



# Evaluation of hematological, biochemical and oxidative stress profile in calves under propofol anesthesia

Pedro Paulo Arcanjo Lima<sup>1</sup> · Luis Gustavo Narciso<sup>2</sup> · Jefferson Filgueira Alcindo<sup>1</sup> · Maurício Deschk<sup>1</sup> · Paulo Cesar Ciarlini<sup>2</sup> · Paulo Sérgio Patto dos Santos<sup>2</sup> · Breno Fernando Martins de Almeida<sup>2,3</sup>

Received: 24 May 2021 / Accepted: 27 August 2021 / Published online: 3 September 2021  
© The Author(s), under exclusive licence to Springer Nature B.V. 2021

## Abstract

Propofol is a widely used drug in veterinary medicine to induce anesthesia; as well as the chosen compound for protocols of intravenous anesthesia. The present study aimed to describe the hematological, biochemical and oxidative stress alterations in calves kept under anesthesia by propofol in different dosages. In order to achieve this, eight Holstein calves were induced using propofol in a 5 mg/kg dosage and maintained under continuous propofol infusion for 60 min, having being administered 0.6 mg/kg/h or 0.8 mg/kg/h in crossover design with seven days interval. Blood samples were collected immediately before the anesthesia induction (baseline), and 30 min, 1, 2, 3, 4 and 5 h after the procedure started. Statistically relevant propofol influence was observed both in blood and biochemical parameters, with differences between dosages according to the time of infusion. The drug action over oxidative stress was also observed, causing a raise of the total antioxidant capacity (TAC) with an uric acid increase. Additionally, the increase of triglycerides, induced by the anesthesia maintenance with propofol, caused lipemia in the samples, which was capable of interfering directly in the measurements made by refractometry and spectrophotometry. It was concluded that, in spite of propofol induced alterations in blood and biochemical parameters, such alterations are subtle. In addition to that, the drug presented an antioxidative effect, which reinstates the safety of anesthesia maintenance with propofol in calves.

**Keywords** Antioxidant · Continuous infusion · Bovine · Hemogram

## Introduction

Developed in the 1970's, propofol—or 2, 6-diisopropylphenol—is a general short-acting anesthetic medication that belongs to the alkylphenol family (Walsh 2018). Since introduced in the market, in 1977, the drug has replaced barbiturates as the most popular inductor and has been widely used as a sedative in intensive care units (Brohan and Goudra

2017; Guo and Ma 2020). Propofol presents itself as a lipid emulsion composed by its active (propofol), soybean oil, glycerol and egg lecithin.

Besides the sedative and hypnotic effects of propofol not being completely understood, it is known that the drug acts potentializing the Gamma-Aminobutyric acid (GABA<sub>A</sub>) inhibitory-transmissor connection to the ionic channels from GABA<sub>A</sub> (GABAAR) receptors, indirectly activating such receptor (Brohan and Goudra 2017; Walsh 2018). Propofol also inhibits *N*-Metil-D-aspartate (NMDA) receptors, contributing to a depression and reduction of activity of the central nervous system (Grimm et al. 2015).

The drug has a 97 to 99% potential to connect with plasma proteins (Cagnardi et al. 2009). Metabolization happens fast and extensively in the liver, forming inactive water soluble metabolites which are excreted by the kidneys (Walsh 2018). It is also suggested a possible existence of extra-hepatic metabolism or extra-renal excretion (Grimm et al. 2015) Other pharmaceutical characteristics fit propofol as an ideal injectable anesthetic, such as fast

✉ Breno Fernando Martins de Almeida  
bfmalmeida@yahoo.com.br; breno.fernando@unifio.edu.br

<sup>1</sup> Faculty of Veterinary Medicine, Federal University of Juiz de Fora (UFJF), Juiz de Fora, Minas Gerais State, Brazil

<sup>2</sup> Faculty of Veterinary Medicine of Araçatuba, São Paulo State University, (FMVA-UNESP), Araçatuba, São Paulo State, Brazil

<sup>3</sup> Department of Veterinary Medicine, University Center of the Integrated Faculties of Ourinhos (Unifio), Rodovia BR 153, km 338, Bairro Água Do Cateto, Ourinhos, SP CEP 19909-100, Brazil

effectively, short-action, absence of cumulative effects and fast recovery. On the other hand, the drug presents side-effects such as post-induction apnea, increased susceptibility to microbial infection, arrhythmia, cardiac, circulatory and breath dose-dependent depression, hypotension and others (Visvabharathy et al. 2015; Brohan and Goudra 2017; Guo and Ma 2020).

