Asian Research Journal of Gynaecology and Obstetrics

2(1): 107-126, 2019; Article no.ARJGO.56384

Effects of Propofol Anaesthesia on Thermoregulation, Blood Constituents, Coagulation Indices and Selected Serum Biochemicals and Enzymes in Pregnant Rabbit Model

Khalid Abbas Owish Sukar[1*], Abdalla Mohamed Abdelatif[2] and Etayeb Mohamed Alfaki[1]

[1]Faculty of Medicine, University of Bakht Alruda, P.O. Box 1311, El-duiam-12556, Khartoum, Sudan.
[2]Faculty of Veterinary Medicine, University of Khartoum, Sudan.

Authors' contributions

This work was carried out in collaboration among all authors. Authors KAOS and Abdalla Mohamed Abadelatif designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Author KAOS and Abdalla Mohamed Abdelatif managed the analyses of the study. Author Etayeb Mohamed Alfaki managed the literature searches. All authors read and approved the final manuscript.

Article Information

Editor(s):
(1) Dr. David Kitara Lagoro, Gulu University, Uganda.
Reviewers:
(1) Vaishali Waindeskar, All India Institute of Medical Sciences (AIIMS), Bhopal, India.
(2) Dennis Amaechi, Veritas University, Nigeria.
Complete Peer review History: http://www.sdiarticle4.com/review-history/56384

Original Research Article

Received 14 February 2020
Accepted 20 April 2020
Published 01 May 2020

ABSTRACT

Aim: This study was conducted to evaluate the effects of propofol anaesthetic on the physiological responses in rabbit model in mid gestation (GD18) period.
Methods: Fourteen rabbits, 7 pregnant and 7 nonpregnant were used in this study. Both groups were induced propofol anaesthetic intravenously maintained for 90 min by constant I.V infusion rate (1mg/kg/min). Measurements of the parameters were performed before and after induction of anaesthesia for pregnant and nonpregnant rabbits.
Results: The RR and HR decreased significantly ($P<0.05$) after propofol anaesthesia in pregnant and nonpregnant rabbits. The PCV, Hb and erythrocytes values were significantly ($P<0.05$) lower

**Corresponding author: E-mail: owishkhalid55@gmail.com;*

after propofol anaesthesia in both groups. Interactions between pregnancy and propofol anaesthesia indicated a decrease in RR, PCV, MCV and increases in PT, serum levels of Na^+, K^+, plasma Osmolality, LDH and CPK enzymes.
Conclusions: The studies provide evidence that pregnancy induces variable alterations in blood profiles in anaesthetized rabbits.

Keywords: Rabbits; propofol; pregnancy; haemetological parameters.

1. INTRODUCTION

Rabbits are used as models for assessment of the effects of anaesthesia and physiological signals, such as heart rate, respiratory rate and body temperature. Although rabbits constitute the most commonly anaesthetized experimental animal species, they have at least seven times more risks of anaesthetic-related death compared to dogs and cats [1]. Advanced diagnostic and surgical procedures requiring safe and adequate anaesthesia are usually performed on rabbits [2]. Propofol is an intravenous anesthetic agent currently popular in humans and animals, both as sole agent and as an adjunct in balanced anesthetic techniques [3,4]. It has been administered successfully to induce anaesthesia in rabbits [5,6]. Previous studies have indicated that propofol impairs platelets aggregation in surgical patients [4]. Such data suggest that the use of propofol infusion for anesthetic maintenance might be undesirable in surgical operations where bleeding may become a problem.

Pregnancy constitutes stressful condition associated with the blood volume increases by 50% while red blood cells increase by 25% causing physiological anemia in pregnancy [7].Thus, there is a higher volume of distribution of drugs [8]. Physiological hypovolemia during gestation is associated with an increase in alpha-1-glycoprotien, changing the free fraction of drugs and increasing their toxicity [9]. Anaesthetic drugs affect cell signaling, mitosis and DNA synthesis which induce effects on organogenesis [8].Recent advanced research indicated that propofol administration during late stages of pregnancy impaired cognitive function of offspring in rats [10]. Propofol is widely used in intensive care and classified as a pregnancy category B agent based on animal data, while clinical use is adopted during caesarean deliveries [11]. Clinical data in maternal critical regarding what care are limited to some case reports during pregnancy [12,13]. This experiment adopted a rabbit model to investigate the effect of propofol on blood constituents and coagulation indices during pregnancy.

2. MATERIALS AND METHODS

2.1 Experimental Animals

Fourteen healthy, sexually mature pregnant and nonpregnant rabbits (*Oryctolagus cuniculus*) were used in the studies. The animals were kept in an animal house at the Department of Physiology. The rabbits were obtained from the local market. The animals were aged 9−12 months with average body weight 1.50±0.30Kg. Female rabbits were isolated for one month individually in cages to ascertain their reproductive status and animals judged to be in oestrus were housed together with sexually mature males in cages for mating. During the studies, the rabbits were offered fresh Lucerne (*Medicago sativa*) and crushed sorghum grains and were given fresh tap water *ad libitum*. Water and food stopped for 60 min prior to induction of anaesthesia.

2.2 Experimental Procedure

The complete randomized design was used to evaluate the effect effects of propofol anaesthetic on the physiological responses in rabbit model in gestation period. Fourteen mature female rabbits were assigned to two equal groups of 7 each, pregnant at mid-gestation (day 18) and nonpregnant group. In all rabbits the skin of the dorsal base of the ear was shaved and one ear was infiltrated with 0.5-1.0 ml of Lidocaine hydrochloride 1% topical anesthetic solution (Kela laboratoria, Hoogstraten- Belgium) to induce vasodilatation of blood vessels of rabbit ears and facilitate venous cannulation. Five minutes later a marginal vein of ear was cannulated by a 24 gauge canula (Harsoria Health Care PVT-India) for IV anaesthetic administration. Blood samples were taken from the marginal vein of the other ear. Rabbits were allowed to rest for 10 min after venous cannulation before pre-anaesthetic blood sampling and data collection. All rabbits breathed room air during the study. In all groups, propofol 1% 10 mg/kg (B. Braun, Melsungen AG, Germany) was administered intravenously over 10 seconds for induction of anaesthesia. The anaesthesia then was maintained for 90min by

constant I.V infusion rate (1 mg/kg/min.) by using an infusion pump (R. 99 EZ Syringe infusion pump, UK). Recovery was confirmed by return of righting reflex. Ten minutes post recovery, post-anesthetic samples were collected. The value of Tr, RR, HR, haematological parameters and biochemical profiles were compared in pregnant and nonpregnant rabbits before and after induction of propofol.

2.3 Rectal Temperature (Tr)

The rectal temperature (Tr) of animals was measured by a certified digital clinical thermometer (Hartman – United Kingdom).The thermometer was inserted into the rectum for a depth of approximately 4 cm for 2 min. The values were obtained with an accuracy of ±0.1℃.

2.4 Respiratory Rate (RR)

The respiratory rate (RR) of rabbits was measured visually by counting the flank movements for 1 min. using a stopwatch. The values were taken with the animals sitting quietly.

2.5 Heart Rate (HR)

The heart rate (HR) was measured by auscultation using a stethoscope on the left ventral chest wall, performed twice for one minute. During the experimental period, the HR was also measured by Pulse-oximetry Patient Monitor (General Meditech Inc, Shenzhen, China).

2.6 Collection of Blood Samples

The area of the collection was shaved and scrubbed by a disinfectant (70% ethanol) before the marginal ear vein was punctured. Then 5 ml of blood was collected using plastic disposable syringes. Immediately after collection, 2 ml of blood was transferred to capped test tube containing di-sodium ethylene diamine tetra-acetate (Na_2 EDTA) as an anticoagulant for measurements of haematological parameters. The rest of the blood was allowed to stay for 2 hrs at room temperature and then centrifuged at 3000 rpm for 15min (Hettich-Zentrifugen-German) and haemolysis-free serum samples were pipetted into clean vials and immediately frozen at -20 ℃ for subsequent analysis. In addition, 2 ml of blood collected in heparinized tubes were centrifuged at 300 rmp for 15 min, and plasma samples obtained were used for determination of prothrombin time (PT) and activated partial thromboplastin (APTT) and osmolality.

2.6.1 Erythrocytic and leukocytes parameters

The standard methods described by Jain (17) were used for the determination of the parameters of erythrocyte series, erythrocytic count, Packed cell volume (PVC), Haemoglobin concentration (Hb),Total leukocyte count (TLC) and Differential leukocyte count (DLC).

2.7 Biochemical Parameters

2.7.1 Serum total protein

Serum total protein concentration was determined by the colorimetric standard calculator (18) using a kit (Cromatest Linear Chemicals S.L, Spain).

2.7.2 Serum albumin

Serum albumin concentration was determined by the colorimetric method (19) using a kit (Cromatest Linear Chemicals S.L, Spain).

2.7.3 Serum cholesterol

Serum cholesterol concentration was determined by the enzymatic-colorimetric method (20) using a kit (Spinreact, Spain).

2.8 Statistical Analysis

The data obtained from the studies were subjected to standard methods of statistical analysis using the Statistical Package of Science and Social (SPSS) version 16.0. The experiments were performed according to the completely randomized design (CRD). Analysis of variance (ANOVA) test was used to evaluate the effect of Propofol anaesthetic on thermoregulation, haematological, biochemical parameters and enzymes level in rabbits. The means values were compared significance at $P \leq 0.05$ and the group results were presented as mean ± SD.

3. RESULTS

The results of the effects of Propofol anaesthesia on thermoregulation, blood constituents and coagulation parameters in pregnant and nonpregnant are presented in Tables 1, 2 and 3 and figures shown in appendices.

3.1 Rectal Temperature (Tr)

Fig. 1 shows the results of the effect of Propofol anaesthesia on Tr in rabbits. There was no significant change in Tr values after induction of Propofol anaesthesia in pregnant and nonpregnant rabbits. However, in both groups, the administration of anaesthesia induced lowering of Tr. No significant interaction between Propofol and pregnancy was detected (Table 1). However, the general trend indicates lower Tr values in pregnant rabbits.

