. Experimental animals

Twelve healthy Nigerian adult dogs comprised six female and six male, weighing an average 10.8 ± 0.7 kg were bought from commercial breeders for the study. The animals were acclimatized for four weeks and the body condition score (BCS) of each dog was determined before they were randomly divided into three group of four animals each. OVH, GAT and IRT were performed on group 1, 2 and 3, respectively. Food and water were provided *ad libitum*. The study was approved by the Ethical Committee, Department of Veterinary Surgery and Diagnostic Imaging, College of Veterinary Medicine, Federal University of Agriculture, Makurdi, Nigeria given the permit number PN 2020-002. Animals were cared for according to laboratory animal guidelines (CIOMS, 1985).

2.2. Preoperative preparation

The dogs were withheld from food and water for a period of 12 and 6 h respectively prior to induction of anaesthesia and surgery. The ventral abdominal area of each animal was shaved and the skin aseptically prepared for surgery using 0.05% chlorhexidine gluconate (purit®) manufactured by Saro Lifecare Limited, Nigeria. An intravenous catheter was placed in the cephalic vein and physiologic saline (0.9% Nacl) produced by Dana pharmaceuticls, Nigeria was infused at 10ml/mg/h. The dogs were thereafter premedicated with intramuscular atropine sulphate (0.04 mg/kg) manufactured by Jiangsu Huayang Pharmaceutical, China and 2% xylazine(2 mg/kg),produced by VMD, Belgium) respectively. Propofol (6 mg/kg) manufactured by Frensenius Kabi AB SE-75174 Uppsala, Sweden, was used for induction of anaesthesia.

2.3. Surgical procedures

2.3.1. Ovariohysterectomy

A ten centimeter (10 cm) skin incision was made with size 20 scalpel blade on the skin along ventral midline, and the subcutaneous tissue to expose the linear alba. A stab incision was then made on the linear alba and the incision extended with scissors. The abdomen was entered into, and the uterus located after retroflexing the bladder. The right and the left uterine horns were identified and the ovaries located. Two hemostatic forceps were placed across the ovarian pedicle which was double ligated using chromic cat gut size 2-0 and the first ovary was removed. The procedure was repeated for the second ovary, after which the uterus was removed. The abdominal and skin incisions were closed using chromic cat gut and nylon respectively (Fossum, 2019).

2.3.2. Intestinal resection and anastomosis

Following celiotomy and entry in to the abdominal cavity, the intestinal tract was exteriorized and 10 cm of the Jejunum was resected, beginning at a point 9 cm from the duoduno-jejunal flexure (treitz ligament). The residual intestinal tract was sutured using end- to- end anastomosis with chromic catgut size 2-0. The anastomostic site covered with omentum was returned to the abdominal cavity and the abdominal incision was closed, using standard surgical technique (Fossum, 2019).

2.3.3. Gastrotomy

Following ventral midline incision and entry into the abdominal cavity, the stomach was exposed and isolated from the abdominal cavity. Incision was made on the body of the stomach between the greater and lesser curvatures, in the least vascularized area of the serosa. Stay sutures were placed on the stomach for easy manipulation. The stomach content was emptied, and the gastrotomy incision was closed in two layers of simple continuous and lembert suture patterns respectively, using chromic catgut size 2-0. The abdominal incisions were closed with chromic catgut size 2-0 using simple continuous suture pattern, whereas skin incision was closed with nylon size 2-o, using horizontal mattress suture pattern (Fossum, 2019).

2.4. Collection of blood samples

Blood samples were collected from the cephalic vein into plain vacuitaner tubes at 0 (pre-operative), 2, 24, 48, 72, 96, day 120 and 144 h posts operatively, for analysis of white blood cells (Villiers, 2016, sodium, potassium, bicarbonate, chloride ion (George, 2011) lactate (Allison, 2012) as well as blood urea nitrogen (BUN) (Manoeuvrier et al., 2017) and serum creatinine (Moore and Sharer, 2017).