Anesthetic agents may induce important alterations over different systems and organs, promoting biochemical and hematologic alterations, but data about such information is scarce. Propofol phenol structure is able to stabilize the structure of cell membranes and, because of that, the drug is related to antioxidant activity by reducing lipid peroxidation (Costa et al. 2013). Propofol is credited for protecting cells against oxidative and reperfusion injuries, caused by ischemia or hypoxia processes in the brain, lungs, heart, kidneys, liver and intestinal tissues (Vasileiou et al. 2012; Costa et al. 2013). When in moderate concentration and duration, propofol can protect organs and cells, as well as exert an anti-tumoral effect regulating autophagy (Guo and Ma 2020). Additionally, the antioxidant protective effect can increase erythrocyte membrane resilience, avoiding their destruction (Costa et al. 2013). The drug also influences the inflammatory-response modulation by reducing the production of pro-inflammatory cytokines, altering nitric oxide expression and inhibiting neutrophil function (Sato et al. 2016). Despite its possible antioxidant action, there are, to date, no studies that have determined the effect of propofol on oxidative stress parameters in cattle. However, when evaluating other anesthetic protocols, it has already been demonstrated an increase of the total oxidant capacity during the use of desflurane, while sevoflurane can significantly increase the antioxidant capacity of the organism (Erbas et al. 2015).

Bearing in mind the possible alterations caused by anesthetic agents in hematological, biochemistry and oxidative stress analyzes, the present study aims to describe alterations in these parameters in calves kept under anesthesia with propofol and clarify propofol effects in these animals.

## Material and methods

### Approval by the Ethics Committee

The study was approved by the Ethics Committee of Animal Usage in Animal Experimentation (CEEA) of the School of Veterinary Medicine at the Araçatuba Campus of São Paulo State University (Unesp), under procedural number FOA-9416/10.

## Animals

Eight male Holstein calves, aged between 6 to 12 months and weighing between 84 and 124 kg, were used, all of them came from the same milking farm. The animals were submitted to clinical examination accordingly to Feitosa (2014) and had a complete blood count (CBC) performed to verify their health conditions. Animals were placed in paddocks and were fed with brachiaria grass, starter and corn silage with supplementing. Water was freely provided.

### Animal preparation and experiment protocol

Animals were kept in food fasting for 36 h and water fasting for 12 h before the experiment began. After physical constraint, the animals had their jugulars catheterized with a 16 gauge 30.5 mm catheter (Catheter BD Intracath 16G—Becton, Dickinson Ind. Cirúrgicas Ltda.—Juiz de Fora, MG, Brazil), the right vein for intravenous propofol administration and the left for the maintenance fluid therapy, with an administration of Ringer with lactate (Ringer com Lactato, Equiplex indústria farmacêutica Ltda., Aparecida de Goiânia, GO, Brazil) in an infusion rate of 5 mL/kg/h.

The animals were kept restrained for a 10-min period in order to minimize the handling's effect over baseline values. Afterwards, the animals were induced with Propofol (Propovan 10 mg/mL Laboratório Cristália—Produtos Químicos Farmacêuticos Ltda, Itapira, SP, Brazil) in a 5 mg/kg dosage administered over 2 min and, immediately after that, intubated with tracheal tubes proportional to their size and positioned in right lateral decubitus, spontaneously breathing the air from the environment. The anesthesia maintenance was made by a continuous propofol infusion, administered by an infusion pump (ST-1000-Samtronic, São Paulo, SP, Brazil) at two different rates: 0.6 mg/kg/min IV (G06) and 0.8 mg/kg/min IV (G08) during 60 min. These rates were established according to Riebold (2007), that observed a superficial anesthetic plane at the rate of 0.4 mg/kg/min, and a pilot study using different rates. All animals were anesthetized twice, participating in both groups, with a 1-week interval between one anesthesia and the other.

The blood samples were collected just right before the anesthesia induction (baseline) and 30 min, 1, 2, 3, 4 and 5 h after the procedure started. Before each sampling, about 3 mL of blood was removed to avoid dilution and contamination of the samples. After each sampling, the catheter was flushed with heparinized solution (5 U/mL). The blood samples destined to the hemogram were

put in tubes with ethylenediaminetetraacetic acid disodium ( $\text{Na}_2\text{EDTA}$ , BD Vacutainer®, Franklin Lakes, NJ, EUA) and the ones destined to biochemical and oxidative stress evaluations were put in tubes with heparin (BD Vacutainer®, Franklin Lakes, NJ, EUA) to obtain plasma after immediate centrifugation in 2,500 rpm for 10 min and stored under light protection at  $-20^\circ\text{C}$  by a maximum period of 15 days.