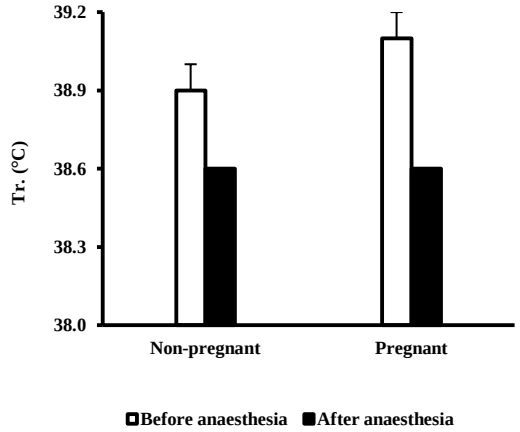

Fig. 1. Effect of propofol anaesthesia on rectal temperature (Tr) in pregnant and non pregnant rabbits

3.2 Respiratory Rate (RR)

The results indicated that RR values decreased significantly (P<0.05) after induction of Propofol anaesthesia in pregnant and nonpregnant rabbits compared to the control values. However, the interaction between pregnancy and Propofol anaesthesia was detected significant changes in rabbits (Table 1).

3.3 Heart Rate (HR)

The HR values were significant (P<0.05) decreased after Propofol anaesthesia in rabbits compared to the control values. The interaction variability between pregnancy and Propofol did not detect significant change after Propofol anaesthesia (Table 1). However, the effect of Propofol on HR was less pronounced in pregnant rabbits.

3.4 Haematological Parameters

The effects of Propofol anaesthesia on haematological parameters in pregnant and nonpregnant rabbits are shown in Table 2 and figures in (A4 –A12).

3.4.1 Packed Cell Volume (PCV)

The PCV values were significantly (P<0.05) decreased in both groups of rabbits after Propofol anaesthesia. No significant interaction between pregnancy and Propofol was detected (Table 2). Lower PCV values were obtained in pregnant group after administration of anaesthesia.

3.4.2 Erythrocyte count

The erythrocytes count value was significantly (P<0.05) reduced in pregnant and nonpregnant rabbits after induction of Propofol anaesthesia (Table, 2). No significant interaction between propofol anaesthesia and pregnancy was detected (Table 2).

3.4.3 Haemoglobin concentration (Hb)

Hb concentration was significantly (P<0.05) reduced in pregnant and nonpregnant groups after induction of anaesthesia. But no significant interactions were recorded between pregnancy and Propofol anaesthesia (Table, 2). Minimal Hb concentration values were recorded in pregnant group after anaesthesia.

3.4.4 Mean Cell Volume (MCV)

The MCV values in the non pregnant group were highly significantly (P<0.01) reduced after anaesthesia. The MCV was higher after Propofol anaesthesia in pregnant rabbits. Significant interactions were detected between pregnancy and anaesthesia (Table, 2).

3.4.5 Mean Cell Haemoglobin (MCH)

The MCH values in the nonpregnant group did not detect significant changes after induction of Propofol anaesthesia. The MCH was lower after propofol anaesthesia in pregnant group, compared to non pregnant. A significant difference was recorded between Propofol and pregnancy (Table 2).

3.4.6 Mean Cell Haemoglobin Concentration (MCHC)

The MCHC values were significantly (P<0.05) increased in pregnant and nonpregnant rabbits after induction of anaesthesia. A significant interaction between propofol anaesthesia and pregnancy was detected (Table 2).

Table 1. Effects of propofol anaesthesia on thermoregulation and heart rate (HR) in nonpregnant and pregnant rabbits before and after anaesthesia

Parameters	Non-pregnant		Pregnant	
	Before anaesthesia	After anaesthesia	Before anaesthesia	After anaesthesia
Tr (°C)	38.90±0.17[a]	38.60±0.18[a]	38.55±0.19[a]	38.55±0.33[a]
RR (breaths/min)	59.00±3.42[a]	47.00±4.16[b*]	60.00±5.73[a]	52.00±11.67[b*]
HR (beats/min)	268.00±5.48[a]	258.00±4.50[b*]	276.00±8.89[a]	268.00±6.00[b*]

*Mean values within the same row bearing different superscripts are significantly different at P<0.05. * P≤0.05*

3.5 Blood Coagulation Parameters

The effect of Propofol anaesthesia on blood coagulation parameters in nonpregnant and pregnant rabbits are presented in Table 2.

3.5.1 Platelets count

Platelets count values were significantly (P< 0.01) decreased in pregnant after anaesthesia (Table 2). A significant interaction between pregnancy and Propofol anaesthesia was detected (Table 2).

3.5.2 Prothrombin Time (PT)

The PT values were significantly (P<0.05) prolonged in pregnant and nonpregnant rabbits after Propofol anaesthesia. Significant interaction between pregnancy and propofol anaesthesia was detected (Table 2).

3.5.3 Activated Partial Thromboplastin Time (APTT)

The nonpregnant rabbits showed significantly prolonged APTT after induction of Propofol anaesthesia. The APTT was greater in pregnant rabbits.

3.6 Biochemical Constituents

The results of the effects of Propofol anaesthesia on serum biochemicals in nonpregnant and pregnant rabbits are presented in Table 3 and Figs. A13 to A 20.

3.6.1 Total protein

The total protein values were no significantly decreased in pregnant and nonpregnant rabbits after Propofol anaesthesia (Table 3). The lowest total proteins concentration after anaesthesia was recorded in pregnant rabbits. No significant interaction between pregnancy and anaesthesia was recorded (Table 3).

3.6.2 Albumin

The albumin concentration values were significant (P<0.05) decreased in nonpregnant group, while in pregnant rabbits albumin, was significantly (P<0.05) increased after Propofol anaesthesia.

3.6.3 Sodium (Na)

The Na concentration values were significantly (P<0.05) decreased in pregnant rabbits after Propofol anaesthesia. A significant interaction was recorded between Propofol anaesthesia and pregnancy (Table 3).

3.6.4 Potassium (K)

The K values were significantly (P<0.05) decreased in rabbits after Propofol anaesthesia. A significant interaction between pregnancy and Propofol anaesthesia was recorded (Table 3).

3.6.5 Calcium (Ca)

The Ca concentration values were significantly (P<0.05) reduced in pregnant while nonpregnant groups were obtained no significant increase of Ca values after induction of Propofol anaesthesia. There was no significant interaction between Propofol anaesthesia and pregnancy (Table 3).

3.6.6 Plasma osmolality

The plasma osmolality value was significantly (P<0.01) increased in pregnant groups after Propofol anaesthesia while nonpregnant obtained no significant changes. A significant interaction was detected after induction of Propofol anaesthesia. But general trend indicates higher plasma osmolality value in pregnant rabbits after administration of Propofol (Table 3).

3.6.7 Serum enzymes

The effects Propofol anaesthesia in nonpregnant and pregnant rabbits on serum enzymes are presented in Table 3.

Table 2. Effect of propofol anaesthesia on haematological parameters in rabbits

Parameters	Non-pregnant		Pregnant	
	Before anaesthesia	After anaesthesia	Before anaesthesia	After anaesthesia
Packed cell volume (%)	39.50±2.08^{a}	36.50±1.29^{b*}	36.00±2.74^{a}	34.65±3.23^{b*}
Erythrocytes (x10^{6}/μL)	4.85±0.13^{a}	4.70±0.19^{b*}	4.95±0.34^{a}	4.85±0.45^{a}
Hemoglobin (g/dL)	10.60±0.59^{a}	10.10±0.62^{b*}	10.60±0.65^{a}	10.30±0.65^{b*}
Mean cell volume ((fl)	82.00±3.70^{a}	80.10±0.96^{b**}	70.00±8.88^{a}	71.00±6.72^{a}
Mean cell hemoglobin (pg)	22.50±2.52^{a}	22.00±1.83^{a}	21.00±2.14^{a}	21.00±0.90^{a}
Mean cell hemoglobin concentration (g/dL)	26.80±2.99^{c}	28.50±2.65^{b*}	19.10±0.99^{b}	29.20±1.09^{a*}
Platelets (x10^{3}/μL)	377.50±17.29^{a}	377.80±8.58^{a}	512.30±187.18^{a}	490.10±161.83^{b**}
Prothrombin time (sec)	7.70±0.36^{b}	8.20±0.13^{a*}	9.00±0.33^{a}	9.10±0.40^{a}
Activated partial thromboplastin time (sec)	17.60±0.68^{a}	18.00±0.76^{b*}	18.10±0.88^{b}	18.60±0.77^{a*}

*Mean values within the same row bearing different superscripts are significantly different at P<0.05. * P≤0.05; ** P≤0.01*

Table 3. Effect of propofol anaesthesia on serum biochemical constituents in rabbits

Parameters	Non pregnant		Pregnant	
	Before anaesthesia	After anaesthesia	Before anaesthesia	After anaesthesia
Total protein (g/dL)	6.65±0.42^{a}	6.35±0.29^{a}	5.95±0.59^{a}	5.60±1.20^{a}
Albumin (g/dL)	4.10±0.18^{a}	3.60±0.19^{b*}	3.65±0.29^{b}	4.15±0.38^{a*}
Sodium Na^{+} (mEq/dL)	137.30±1.71^{a}	137.80±3.86^{a}	139.40±2.00^{a}	135.50±1.60^{b*}
Potassium K^{+} (mEq/dL)	6.01±0.24^{a}	5.61±0.26^{b*}	5.50±0.46^{a}	4.30±0.55^{b*}
Calcium Ca^{2+} (mg/dL)	9.80±0.66^{a}	9.50±0.55^{a}	10.10±0.25^{a}	9.70±0.24^{b*}
Osmolality (moms/L)	296.80±12.18^{a}	297.50±12.82^{a}	274.80±19.00^{b}	300.00±15.33^{a**}
LDH (IU/L)	185.75±17.75^{b}	293.00±97.22^{a**}	208.39±90.95^{a}	193.50±77.01^{b**}
CPK (IU/L)	231.00±95.10^{b}	296.00±115.45^{a**}	261.00±79.49^{b}	291.00±119.45^{a**}

Mean values within the same row bearing different superscripts are significantly different at P<0.05. P≤0.05; ** P≤0.01*

3.6.7.1 Lactate Dehydrogenase (LDH)

The LDH value was significantly (P<0.01) increased in nonpregnant and decreased in pregnant rabbits after Propofol anaesthesia.

3.6.7.2 Creatine Phosphokinase (CPK)

The CPK level was significantly (P<0.01) increased in pregnant and nonpregnant groups after Propofol anaesthesia compared to the control values.

4. DISCUSSION

In this experiment, the effects of pregnancy and Propofol anaesthesia on thermoregulation, blood constituents and blood coagulation indices were investigated in rabbits. The results indicate that the rectal temperature (Tr) values were decreased after administration of Propofol anaesthesia in pregnant and nonpregnant rabbits (Table 1).That could be related to Propofol produced hypothermia by redistribution of temperature [14]. The interaction between Propofol and pregnancy was not associated with significant variation in Tr values (Table 1). But the general trend indicates lower Tr values in pregnant rabbits following administration of Propofol. The lower Tr in pregnant rabbits could be related to increasing in thyroxin binding globulin (TBG) during pregnancy and decreases in free T3 and T4 level during second and third trimester were reported in pregnant women [15]. Hypothyroidism reduces basal metabolic rate, thereby reducing core body temperature [16]. The current results are in agreement with the findings which reported decreased body temperature in Propofol anaesthetized rats [17].