2.5. Mathematical determination of biochemical parameters

Mathematical formulas were used to calculate plasma creatinine, mean creatinine clearance, mean creatinine half life ($Cr^{1/2}$), urine volume and urine creatinine (Saganuwan, 2018).

$$\text{Meanplasmacreatinine(Pcr)} = [\text{Ucrx144}] \div \text{Pcl} \quad (1)$$

Ucr = Urine creatinine; Pcl = Plasma clearance

$$\text{Meancreatinineclearance(CrCl)} = [\text{Ucr} \div \text{Pcr}]\text{x}[1440 \div 10] \quad (2)$$

Where Ucr = Urine creatinine; Pcr = Plasma creatinine; Pcl = Plasma clearance

$$\text{Creatininehalflife}\left(\text{Cr}^{1/2}\right) = 14616.8 \div [\text{Pcl} - \ - 25] \quad (3)$$

$$\text{Urinecreatinine(Ucr)} = [\text{CrClxPcr}] \div 144 \quad (4)$$

Where CrCl = creatinine clearance; Pcr = Plasma creatinine

$$\text{Urinevolume(Uv)} = [\text{CrClxPcr}] \div \text{Ucr} \quad (5)$$

Where Crcl = Creatinine clearance; Pcr = Plasma creatinine; Ucr = Urine creatinine

$$\text{Plasmaclearance(Pcl)} = \text{CrCl} + 25 \quad (6)$$

$$\text{Glomerularfiltrationrate(GFR)} = \text{Pcl} - \ - 25 \quad (7)$$

$$\text{Areaundercurve(AUC)} = \text{Dose} \div \text{Pcl} \quad (8)$$

$$\text{Totalbodyclearance(Tbcl)} = \text{Totaldose} \div \text{AUC} \quad (9)$$

2.6. Statistical Analyses

Two-way analysis of variance (ANOVA) was used to analyze the data. Turkey's multiple comparison test was used to detect significance

difference among all the groups at 0.01% level of significance (Daniel, 2010).

3. Results

The effects of time and surgical procedures on electrolytes are presented in Table 1. Sodium and chloride ions were significantly increased ($p \leq 0.05$) in ovariohysterectomy and gastrotomy, but decreased significantly in intestinal resection and anastomosis ($p \leq 0.05$). Biocarbonate ion increased significantly on day 2, and later decreased significantly for the rest period of experimentation. Potassium ion was not significantly affected. Lactate was significantly increased ($p \leq 0.05$) in the OVH and GAT dogs but decreased significantly ($p \leq 0.05$) in the ITR dogs (Table 2). Blood urea nitrogen was significantly increased ($p \leq 0.05$) at various time intervals in the OVH, GAT and ITR dogs. Significantly decreased serum creatinine level was observed in ITR dogs only ($p \leq 0.05$). Nevertheless, plasma creatinine level was significantly increased and decreased in the OVH and ITR dogs respectively ($p \leq 0.05$). Creatinine half-life was significantly increased and decreased in GAT and ITR as well as OVH, respectively. Urine creatinine, urine volume and plasma clearance were not affected significantly ($p \geq 0.05$). GFR increased significantly ($p \leq 0.05$) in OVH, GAT and ITR dogs and later decreased significantly ($p \leq 0.05$) at 24 h, 72 h, 96 h and 120 h in OVH dogs. AUC was significantly decreased ($p \leq 0.05$) at 24 h in GAT and ITR dogs. TBCL increased significantly ($p \leq 0.05$) at 24 h in GAT and ITR dogs. Values of neutrophils were significantly increased in OVH, GAT and ITR dogs ($p \leq 0.05$), but lymphocytes were significantly increased and decreased at various periods of time, whereas monocytes were significantly increased in GAT dogs only ($p \leq 0.05$) (Table 2). Neutrophils were significantly increased ($p \leq 0.05$) in OVH, GAT and ITR dogs, as lymphocytes were significantly increased at 24 and 96 h and decreased significantly at 2, 48 and 120 h, respectively. Nevertheless, lymphocytes was decreased significantly ($p \leq 0.05$) in GAT and ITR dogs throughout the period of study, except at 48 h when lymphocytes increased significantly in ITR dogs ($p \leq 0.05$). Monocytes decreased significantly ($p \leq 0.05$) at 2 h in OVH group and at 96 h in GAT group, respectively (Table 3).

4. Discussion

Hypernatremia and hyperchloraemia observed in the study agree with the report, indicating that surgery caused hypernatremia and hyperchloraemia (Flear, 1970). Acid-base and electrolyte imbalance are common in dogs with gastrointestinal disturbances (Boag et al., 2005). Normal potassium level observed, disagrees with the report of Tetzlaff et al., (1993) indicating that potassium is required during anaesthesia. Hyperchloraemia observed may cause metabolic acidosis (West et al., 2013) with adverse effect on respiration (Bunker, 1962).