### Laboratorial analysis

For the CBC's realization, counts of red blood cells (RBC) and white blood cells (WBC), as well as the measurement of hemoglobin were done in a veterinarian automated cell counter (BC-2800Vet, Shenzhen Mindray Bio-Medical Electronics Co., Nanshan, China). Hematocrit (HCT) was determined by Strumia's microcapillary method, centrifuged in 11,400 rpm during 5 min. The differential leukocyte counts and the determination of platelets by  $1,000\times$  oil immersion field ( $1000\times$  field) were done in a blood smear colored by commercial stain (Instant-Prov, Newprov, Pinhais, PR, Brasil) and, altogether with icterus levels, followed what was recommended by Jain (1986). Total plasma protein (TPP) was determined in a portable clinical refractometer (ATAGO, Mod. Master-SUR-NM, Tokio, Japan) and plas-matic fibrinogen (PF) was measured after its precipitation under  $56^\circ\text{C}$ . The blood indicators of mean corpuscular hemoglobin concentration (MCHC) and mean corpuscular volume (MCV) were measured as previously described (Jain 1986).

Biochemical evaluations were done with an automated photocolormeter (BS 200, Shenzhen Mindray Bio-Medical Electronics Co., Nanshan, China) using commercial reagents (Biosystems, Barcelona, Spain) according to the producer's recommendation. The biochemical determinations were made in a duplicate in  $37^\circ\text{C}$  after calibration with a commercial calibrator and checked with commercial controls levels I and II (Biosystems, Barcelona, Spain). Uric acid, glucose, total cholesterol and triglycerides levels were measured by Trinder-enzymatic method, AST activity by ultraviolet (UV) kinaesthetic method, albumin levels by colorimetric method using bromocresol green, total bilirubin by Sims-Horn colorimetry, creatinine by alkaline picrate colorimetric method, GGT activity by modified-Szasz, total protein by biuret colorimetric method and urea by enzymatic UV method. Globulin levels were obtained subtracting the albumin from the total protein levels.

To evaluate the oxidative stress, the determinations were also made in the same automated photocolormeter. The total antioxidant capacity (TAC) was determined by the cation 2,2'-azino-bis 3-ethylbenzthiazoline-6-sulphonic acid (ABTS) inhibition, described by Erel (2004). The total oxidant capacity (TOC) was measured by the orange xilenol

colorimetric method described by Erel (2005). Lipid peroxidation was measured by substances reactive to the thiobarbituric acid (TBARS) according the methodology described in Hunter et al. (1985) at 545 nm, in which the results were obtained after a comparison of the samples with a standard curve from 0 to  $100\ \mu\text{mol}$  de malondialdehyde/L. All the compounds used to make the reagents were from Sigma-Aldrich Chemical Co.

### Statistical analysis

The variables were tested in normality using Shapiro–Wilk Test and the differences between the groups and time points (TP) were tested by two-way repeated measures ANOVA and Sidak's post-testing. All statistical analysis was done in a computer program (GraphPad Prism, v.6.00 para Windows, GraphPad Software, La Jolla, CA, USA, [www.graphpad.com](http://www.graphpad.com)), being considered significant when  $p < 0.05$ .

## Results

### Hematology

When analyzing the erythrogram parameters, the anesthesia with propofol in a  $0.6\ \text{mg/kg/min}$  infusion rate caused an elevation of HCT and hemoglobin in TP30min, TP1h and TP2h after the procedure in comparison with the baseline; there was no difference from the infusion rate of  $0.8\ \text{mg/kg/minute}$ . The other variables from the erythrogram were not affected nor by the anesthesia time nor by the propofol's dosage (Table 1).

As for the leukogram, the propofol anesthesia in a  $0.6\ \text{mg/kg/minute}$  infusion rate caused an elevation of WBC from the first 30 min up to the last evaluated TP (TP5h), while when in the infusion rate of  $0.8\ \text{mg/kg/minute}$ , such raise just became evident 3 h after the procedure began. In addition to that, the WBC counts in TP1h, TP2h and TP3h from the G06 were superior to G08. This increase of total leukocytes happened because of the segmented neutrophil increase, observed in both groups during all moments evaluated in relation to the baseline, not being verified any difference related to the propofol's dosage. The propofol usage in a rate of  $0.8\ \text{mg/kg/minute}$  reduced the lymphocyte number 1 h after the procedure. Calves under a  $0.6\ \text{mg/kg/minute}$  rate anesthesia presented more lymphocytes 2 h after the procedure than those put under the  $0.8\ \text{mg/kg/minute}$  rate at the same moment. Calves under the infusion rate of  $0.8\ \text{mg/kg/minute}$  presented more eosinophils than those under the  $0.6\ \text{mg/kg/minute}$  rate in TP5h. As for the other parameters, the leukogram did not have any differences in relation to time and dosage (Table 1).