The studies indicate that the respiratory rate (RR) values in pregnant and nonpregnant rabbits were significantly decreased after induction of propofol (Table 1). That could be related to the fact that Propofol causes depression of the respiratory centre and decreases respiratory rate [18]. Propofol caused bradypnoea which may induce apnoea as a main undesirable effect. The current result is in agreement with the findings of [19] who found Propofol anaesthesia decreased respiratory rate in rabbits. However, there was a significant interaction between pregnancy and Propofol anaesthesia (Table 1), detected that RR was decreased slightly after induction of Propofol anaesthesia in pregnant rabbits. The minimal effect of Propofol on RR during gestation in humans was reported [20]. In the current study, the HR decreased significantly after administration of Propofol anaesthesia in pregnant and nonpregnant rabbits (Table 1). This response is related to negative inotropic and chronotropic effect of Propofol anaesthesia, which is mediated by activation of subtype of M2 acetylcholine receptor which enhanced nitric oxide production in cultured rat myocytes [21]. Propofol administration induces hypotension, negative effect inotropic and decreased systemic vascular resistance, resulting in lowering of the cardiac output [22,18,23,6]. A slight decrease on HR was detected after Propofol anesthesia in pregnant rabbits in the present study (Table 1) probably because Propofol modifies sympathetic tone during pregnancy and contributes to maintenance of resting vasomotor tone [23].

The results indicate that, PCV and RBCs count values were significantly decreased after administration of Propofol anaesthesia in pregnant and nonpregnant rabbits (Table 2). However, there was no significant interaction between pregnancy and Propofol. But the

general trend indicates lower Hb and PCV values in pregnant group after induction of Propofol anaesthesia. The cause of decline in these parameters may be related to the fact that Propofol decreases circulating halflife of erythrocytes. Propofol products diminish the deformability and survival of erythrocytes [24]. The current results are in agreement with the findings who found decline in PCV, Hb and RBCs count values after induction of Propofol anaesthesia in rabbits [19].

The current results indicate that the values of MCV, MCH and MCHC were significantly increased in pregnant group, while nonpregnant rabbits showed significant decrease in MCV and MCH values after propofol anaesthesia (Table 2). No significant interaction was detected between pregnancy and Propofol anaesthesia (Table 2).The results are generally in agreement with the findings [25] which reported no significant changes in RBC, Hb, and MCH, MCHC in dogs anaesthetized by products of emulsion of Propofol.

The findings of this study showed that the platelets count significantly decreased in pregnant rabbits after Propofol anaesthesia (Table 2). Significant interaction between pregnancy and Propofol in platelet count was obtained (Table 2). That could be related to decrease in platelet production during gestation. In women, normal pregnancy is associated with a physiological decrease in platelets count characterized by leftward shift in the platelet count distribution [26]. Propofol inhibited platelet aggregation as results of the inhibition of thromboxane A2 synthesis and increase of Nitric oxide production [4]. Propofol anaesthesia inhibits platelet-derived thromboxane A2 in surgical patients, whereas the plasma concentration NO is major metabolites [27]. Propofol related to thromboxane A2 inhibition platelets and concurrent enhancement of NO synthesis [28].The current results are in agreement with findings [4] who found that platelets count was dramatically decreased after Propofol anaesthesia in humans.

The current study showed significant increase in PT and APPT in pregnant and nonpregnant rabbits after induction of Propofol anaesthesia (Table 2). A significant interaction between pregnancy and Propofol anaesthesia detected higher PT values in pregnant rabbits (Table 2). Prolonged PT is related to impairment of production of fibrinogen and clotting factors active tissue factor VII, VIII, X and XII synthesis during pregnancy [29].Prothrombin time was significantly prolonged during organogenesis and was shortened in late foetal stage and APTT was prolonged in foetal stage in pregnant rabbits [30]. Also prolonged APTT was reported in pregnant rats [31]. A slight increase in PT and APTT after induction of Propofol anaesthesia in dogs was documented [25]. However, comparative studies reported that PT was decreased during normal pregnancy in women [32]. The observed variation could be species specific.

The present results showed that the concentration of plasma total proteins numerical decreased after induction of Propofol anaesthesia in pregnant and nonpregnant rabbits (Table 3), but no significant interaction between pregnancy and Propofol was obtained (Table 3). However, lower values of plasma total proteins were reported in pregnant rabbits. This response could be related to increase in plasma volume in pregnancy associated with haemodilution [33]. The albumin concentration values were significantly decreased in nonpregnant rabbits, while in pregnant rabbit's albumin concentration increased to the upper physiological limit after Propofol anaesthesia compared to the control values (Table 3). The serum concentration of total protein and globulins were gradually increased for 12 hours in rabbits sedated by Propofol [34]. The current results are in agreement with the findings [35] which revealed significant increase in serum total protein and albumin values after Propofol anaesthesia in dogs.

The current results showed that induction of Propofol anaesthesia was associated with significant decrease in plasma Na and K concentration in pregnant rabbits (Table 3).The decline could be related to the fact that propofol anaesthesia decreases renal tubular Na and water reabsorption. Significant changes in Na concentration after administration of Propofol anaesthesia were reported in calves [36].

The present results showed significant decrease in plasma Ca level in pregnant rabbits and no significant change in nonpregnant rabbits after induction of Propofol anaesthesia (Table 3). No significant interaction was noted between pregnancy and Propofol, but a decrease in Ca level was obtained in pregnant rabbits that could be related to increase of fetal demand for Ca. However, plasma Ca level increased during organogenesis stage on gestation day 18 in

rabbits [30]. Propofol has negative inotropic effect, partly mediated by decreased uptake of Ca into the sarcoplasmic reticulum via IP3 receptors channels [37]. Previous studies inducted that Propofol can block Ca channels by inhibiting the L- type Ca current [38,39].

There was significant increase in plasma osmolality in pregnant and no significant change in nonpregnant rabbits after Propofol anaesthesia (Table 3). Significant interaction was detected between pregnancy and Propofol anaesthesia. However, the general trend indicates higher plasma osmolality in pregnant group. The plasma osmolality is related mainly to glucose and sodium levels [40] and both of these elements increase during gestation [41]. Propofol anaesthesia induces systemic insulin resistance along with decreases in insulin stimulated glucose uptake in muscles. Attenuation of insulin mediated suppression of hepatic glucose output in rats lead to hyperglycemia and increase in osmolality [42].

The results showed significant decrease in LDH and increase in CPK concentration after Propofol anaesthesia in pregnant rabbits (Table 3). Significant interaction was detected between pregnancy and Propofol. This response could be related to the fact that propofol impairs the oxidation of fatty acids which constitute primary energy source of muscle, by inhibition of transport protein and failure of respiratory chain complex II [43] consequently, the imbalance between demand and supply may increase CPK concentration. Previous studies found that LDH increased on day 18 of gestation and then decreased with CPK during fetal development in rabbits [30]. However, LDH concentration increases slightly in pregnant women [29].

5. CONCLUSION

The results provide evidence that Propofol induces variable alterations in thermoregulation, heart rate, blood profile and serum biochemicals in pregnant rabbits. The information generated could be used in monitoring maternal health during pregnancy and risks of changes associated with anaesthesia in mammals.

CONSENT

It is not applicable.

ETHICAL APPROVAL

The ethical issues were addressed adequately according to veterinary and institutional guidelines.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Brodbelt D. Perioperative mortality in small animal anaesthesia. Vet. J. 2009;182(2):152-161.
2. Luo Z, Wang P, Zhang A, Zuo G, Zheng Y, et al. Evaluation of the microcirculation in a rabbit haemorrhagic shock model using laser Doppler Imaging. PLOS ONE. 2015;10(2):e0116076.
3. Mama KR, Steffey EP, Pascoe PJ. Evaluation of propofol as a general anaesthetic for horses.Vet. Surg.1995; 24(2):188-194.
4. Shabir N, Iqbal R, Abbas MN. Effect of propofol on haemodynamics and blood profile of humans. World J. Med. Sci. 2014;10(1):74-77.
5. Harcourt-Brown F. Textbook of Rabbit Medicine.Reed Educational and Professional Publishing Ltd; 2002.
6. Baumgartner CM, Koenighaus H, Ebner JK, Henke J, Schuster T, et al. Cardiovascular effects of dipyrone and propofol on haemodynamic function in rabbits. Am. J. Vet. Res. 2009;70(11):1407-1415.
7. Moreira CES, Ogino MAS, de Moraes, ACR. Haemostasis na gravidez: um estudo prospective. R.B.A.C., 2008;40:111-113.
8. Cheek TG, Baird E. Anaesthesia for non-obstetric surgery: Maternal and foetal considerations. Clin. Obstet. and Gynecol. 2012;52(4):535-545.
9. Ni Mhuireachtaigh, R. and O'Gorman, D.A. Anaesthesia in pregnant patients for non-obstetrics surgery. J. Clin. Anesth. 2006;18(1):60-66.
10. Xu Z, Dong M, Fang L, Dong R, Li S. The effect of propofol on the expression of rabbit ischemia reperfusion injury- related proteins. Cell Biochem. Biophysics.2015; 71(2):1165-1170.
11. Briggs GA, Freeman RK, Yaffe SJ. Drugs in pregnancy and lactation. A reference guide to foetal and neonatal risk. 8th ed. Lippincott Williams and Wilkins, Philadelphia. 2008;1178.
12. Bacon RC, Razis PA. The effect of propofol sedation in pregnancy on neonatal condition. Anaesthesia. 1994;49 (12):1058- 1060.