The significant increase in mean sodium, chloride and bicarbonate concentration observed after OVH and GAT (OVH and GAT) might be due to dehydration. Dehydration has been reported as non renal or extra renal cause of hypernatremia, hyperchloremia and hypercarbonatemia (Arneson, 2014). The non significant changes in potassium concentrations in this study suggest healthy kidney function and normal urine output (Silverstein et al., 2017). The significant decrease in sodium, chloride and bicarbonate especially in ITR group was due to gastrointestinal loss, postoperative stress, third- space loses and sodium and water retention in the intracellular space (Silverstein et al., 2017). Surgical stress triggered by anaesthesia and surgery, exacerbates sodium and water retention, which is a compensatory mechanism, initiated to improve cardiac output and renal perfusion, but conversely can be associated with myriads of adverse clinical effects including impaired gastrointestinal function and multiple organ dysfunctions (Chowdhury and Lobo, 2011). Water retention is proportional to the extent of surgery (Rassam and Counsel, 2005), suggesting that fluid shift and losses could result in hypovolaemia, if preoperative fluid therapy is not administered (Rassam and Counsel, 2005). There may be need for perioperative electrolytes (Rassam and Counsel, 2005) as electrolyte disturbances are also associated with non-survival in dogs (Goggs et al., 2017).

Increased lactate values at 2 h post GAT and ITR may be due to combination of surgical trauma, surgical stress, pain, circulating catecholamines and accumulation of leukocytes at the site of inflammation (Rosenstein et al., 2018; Velickovic et al., 2019). Propofol and xylazine cause type B hyperlactatemia, whereas xylazine triggers the release of catecholamines which increase lactate concentrations (Levy et al., 2008). Propofol caused lactic acidosis in humans (Loh and Nair, 2013) and dogs. Increased lactate concentrations at 72 h (GAT), 96 h, 120 h and 144 h post OVH, GAT and ITR may be due to struggling during restraint (Redavid et al., 2012) which increased blood lactate concentrations in pigs (Jensen-Waern and Nyberg, 1993). Adeva-Andany et al., (2014) reported association between increased initial lactate and mortality in dogs. Hyperlactatemia was the cause of mortality in critically ill patients after major surgery (Velickovic, 2019).The upper limit of lactate needed to cause mortality in patients undergoing an elective abdominal surgery is not the same with that of patients undergoing surgery as a result of infection (Velickovic et al., 2019).The decreased lactate values in dogs subjected to OVH post-surgery compared to the presurgical value cannot be explained. Similar finding was reported by Mathews et al., (2014) in healthy anesthetized sheep.

The low serum and plasma creatinine observed for OVH, GAT and ITR might be due to perioperative fluid administration and low muscle mass. This agree with the report of Ostermann et al., (2016)indicating that perioperative fluid administration decreases serum creatinine concentrations, by increasing renal blood flow and clearance, with the net effect increase in creatinine filtration. However, the observed increases in serum and plasma creatinine for OVH post-surgery might be as a result of dehydration and neuroendocrine response to anaesthesia and surgery. Pre and post-operative plasma creatinine in patients

Table 1
The effects of time and surgical procedures on electrolytes of Nigerian indigenous dogs.