**Table 1** Blood evaluation made in calves put under continuous propofol infusion in the rates of 0.6 mg/kg/minute and 0.8 mg/kg/minute

Variable	Propofol infusion rate	Baseline	TP30min	TP1h	TP2h	TP3h	TP4h	TP5h
HCT (%)	0.6	27,1 ± 3,27	29,2 ± 2,86 *	29,0 ± 3,66 *	29,2 ± 3,99 *	28,3 ± 4,06	27,8 ± 3,94	27,3 ± 4,06
	0.8	28,0 ± 3,20	29,0 ± 3,54	29,3 ± 3,42	29,0 ± 3,29	28,6 ± 4,27	28,1 ± 4,91	27,5 ± 4,47
RBC (× 10 <sup>6</sup> /μL)	0.6	6,48 ± 0,9	6,81 ± 0,6	6,79 ± 0,98	6,84 ± 0,78	6,76 ± 0,94	6,47 ± 1,02	6,61 ± 1,55
	0.8	6,54 ± 0,82	6,66 ± 0,87	6,71 ± 0,82	6,71 ± 0,93	6,63 ± 1,21	6,54 ± 1,25	6,42 ± 1,14
Hemoglobin (g/dL)	0.6	9,2 ± 1,16	9,5 ± 1,09 *	9,4 ± 1,11 *	9,5 ± 1,31 *	9,2 ± 1,13	9,1 ± 1,13	9,0 ± 1,19
	0.8	9,3 ± 1,18	9,5 ± 1,22	9,6 ± 1,33	9,8 ± 1,47	9,6 ± 1,56	9,6 ± 1,69	9,3 ± 1,54
MCV (fL)	0.6	41,9 ± 2,64	42,9 ± 2,74	42,8 ± 2,95	42,6 ± 2,35	42,0 ± 2,74	43,2 ± 2,49	43,3 ± 2,03
	0.8	42,8 ± 1,94	43,5 ± 1,73	43,8 ± 1,62	43,3 ± 1,73	43,3 ± 1,88	43,0 ± 1,43	42,8 ± 1,21
MCHC (%)	0.6	33,9 ± 2,10	32,6 ± 1,45	32,7 ± 0,84	32,7 ± 0,81	32,6 ± 1,33	32,8 ± 1,40	33,1 ± 1,55
	0.8	33,4 ± 0,92	32,9 ± 1,15	32,9 ± 1,13	33,8 ± 2,94	33,8 ± 1,95	34,2 ± 1,44	34,1 ± 2,07
WBC (× 10 <sup>3</sup> /μL)	0.6	10,8 ± 4,10	14,0 ± 5,23 *	13,4 ± 5,57 *	15,5 ± 5,49 *	16,2 ± 5,64 *	14,8 ± 3,46 *	14,4 ± 3,95 *
	0.8	10,9 ± 3,72	12,5 ± 4,43	11,3 ± 2,50 §	12,6 ± 3,48 §	13,3 ± 3,31 *§	13,7 ± 3,41 *	13,0 ± 3,69 *
Segmented neutrophils (μL)	0.6	2924 ± 1168	5518 ± 2300 *	6206 ± 2465 *	6272 ± 2731 *	6400 ± 2357 *	6064 ± 1768 *	5054 ± 1574 *
	0.8	2206 ± 714	5054 ± 2238 *	4825 ± 1216 *	5553 ± 1453 *	5311 ± 1783 *	5109 ± 1691 *	5039 ± 1824 *
Lymphocytes (μL)	0.6	7472 ± 3703	7935 ± 3292	6726 ± 3416	8869 ± 3883	9318 ± 4700	8385 ± 2745	8972 ± 3048
	0.8	8091 ± 3725	6762 ± 2504	5957 ± 1738 *	6428 ± 2042 §	7668 ± 2356	8073 ± 2949	7453 ± 2135
Monocytes (μL)	0.6	366 ± 301	425 ± 314	397 ± 263	274 ± 217	361 ± 249	417 ± 120	407 ± 180
	0.8	413 ± 306	422 ± 208	333 ± 347	365 ± 234	243 ± 155	271 ± 204	259 ± 146
Eosinophils (μL)	0.6	124 ± 144	208 ± 264	120 ± 160	133 ± 224	120 ± 156	37 ± 74	53 ± 80
	0.8	188 ± 195	335 ± 453	183 ± 144	327 ± 273	114 ± 129	258 ± 258	323 ± 484 §
TPP (g/dL)	0.6	6,77 ± 0,65	7,12 ± 0,53 *	7,32 ± 0,67 *	7,10 ± 0,58 *	6,76 ± 0,42	6,70 ± 0,30	6,57 ± 0,31
	0.8	6,20 ± 0,61	6,37 ± 0,64 §	6,62 ± 0,69 *§	6,60 ± 0,57 *§	6,35 ± 0,56	6,22 ± 0,68	6,20 ± 0,61
PF (g/dL)	0.6	0,45 ± 0,17	0,47 ± 0,10	0,50 ± 0,18	0,45 ± 0,09	0,47 ± 0,18	0,50 ± 0,10	0,42 ± 0,17
	0.8	0,45 ± 0,20	0,45 ± 0,14	0,50 ± 0,18	0,47 ± 0,14	0,45 ± 0,17	0,45 ± 0,09	0,47 ± 0,14
Platelets (1000 × field)	0.6	46 ± 11	48 ± 8	54 ± 11 *	53 ± 13 *	50 ± 10	53 ± 12 *	52 ± 10
	0.8	53 ± 8	49 ± 13	48 ± 9	50 ± 8	53 ± 9	53 ± 6	52 ± 6