13. Hilton G, Haase R, Sauer H, Eichler G. Prolonged propofol infusion in pregnant neurosurgical patients. J. Neurosurg. Anaesthesiol. 2007;19(1):67-68.
14. Ikeda T, Sessler DI, Kikura M, Kazama T, Ikeda K, et al. Less core hypothermia when anaethesia is induced with inhaled sevoflurine than with intravenous propofol. Anaesth. Analg. 1999;88(4):921-924.
15. Soma-Pillay P, Nelson-Piercy C, Tolpanen H, Mebazaa A. Physiological changes in pregnancy. Cardiovasc. J. Afr. 2016;27(2):89-94.
16. Silva JE. Thermogenic effect of thyriod hormone and its clinical implication. Ann. Inter. Med. 2003;139(3):205-213.
17. Dispersyn G, Pain L, Touitou Y. Circadian disruption of body temperature and rest activity rhythms after general (propofol) anaesthesia in rats. Anaesthesiology, 2009;110(6):1305-1315.
18. Glowaski MM, Wetmore LA. Propofol: application in veterinary sedation and anesthesia. Clin. Tech. Small Anim. Pract. 1999;14(1):1-9.
19. Mazaheri-Khameneh R, Sarrafzadeh-Rezaei F, Asri-Rezaei S, Dalir-Naghadeh B. Evaluation of clinical and paraclinical effects of intraosseous vs intravenous administration of propofol on general anaesthesia in rabbits. Vet. Res. Forum., 2012;3(2):103-109.
20. Chesnutt AN. Physiology of normal pregnancy. Crit. Care Clin. 2004;20(4): 609-615.
21. Yamamoto S, Kawana S, Miyamoto A, Ohshika H, Namiki A. Propofol induced depression of cultured rat ventricular myocytes is related to the M2 acetylcholine receptor-NO-cGMP signaling pathway. Anaesthesiology. 1999;91(6):1712-1719.
22. Lercheet P, Nolan AM, Reid J. Comparative study of propofol or propofol and ketamine for induction of anaesthesia in dogs. Vet. Rec. 2000;146(20):571-574.
23. Krassioukov AV, Gelb AW, Weaver LC. Action of propofol on central sympathetic mechanisms controlling blood pressure. Can. J. Anaesth. 2014;40(8):761-769.
24. Sivilotti ML. Oxidant stress and haemolysis of the human erythrocytes. Toxicol. Rev. 2004;23(3):169-188.
25. Morey TE, Modell JH, Shekhawat D, Shekhawat DO, Klatt B, et al. Anaesthetic properties of a propofol microemulusion in dogs. Anaesth. Analg. 2006;103(4):882-887.
26. Boehlen F, Hohlfeld P, Extermann P, Pernerger TV, de Moerloose P. Platelet count at term pregnancy: A reappraisal of the threshold. Obstet. Gynecol. 2000;95(1):29-33.
27. Tsikas D, Gutzki FM, Stichtenoth DO. Circulating and excreting nitric and nitrate as indicators of nitric oxide synthesis in humans: methods of analysis. Eur. J. Clin. Pharmacol. 2006;62(Suppl.13):51-59.
28. Mendez D, Del La Cruz JP, Arrebolla MM, Gonzalez-Correa JA, Garcia-Temboury A, et al. The effect of propofol on the interaction of platelets with leukocytes and erythrocytes in surgical patients. Anaesth. Analg. 2003;96:1361-1366.
29. O'Danoghue K. Physiological changes in pregnancy. In: Respiratory tract. Obstetrics (Editors: Baker P and Kenny L). Hodder Arnold. London. 2013;24-37.
30. Mizoguchi Y, Matsuoka T, Mizuguchi H, Endon T, Kamata R, et al. Changes in blood parameters in New Zealand White rabbits during pregnancy. Lab. Anim. 2010;44(1):33-39.
31. Papworth T, Clubb S. Clinical pathology in the female rat during the pre and postnatal period. Comp. Haematol. Int. 1995;5(1):13-24.
32. Srimala P, Khan I, Hari PS. Estimation of prothrombine time in pregnancy compared with normal controls. J. Evol. Med. Dent. Sci. 2013;2(2):72-78.
33. Andersson A, Hultberg B, Brattstrom L, Isaksson A. Decreased serum homocysteine in pregnancy.Eur. J. Clin. Chem. Clin. Biochem. 1992;(6)30:377-379.
34. Ypsilantis P, Politou M, Mikroulis D, Pitiakoudis M, Lambropoulou M, et al. Organ toxicity and mortality in propofol-sedated rabbits under prolonged mechanical ventilation. Anaesth. Analg. 2007;105(1):155-166.
35. Kim J, Jang I. The effect of xylazine premedication on *Propofol anaesthesia* in the dog. Kor. J. Vet.Clin. Med. 1999;16:86-94.
36. Genccelep A, Aslan L, Sindak N. Effect of propofol anaesthesia in claves. Ind. Vet. J. 2005;82(5):516-518.
37. LinK, Sadee W, Quillan JM. Rapid measurement of intracellur calcium using fluorescence plate reader.Biotechniques. 1999;26(2):318- 322.
38. Yang CY, Wong CS, Yu CC, Luk HN, Lin CI. Propofol inhibits cardiac L-type calcium

current in guinea pig ventricular myocytes. Anaesthesiology. 1996;84(3):626-635.
39. Zhou W, Fontenot HJ, Liu S, Kennedy RH. Modulation of cardiac calcium channels by propofol. Anaesthesiology. 1997;86(3):70-675.
40. Faust R. Anesthesiology review" 2nd ed, Churchil Livingstone, New York. 1994; 35.
41. Akinloye O, Obikoya OM, Jegede AI, Oparinde DP, Arowojolu AO. Cortisol plays central role in biochemical changes during pregnancy. Int. J. Med. Biomed. Res. 2013;2(1):3-12.
42. Yasuda YY, Fukushima Y, Keneki M, Jeevenda Martyn JA. Anaesthesia with propofol induces insulin resistance systemically in skeletal and cardiac muscles and liver of rats. In Biochem.Biophys. Res. Commun, 2013; 431(1):81-85.
43. Wolf A, Weir P, Segar P, Storne J, Shield J. Impaired fatty acid oxidation in propofol infusion syndrome. Lancet. 2001;357 (9256):606-607.

APPENDICES

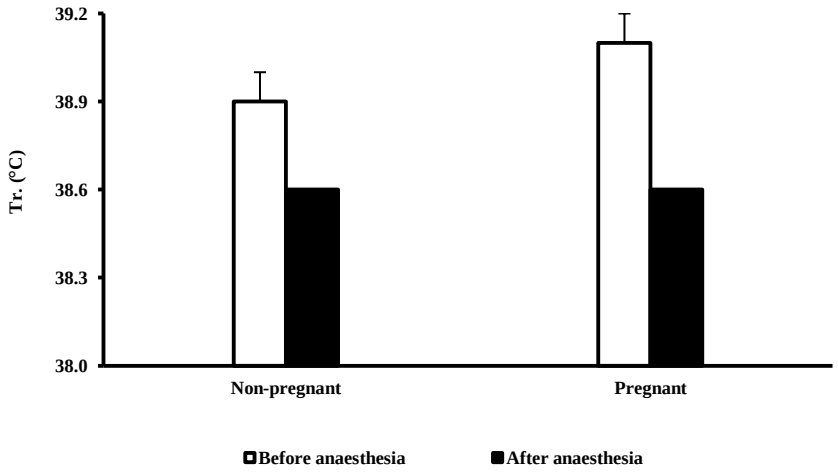

Fig. 1. Effect of propofol anaesthesia on rectal temperature (Tr) in pregnant and nonpregnant rabbits

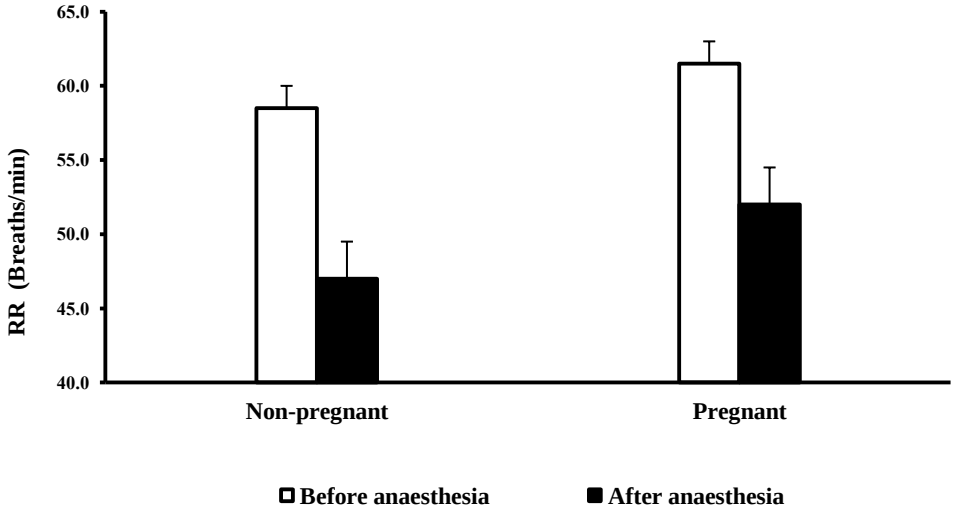

Fig. 2. Effect of propofol anaesthesia on respiratory rate (RR)in nonpregnant and pregnant rabbits

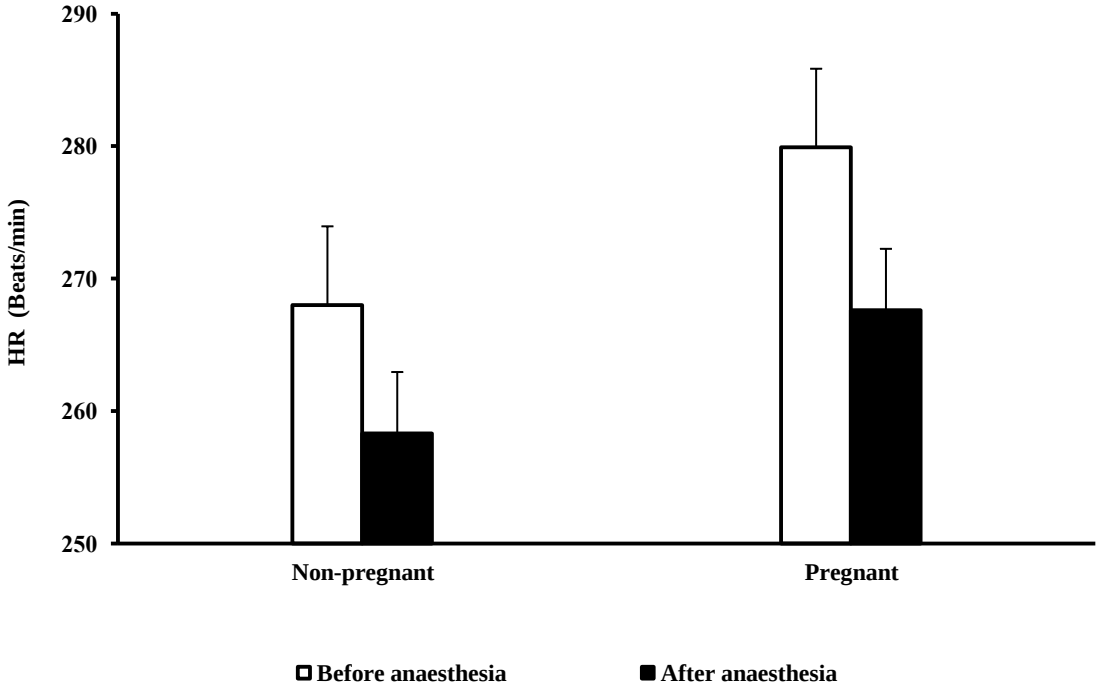

Fig. 3. Effect of propofol anaesthesia on heart rate (HR) in nonpregnant and pregnant rabbits