Parameters	Surgical procedure	Period of treatment (Hours)							
		0	2	24	48	72	96	120	144
Sodium	OVH	137.8±5.48	154.0±4.42[a]	185.0±18.42[a]	153.8±6.07[a]	203.8±16.26[a]	191.0±10.23[a]	170.0±15.03[a]	150.5±19.19[a]
(mmol/L)	GAT	158.3±13.49	152.8±2.49	166.8±14.68[a]	180.0±12.07[a]	203.3±10.80[a]	201.5±13.96[a]	169.3±9.52[a]	174.3±15.27[a]
	ITR	156.3±17.59	150.8±15.09	138.3±2.63[b]	151.8±13.09	138.8±1.5[b]	135.3±1.97[b]	149.8±15.76	133.3±0.63[b]
Potassium	OVH	5.02±0.36	4.26±0.26	5.76±0.38	4.98±0.31	6.36±0.29	6.19±0.22	5.59±0.48	4.97±0.02
(mmol/L)	GAT	6.15±0.99	4.17±0.22	5.78±0.39	5.89±0.43	6.20±0.40	6.07±0.48	5.76±0.25	6.46±0.55
	ITR	5.28±0.46	4.61±0.53	4.60±0.13	6.53±0.03	4.66±0.25	4.45±0.32	4.98±0.97	3.97±0.09
Chloride	OVH	99.23±3.07	116.7±3.10[a]	138.9±15.65[a]	112.60±4.27[a]	154.5±14.60[a]	154.1±14.50[a]	126.20±12.79[a]	131.40±19.8[a]
(mmol/L)	GAT	113.8±8.34	111.0±3.98	124.5±14.91	134.1±6.67[a]	151.9±9.58[a]	156.5±13.17[a]	133.2±10.52[a]	126.1±10.69[a]
	ITR	111.9±12.52	108.7±11.65	100.3±1.90[b]	106.0±12.19	101.8±0.99[b]	97.43±1.01[b]	106.6±12.63	96.13±0.90[b]
Bicarbonate	OVH	21.67±4.41	25.00±3.54[a]	17.50±3.23[b]	27.50±4.79[a]	18.33±1.67[b]	23.33±3.33	18.75±2.39[b]	21.25±3.15
(mmom/L)	GAT	23.75±3.75	26.25±1.25[a]	16.25±1.25[b]	23.75±3.15	25.00±2.89	27.25±4.09[a]	22.50±1.44	18.75±4.27[b]
	ITR	31.37±4.40	35.00±3.54[a]	32.25±4.66	23.75±5.54[b]	23.75±3.75[b]	25.00±4.08[b]	20.00±3.54[b]	23.75±4.27[b]

Keys: a=significantly higher (p< 0.05); b= significantly lower (p< 0.05).

Table 2
The effects of time and surgical procedures on biochemical parameters of Nigerian indigenous dogs.