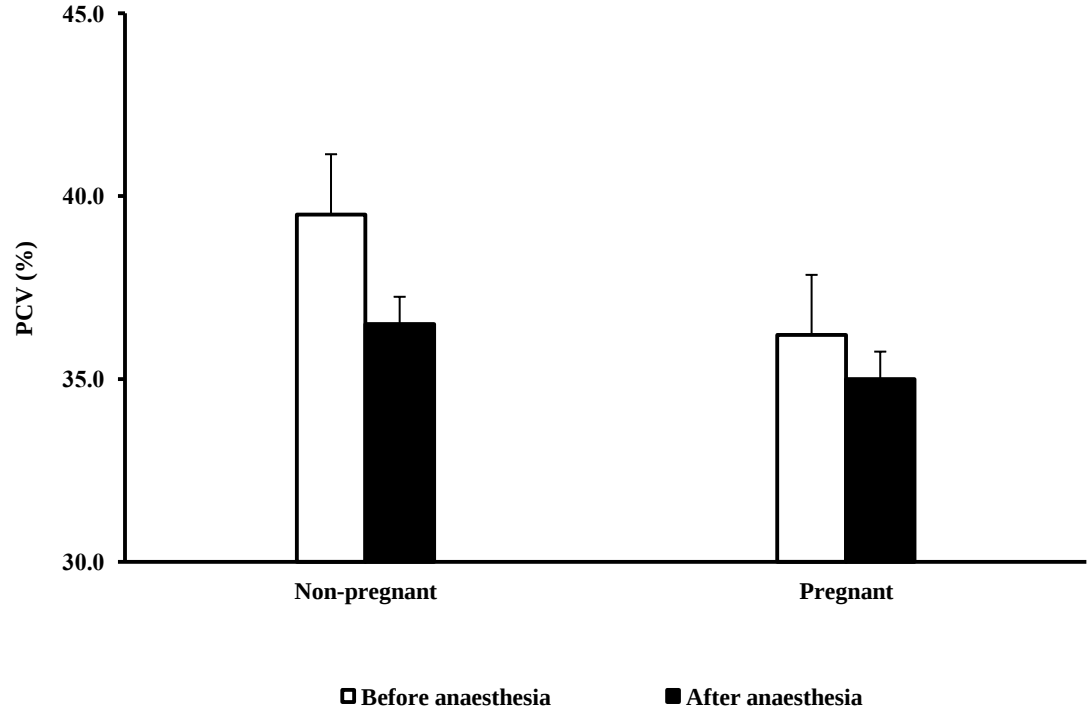

Fig. 4. Effect of propofol anaesthesia on packed cell volume (PCV) in nonpregnant and pregnant rabbits

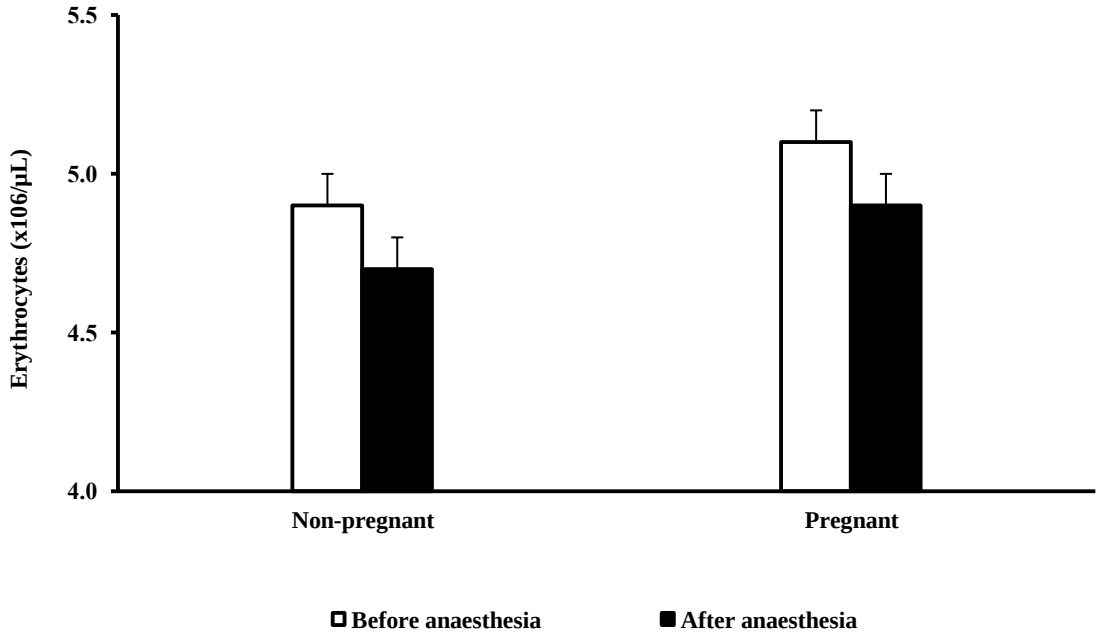

Fig. 5. Effect of propofol anaesthesia on erythrocytes count in pregnant and nonpregnant rabbits

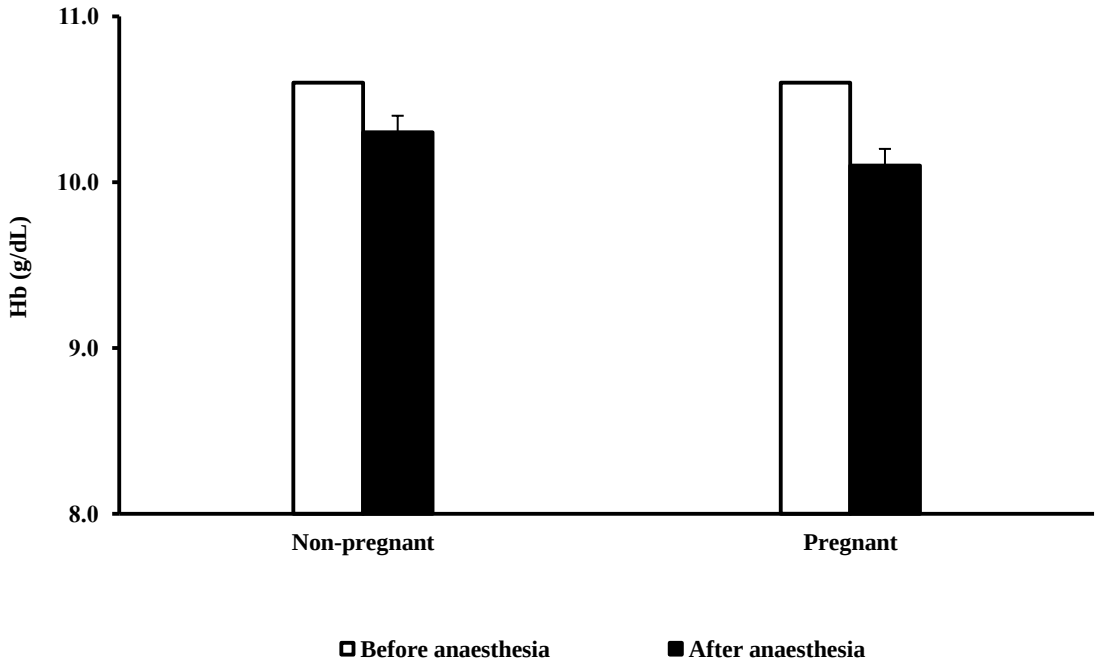

Fig. 6. Effect of propofol anaesthesia on Hb concentration in nonpregnant and pregnant rabbits

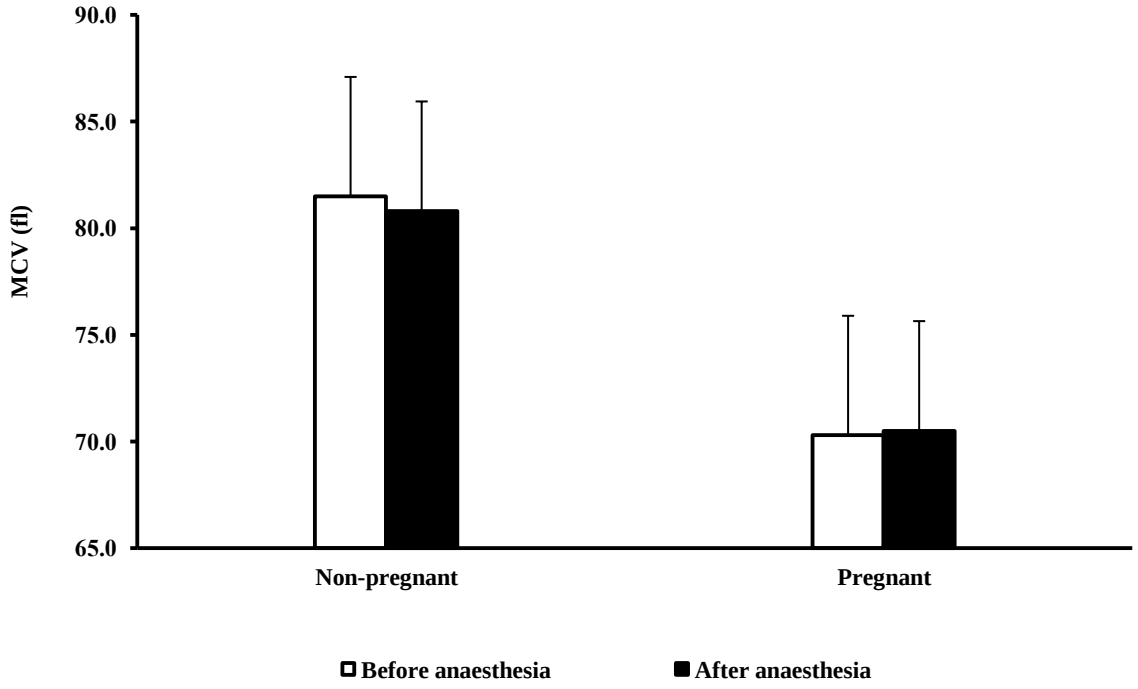

Fig. 7. The effect of propofol anaesthesia on mean cell volume (MCV) in nonpregnant and pregnant rabbits

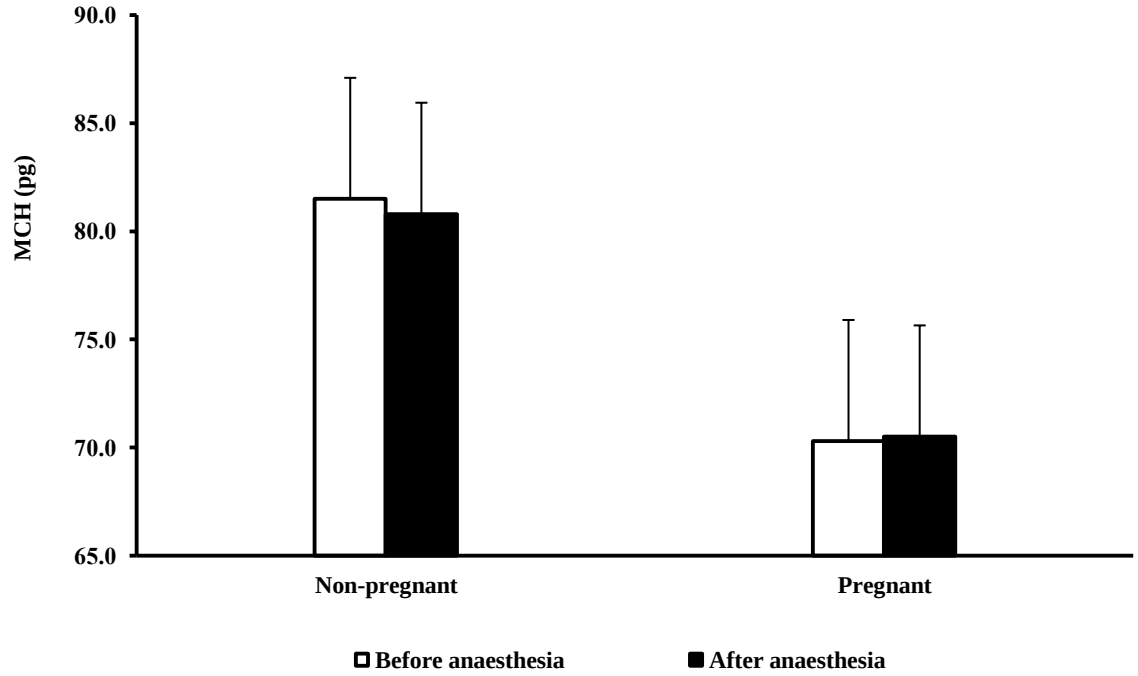

Fig. 8. Effect of propofol anaesthesia on mean cell haemoglobin (MCH) in nonpregnant and pregnant rabbits

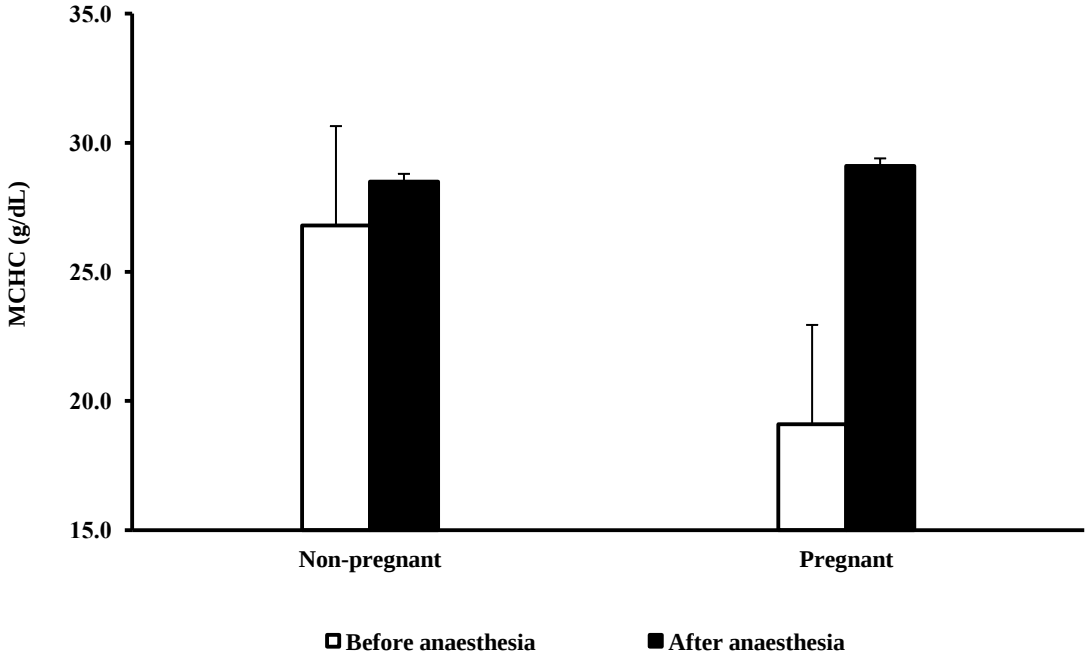

Fig. 9. Effect of propofol anaesthesia in Mean cell haemoglobin concentration (MCHC) in nonpregnant and pregnant rabbits

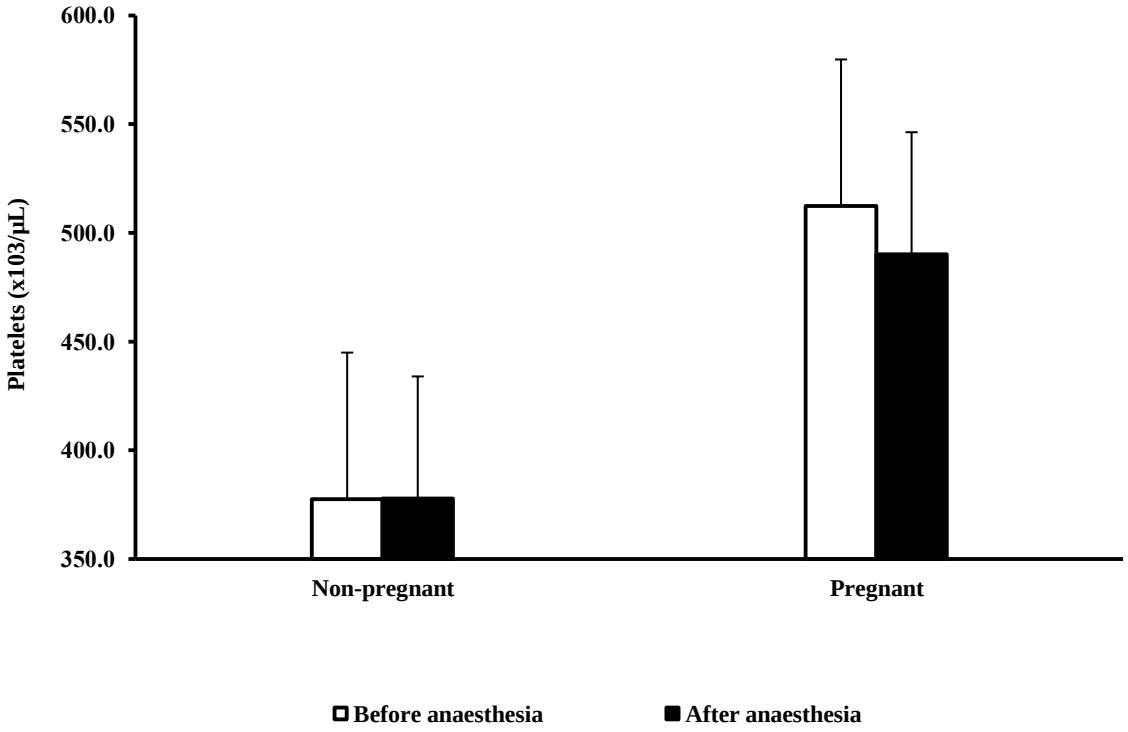

Fig. 10. The effect of propofol on platelets in nonpregnant and pregnant rabbits

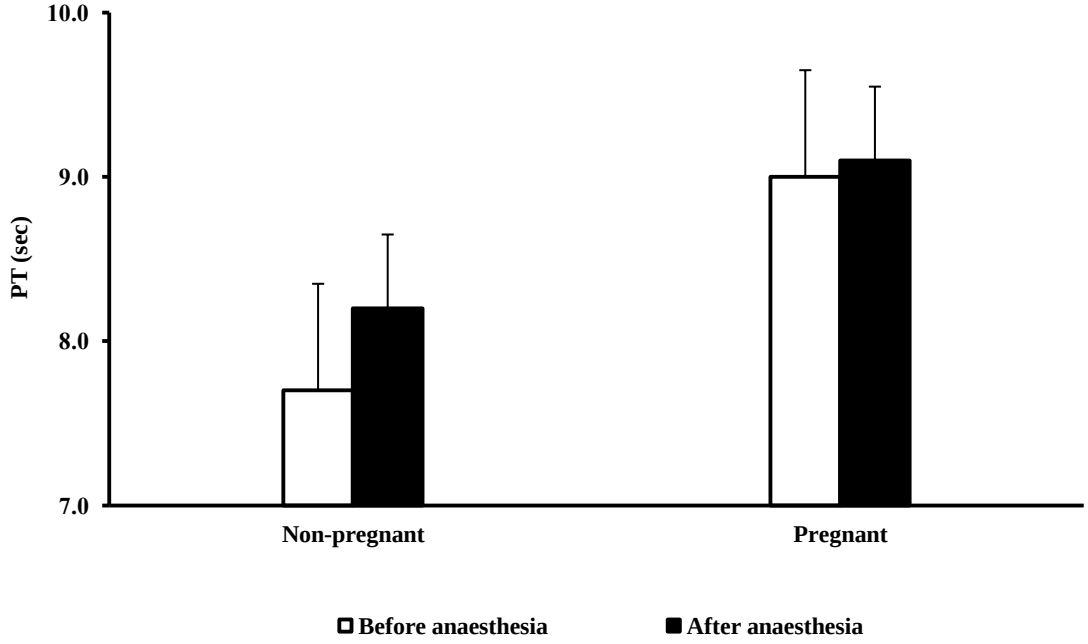

Fig. 11. Effect of propofol anaesthesia on prothrombin time(PT) in nonpregnant and pregnant rabbits