Parameters	Surgical procedure	period of treatment (Hours) 0	2	24	48	72	96	120	144
Lactate (μmmol/L)	OVH	268±32.0	262.1±61.4	232.8±34.1[b]	238.4±44.0[b]	229.3±25.9[b]	290.7±34.4[a]	309.3±65.2[a]	289.9±137.7[a]
	GAT	188.0±1.8	284.9±42.2[a]	176.8±10.4	177.6±36.7	260.5±19.6[a]	264.9±34.5[a]	496.1±47.9[a]	835.0±169.4[a]
	ITR	414.2±192.2	424.7±86.9	421.40±180.8	653.0±373.1[a]	312.8±21.9	391.0±170.1	394.8±57.8	488.9±76.9
BUN (mg/dL)	OVH	2.3±0.6	3.3±0.6[a]	2.7±0.5[a]	1.9±0.3	2.6±0.6[a]	2.7±0.7[a]	2.4±0.5	2.3±0.7
	GAT	2.2±0.3	3.8±0.3[a]	2.0±0.3	1.2±0.4[b]	1.8±0.6	1.6±0.8	2.9±1.0	2.4±0.6
	ITR	2.2±0.5	3.9±0.5[a]	3.2±0.9[a]	3.4±1.8[a]	2.8±0.8	2.4±0.5	3.2±0.4[a]	2.4±0.4
Serum creatinine(mg/dL)	OVH	0.61±0.02	0.58±0.04	0.68±0.08	0.70±0.03	0.82±0.10	0.71±0.10	0.78±0.07	0.63±0.04
	GAT	0.70±0.13	0.61±0.02	0.50±0.06	0.76±0.03	0.71±0.02	0.71±0.06	0.63±0.04	0.80±0.07
	ITR	0.83±0.06	0.81±0.07	0.57±0.06[b]	0.85±0.07	0.64±0.06	0.59±0.04[b]	0.81±0.07	0.86±0.07
Plasma creatinine (mg/dL)	OVH	0.88±0.03	0.84±0.06	0.98±0.12	1.01±0.04[a]	1.18±0.14[a]	1.02±0.14[a]	1.12±0.10[a]	0.91±0.16
	GAT	1.01±0.19	0.88±0.03	0.72±0.09	1.09±0.04	1.02±0.03	1.02±0.09	0.91±0.06	1.15±0.10
	ITR	1.19±0.09	1.17±0.10	0.82±0.09[b]	1.22±0.10	0.92±0.09	0.85±0.06[b]	1.15±0.10	1.24±0.10
Creatinine half life ($Crt^{1}/_{2}$) (h)	OVH	1.49±0.03	1.66±0.06	1.66±0.12[a]	1.56±0.43	1.66±0.14	1.73±0.14	1.72±0.83	1.54±0.62
	GAT	1.71±0.19	1.49±0.03[b]	1.35±0.09[b]	1.68±0.10	1.73±0.09	1.73±0.09	1.54±0.10	1.77±0.10
	ITR	1.83±0.09	1.80±0.10	1.39±0.09[b]	1.88±0.10	1.56±0.09[b]	1.44±0.06[b]	1.77±0.10	1.91±0.10
Urine creatinine (mg/24 h)	OVH	1.0±0.0	1.0±0.0	1.0±0.0	1.1±1.7	1.2±0.0	1.0±0.0	1.1±0.83	1.0±0.0
	GAT	1.0±0.0	1.0±0.0	0.9±0.0	1.1±0.0	1.0±0.0	1.0±0.0	1.0±0.0	1.1±0.0
	ITR	1.1±0.0	1.1±0.0	1.0±0.0	1.1±0.0	1.0±0.0	1.0±0.0	1.1±0.0	1.1±0.0
Creatinine clearance (Crcl) (mL/min)	OVH	2.73±0.03	2.86±0.06	2.45±0.12[b]	2.61±0.43	2.44±0.14[b]	2.35±0.14[b]	2.36±0.83	2.64±0.62
	GAT	2.38±0.19	2.73±0.03[a]	3.0±0.09	2.42±0.04	2.35±0.03	2.35±0.09	2.64±0.06	2.30±0.10
	ITR	2.22±0.09	2.26±0.10	2.93±0.09[a]	2.16±0.10	2.61±0.09	2.82±0.06[a]	2.30±0.10	2.13±0.10
Plasma clearance (Pcl) (mL/min)	OVH	27.73±0.03	27.86±0.06	27.45±0.12	27.61±42.4	27.44±0.14	27.35±0.14	27.36±8.3	27.64±6.2
	GAT	27.38±0.19	27.73±0.03	28.0±0.09	27.42±0.10	27.35±0.09	27.35±0.09	27.64±0.10	27.30±0.10
	ITR	27.22±0.09	27.26±0.10	27.93±0.09	27.16±0.10	27.61±0.09	27.82±0.06	27.30±0.10	27.13±0.10
Urine volume (mL/min)	OVH	2.4±0.0	2.4±0.0	2.4±0.01	2.4±1.0	2.4±0.02	2.4±0.02	2.4±0.10	2.4±1.0
	GAT	2.4±0.04	2.4±0.0	2.4±0.01	2.4±0.0	2.4±0.0	2.4±0.01	2.4±0.0	2.4±0.01
	ITR	2.4±0.01	2.4±0.01	2.4±0.01	2.4±0.01	2.4±0.01	2.4±0.0	2.4±0.01	2.4±0.01
Glomerular filtration rate (GFR) (ml/min/kg)	OVH	2.73±0.3	2.86±0.06[a]	2.45±0.12[b]	2.61±4.24	2.44±0.14[b]	2.35±0.14[b]	2.36±8.3[b]	2.64±6.2
	GAT	2.38±0.19	2.73±0.03[a]	3.0±0.09[a]	2.42±0.10	2.35±0.09	2.35±0.09	2.64±0.10[a]	2.30±0.10
	ITR	2.22±0.09	2.26±±0.10	2.93±0.09[a]	2.16±0.10	2.61±0.09[a]	2.82±0.06[a]	2.30±0.10	2.13±0.10
Area under curve (AUC)	OVH	0.22±0.03	0.22±0.06	0.22±0.12	0.22±42.4	0.22±0.14	0.22±0.14	0.22±8.3	0.22±6.2
	GAT	0.22±0.19	0.22±0.03	0.21±0.09[b]	0.22±0.10	0.22±0.09	0.22±0.09	0.22±0.10	0.22±0.10
	ITR	0.22±0.09	0.22±0.10	0.21±0.09[b]	0.22±0.10	0.22±0.09	0.22±0.06	0.22±0.10	0.22±0.10
Total body clearance (cl(mi)	OVH	306.8±34.	306.8±34.09	306.8±34.09	306.8±34.09	306.8±34.09	306.8±34.09	306.8±34.09	306.8±34.09
	GAT	252.3±13.06	252.3±13.06	264.3±13.68[a]	252.3±13.06	252.3±13.06	252.3±13.06	252.3±13.06	252.3±13.06
	ITR	300.0±33.40	300.0±33.40	314.3±34.99[a]	300.0±33.40	300.0±33.40	300.0±33.40	300.0±33.40	300.0±33.40

Keys: a=significantly higher ($p< 0.05$); b= significantly lower ($p< 0.05$).