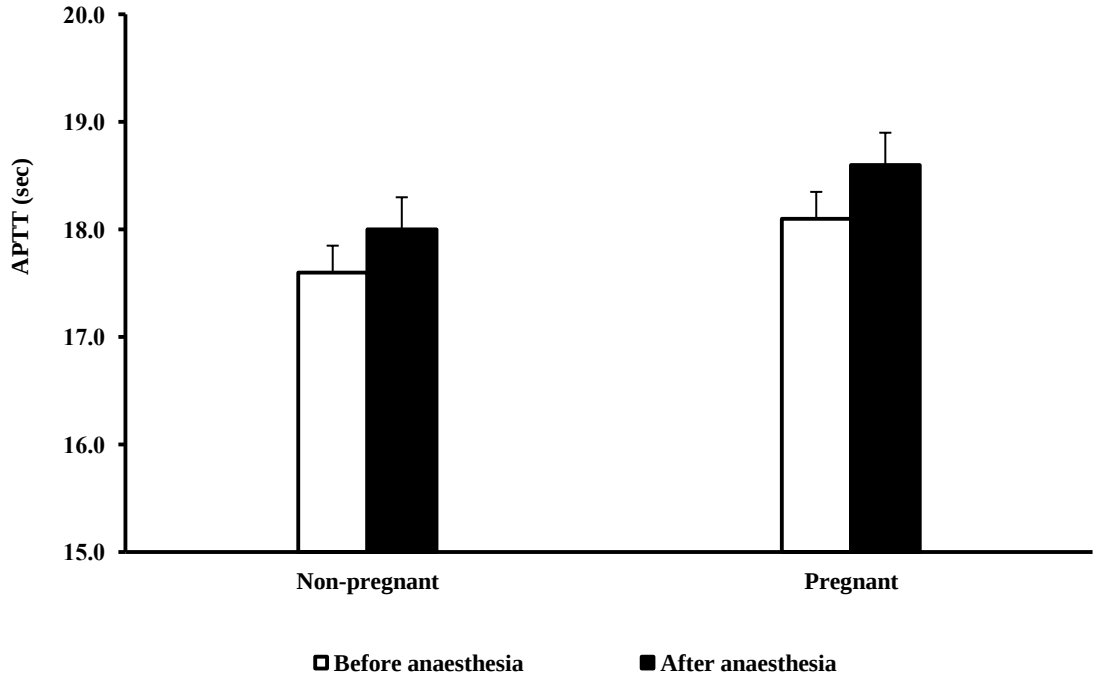

Fig. 12. Effect of propofol anaesthesia on activated partial thromboplastin time (APTT) in nonpregnant and pregnant rabbits

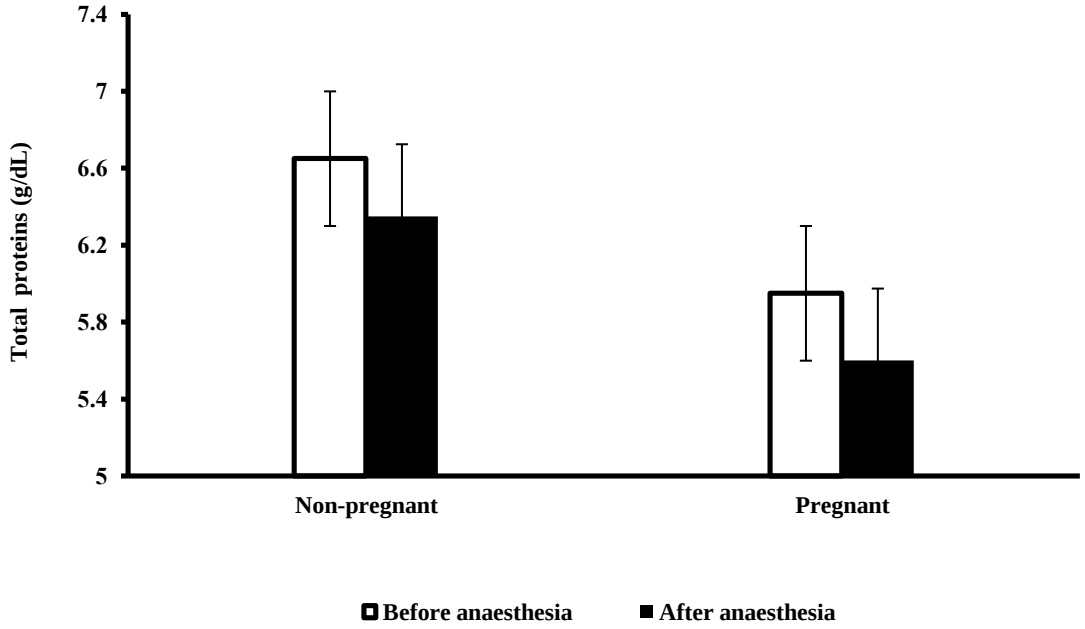

Fig. 13. Effect of propofol anaesthesia on the total proteins concentration in pregnant and nonpregnant

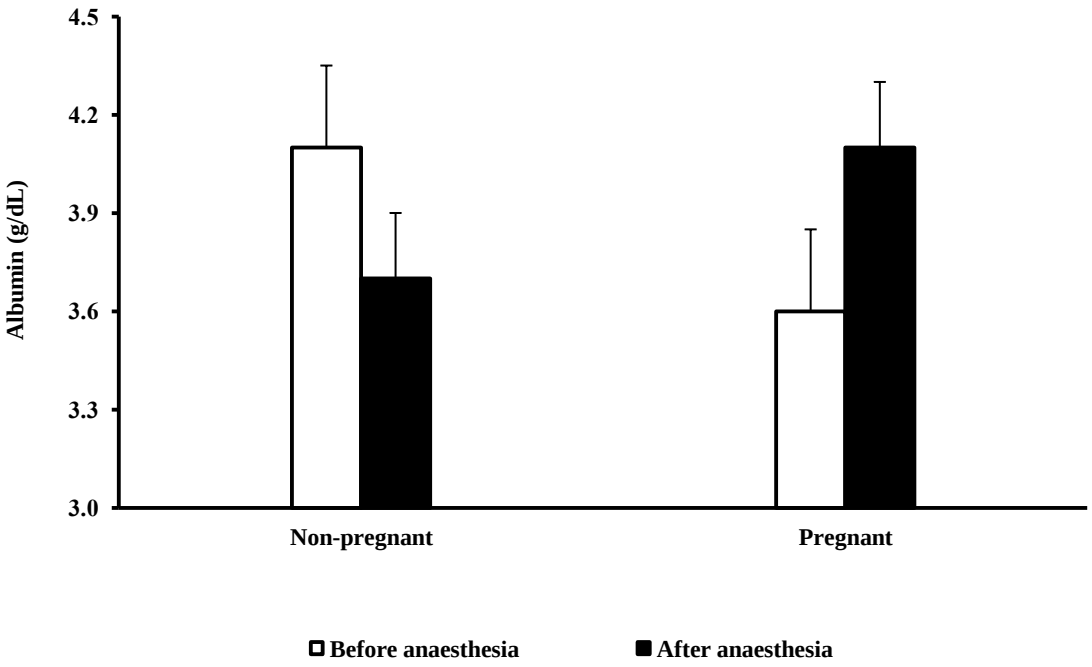

Fig. 14. Effect of propofol anaesthesia on plasma albumin concentration in nonpregnant and pregnant rabbits

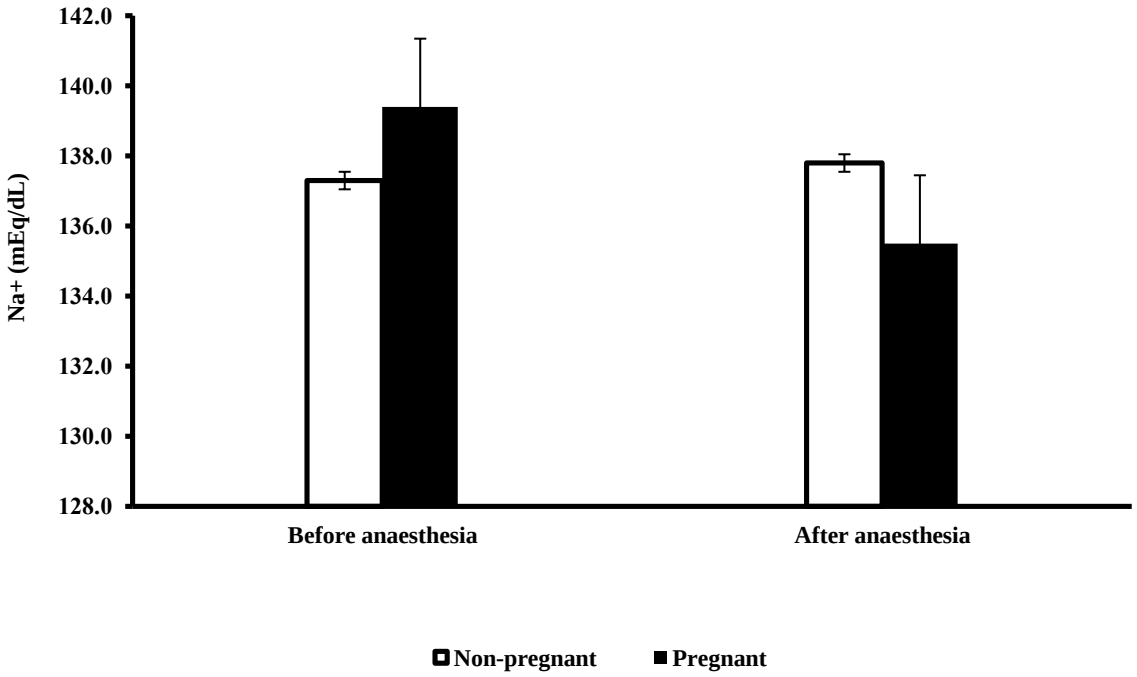

Fig. 15. Effect of propofol anaesthesia on sodium (Na+) concentration in non pregnant and pregnant rabbits