Table 3
The effects of time and surgical procedures on differential leucocyte counts of Nigerian indigenous dogs.

Parameters	Surgical procedure	period of treatment (Hours) 0	2	24	48	72	96	120	144
Neutrophil	OVH	67.5±5.9	83.7±1.3[a]	58.4±10.1	73.6±1.4	69.4±4.7	69.0±5.1	78.4±1.5[a]	66.9±4.0
	GAT	68.2±2.2	81.5±1.6[a]	73.2±3.5[a]	74.2±1.2[a]	70.5±4.4	71.8±4.4	76.2±2.7[a]	75.9±2.3[a]
	ITR	74.3±4.0	81.8±1.5[a]	82.2±4.8a	72.7±4.5	76.0±1.6	78.2±2.2	79.2±2.4	80.4±1.8[a]
Lymphocyte	OVH	22.4±4.7	10.9±0.7[b]	26.5±8.1[a]	20.0±1.0[b]	24.7±3.5	24.6±4.5[a]	17.28±3.7[b]	24.6±3.2
	GAT	21.7±1.3	11.8±0.8[b]	16.5±2.0[b]	17.3±1.7[b]	18.9±0.7	17.0±0.9[b]	18.4±0.3[b]	15.3±0.9[b]
	ITR	17.8±2.6	13.7±1.2[b]	11.2±1.0[b]	21.2±4.9[a]	18.9±1.3	16.7±2.5	13.8±2.3[b]	13.8±1.3[b]
Monocyte	OVH	3.5±0.4	2.6±0.2[b]	4.7±1.3	4.0±0.1	3.9±0.5	4.0±0.8	3.6±0.4	4.4±0.8
	GAT	3.7±0.5	2.9±0.5	3.5±0.4	3.9±0.3	3.4±0.2	3.1±0.3[b]	3.4±0.3	3.7±0.1
	ITR	3.5±0.4	3.1±0.2	4.2±1.6	3.7±0.3	4.0±0.4	4.0±0.6	3.3±0.5	3.9±1.0

Keys: a=significantly higher ($p< 0.05$); b= significantly lower ($p< 0.05$).

undergoing elective coronary artery surgery under isoflurane, sevoflurane and propofol anaesthesia could be increased (Story et al., 2001). Waikar and Bonventre (2009) also reported increased in serum creatinine following renal insult. This might have contributed to the observed hypercreatinaemia after the initial drop 2 h post surgery. Kork et al., (2015) reported that increases in post-operative creatinine during acute kidney injury resulted in mortality. However, in the present study, no mortality was recorded despite increases in post-operative creatinine. Propofol has been reported to prevent as well as treat acute kidney injury and ischemia reperfusion injury (Motayagheni et al., 2017). The higher urea concentrations observed for OVH, GAT and ITR might be due to dehydration, pain and surgical stress. Dehydration increases absorption of urea and makes its concentration in serum higher (Meuten, 2012). Creatinine clearance gives accurate assessment of glomerular filtration rate (Nankivell, 2001) and is useful in identifying early stage of renal disease (Mauten, 2012). The calculated creatinine clearance method is more accurate than the measuring method, which underestimates renal function (Saganuwan, 2018). The use of mathematical formula to determine creatinine clearance is important, as it helps in determining the dose of drugs that are eliminated by the kidney (Saganuwan, 2018). Creatinine half-life ($Cr^{1/2}$) and creatinine clearance are inversely proportional. The increased creatinine clearance in GAT, ITR and OVH, resulted in corresponding decrease in creatinine half-life, decreased creatinine clearance and increased creatinine half-life. Urinary elimination of creatinine is constant over time and is not affected by extra renal factor (Braun et al., 2003). Food can be responsible for the differences in the amount of urine creatinine (Uechi et al., 1997).

Urine volume is a measure of renal perfusion and function (MC ilroy

and Sladen, 2015). The non significant difference in urine volume in this present study agrees with the report of Brown, (1993) indicating that dogs under anaesthesia and surgery maintain normal urine volume, because renal blood flow and glomerular filtration rate remain constant, due to the intrinsic auto regulatory capacity of the kidney. However, the urine volume for dogs in the present study agrees with the reported value (2.4 ml/min) in various species (Saganuwan, 2018).The non significant difference in plasma clearance agrees with the report of Braun et al., (2003) indicating that urinary elimination of creatinine remained unchanged since concentration of creatinine in plasma is largely influenced by muscle mass.

The decrease in AUC and increase in GFR at 24 h shows that propofol was eliminated faster in GAT and ITR. This finding agrees with the report indicating that many pharmacokinetic and pharmacodynamic models for propofol exist (Sahinovic et al., 2018). Therefore, the onset of hypnotic effect of propofol has to be titrated with boluses of administered propofol over a period of time with maintenance dose of 6-12 mg/kg/h (Sahinovic et al., 2018). However, obesity could affect pharmacokinetic of propofol by changing body composition, regional blood flow, haemodynamic, liver and kidney functions (De Baerdemaeker et al., 2004). The AUC of propofol in the present study could predict renal function capacity of the kidney in relation to propofol elimination during 3 stage infusion so as to avoid propofol infusion syndrome (Figs. 1–4).

The increase in total body clearance observed in dogs that underwent GAT and ITR suggests that multiple infusion of propofol did not markedly affect renal function because of high renal clearance of the drug (Ickx et al., 1998). However, propofol could cause renal impairment that may be characterized by high plasma creatinine and low creatinine clearance (Ickx et al., 1998; Story et al., 2001).

Neutrophilia, lymphocytopenia and monocytopenia agrees with the report of Iwase et al., (2006) indicating that inflammation could modulate the release of leucocytes. It could be attributed to surgical trauma (Helmy et al., 1999), anaesthetic technique (Ke et al., 2008) and inflammatory response (Blackwood, 2016).

Anaesthesia and surgery cause cell mediated immune response by interfering with some functional activities of neutrophils, monocytes and macrophages (Kawasaki et al., 2007). Hogan et al., (2011) reported that neutrophilia during surgery is important in immune protection and wound healing. It also activates inflammatory response and autoimmune or graft rejection (Volker-Dieben, 1982). Lymphopenia and monocytopenia expression are associated with immune suppression, delayed wound healing, respiratory diseases and sepsis (Kim et al., 2011) indicating that GAT and ITR wound healings were relatively delayed. All the abnormal parameters observed in the present study are

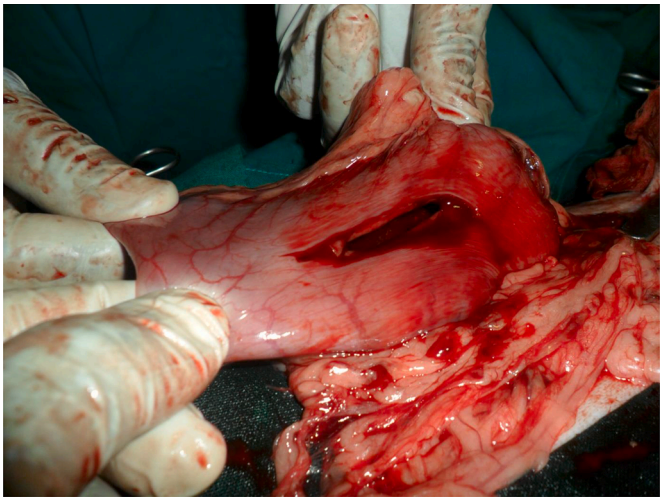

Fig. 1. PThe exteriorized incised stomach.

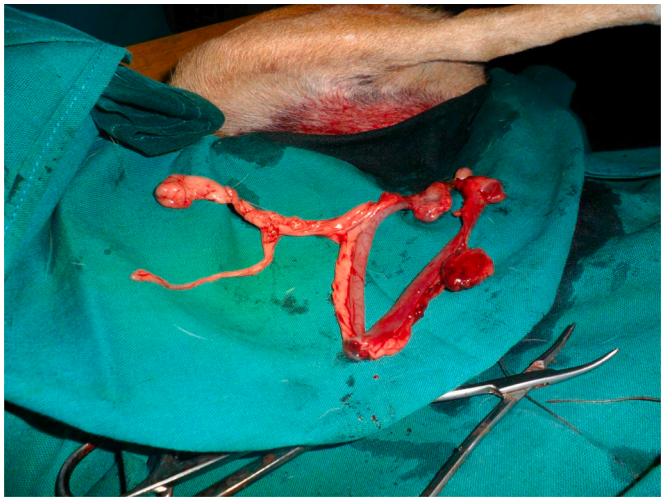

Fig. 2. Removed ovaries and uterus.