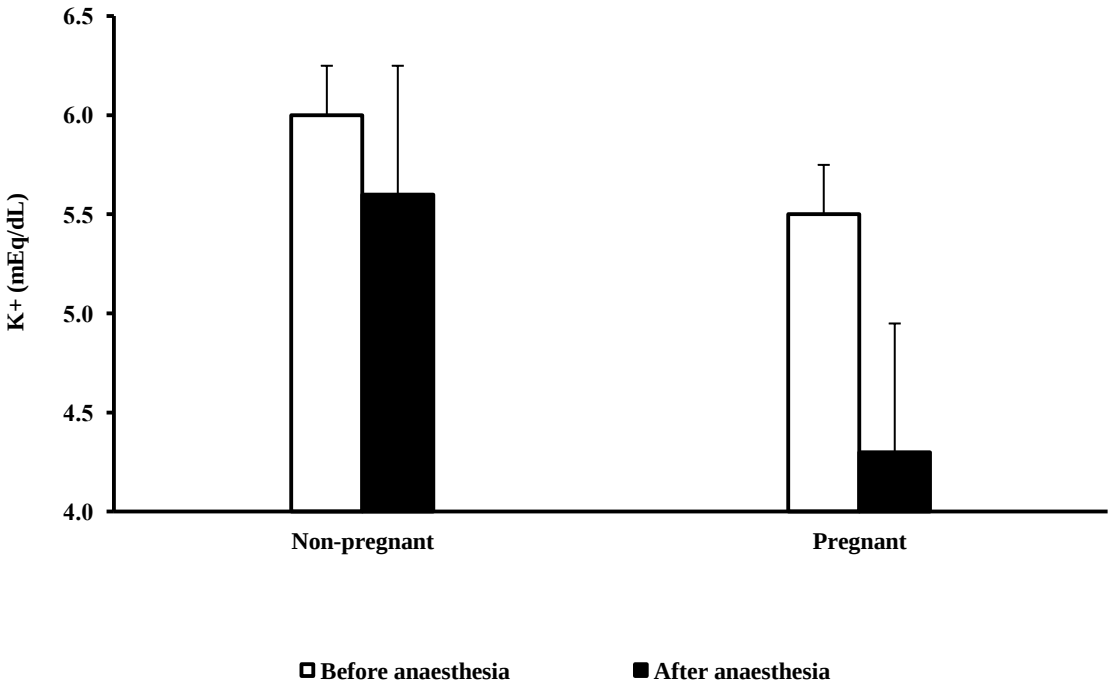

Fig. 16. Effect of propofol anaesthesia on potassium (K+) concentration in non pregnant and pregnant rabbits

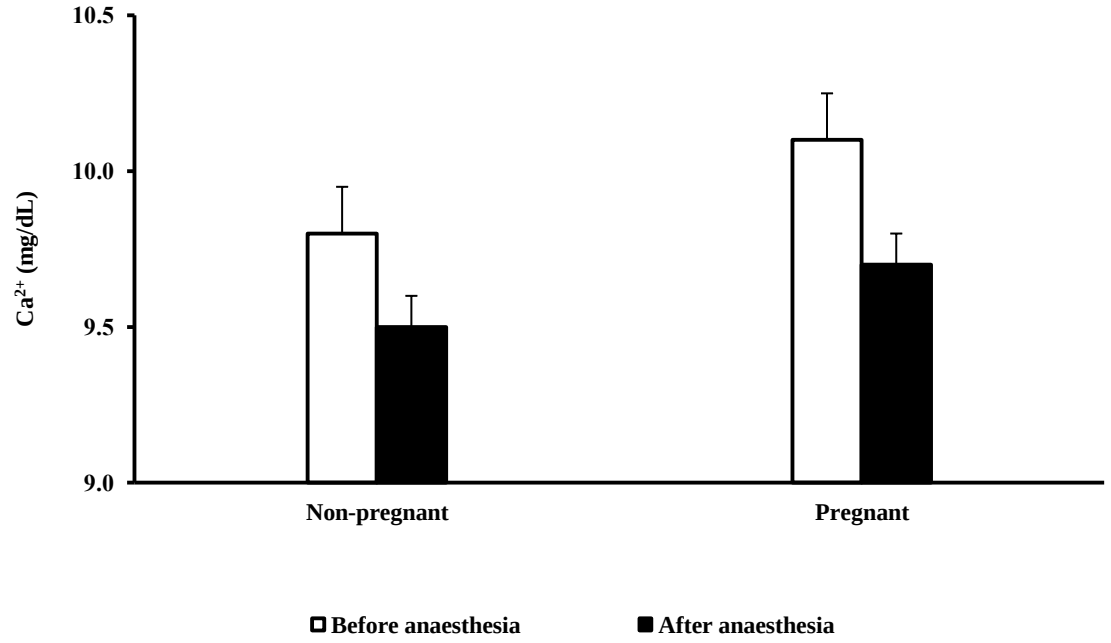

Fig. 17. Effect of propofol anaesthesia on plasma calcium (Ca2+) concentration in pregnant and non pregnant rabbits

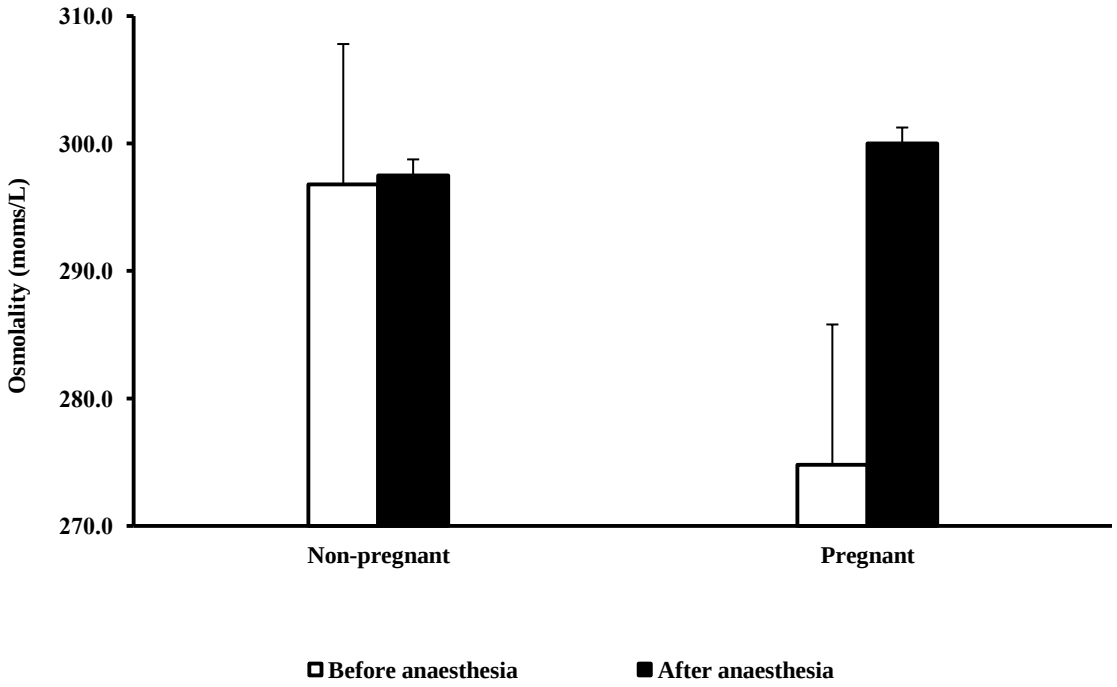

Fig. 18. Effect of propofol anaesthesia on plasma osmolality in non pregnant and pregnant rabbits

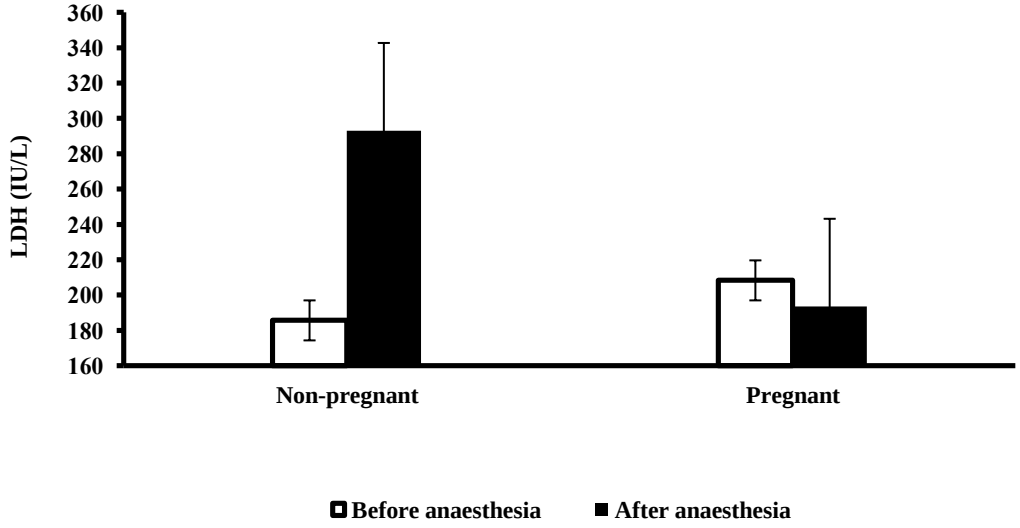

Fig. 19. Effect of propofol anaesthesia on lactate dehydrogenase (LDH) level in non pregnant and pregnant rabbits

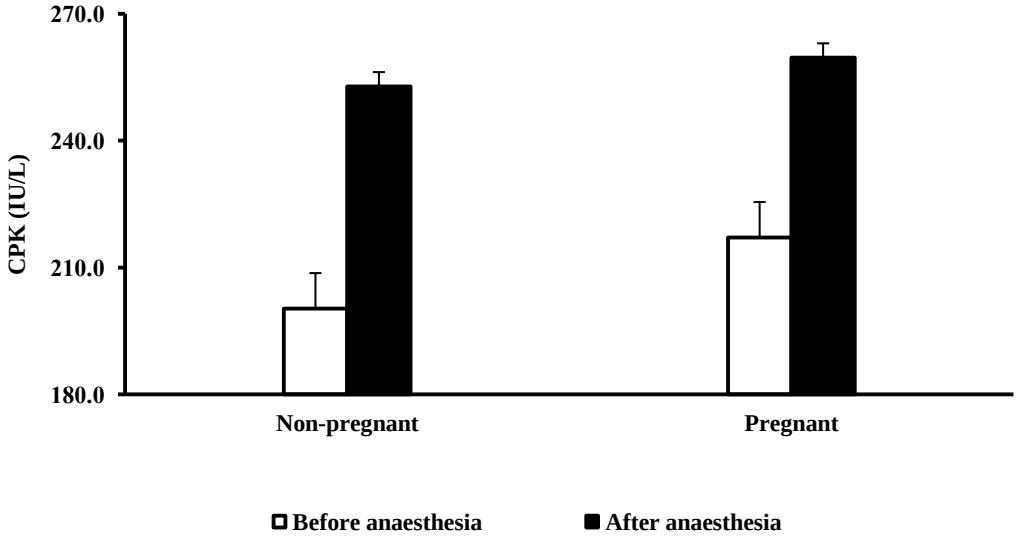

Fig. 20. Effect of propofol anaesthesia on creatinine phosphokinase (CPK) level in pregnant and non pregnant rabbits

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/56384