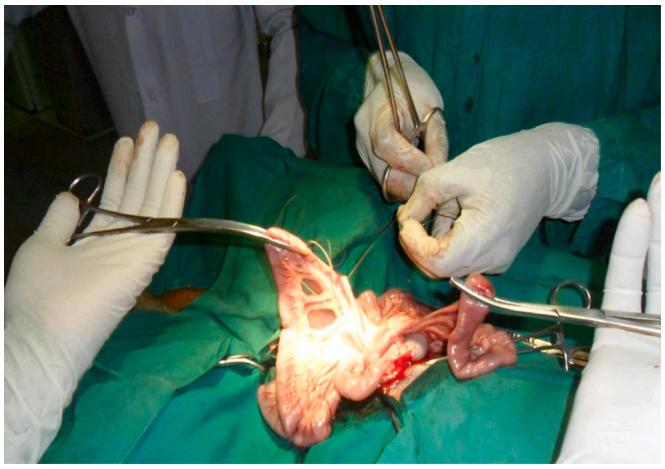

Fig. 3. Showing ligation of small blood vessels that supply small intestine for resection and anastomosis.

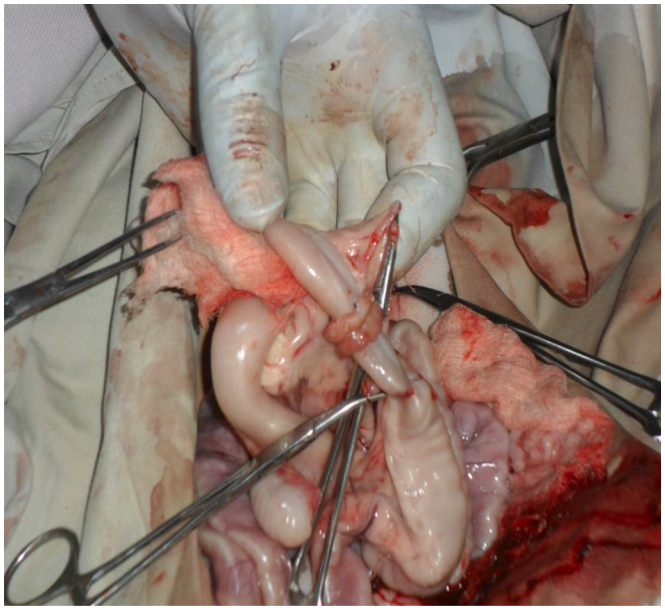

Fig. 4. Anastomosed resected small intestine.

not specific to any of the surgical procedures in the study (Kisani et al., 2018). Urea and creatinine were observed in chronic kidney disease (Tvarijonaviciute et al., 2018), and decreased sensitivity of creatinine during early phase of the study. Cobrin et al., (2013) reported that no any single biomarker is specific for acute and chronic kidney problem. Neutrophilia and lymphopenia observed in the study could be predictive biomarkers for the entire surgical wound healing, except ITR (Paliogiannis et al., 2020). Unfortunately monocytes are inactivated in the present study as opposed to report by Klava et al., (1997).

5. Conclusion

Sodium, chloride, bicarbonate,creatinine, blood urea nitrogen, lactate, neutrophils, monocytes and lymphocytes should be monitored seriously, for a period of seven days, after gastrotomy, intestinal resection and anastomosis, and ovariohysterectomy, in order to avoid post-surgical complication, that may ensue due to pathophysiological, haematological and biochemical changes.

Ethical approval

The study was approved by the Ethical Committee, Department of Veterinary Surgery and Diagnostic Imaging, College of Veterinary Medicine, Federal University of Agriculture, Makurdi, Nigeria given the permit number PN 2020-002.

Funding

The study was funded by the authors.

Author contribution

ATE designed the study. AIK and TON performed the surgery. Data was analysed by TON. AIK wrote the manuscript, ATE revised the manuscript and all authors read and approved the manuscript.

Declaration of Competing Interest

The authors declare that they have no conflict of interest

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