(\*) Indicates a significant difference between the value and the baseline, meanwhile the (§) indicates a difference from the infusion rate dosage

The TPP values increased in TP30min, TP1h and TP2h in the G06 and in TP1h, and TP2h in the G08, so that the observed values in TP30min, TP1h and TP2h in G06 were superior than to the ones observed in G08. Propofol anesthesia did not alter the PF in either dosage (Table 1).

Propofol anesthesia in G06 caused an elevation of platelets in TP1h, TP2h and TP4h in relation to the baseline independently of the dosage evaluated (Table 1).

## Biochemical

Propofol anesthesia caused an elevation of albumin, AST, cholesterol, glucose, globulins, total protein and triglycerides and a reduction in the amounts of bilirubin, creatinine and GGT in different moments in both dosages. There was a significant difference between both dosages evaluated, with a reduction of creatinine and increase of glucose, globulin

and triglycerides in the calves under anesthesia rate of 0.8 mg/kg/minute if compared to the 0.6 mg/kg/minute rate (Table 2).

## Oxidative stress

Propofol anesthesia in an infusion rate of 0.6 mg/kg/minute caused and elevation in the levels of uric acid in TP1h in relation to baseline, so that the infusion rate of 0.8 mg/kg/min there was also an elevation in TP30min and TP2h, in a way which the differences in all these 3 time points were bigger than in G06. There was a TAC increase in TP30min, TP1h and TP2h in relation to the baseline in G06 and G08, with no difference in these time points regardless of the infusion rate. However, in TP3h, TAC was lower in the G08 than in G06. There was a lipid peroxidation increase in TP1h under the rate of 0.6 mg/kg/min and in TP1h and TP2h under the infusion rate of 0.8 mg/kg/min. Because

**Table 2** Biochemical parameters in calves under continuous propofol infusion in the rates of 0.6 mg/kg/minute and 0.8 mg/kg/minute

Variable	Propofol infusion rate	Baseline	TP30min	TP1h	TP2h	TP3h	TP4h	TP5h
Albumin (g/L)	0.6	24,26 ± 3,46	26,08 ± 3,17	28,20 ± 5,44 *	24,98 ± 3,49	24,68 ± 2,49	24,46 ± 2,55	23,99 ± 2,54
	0.8	23,00 ± 2,06	26,83 ± 5,09 *	29,76 ± 7,23 *	28,02 ± 4,22 *	23,85 ± 2,41	23,05 ± 2,31	22,95 ± 1,93
AST (UI/L)	0.6	50,92 ± 14,67	72,87 ± 22,60 *	82,12 ± 32,33 *	65,23 ± 22,83 *	65,89 ± 20,41 *	67,71 ± 16,57 *	67,69 ± 16,29 *
	0.8	50,10 ± 14,71	60,02 ± 15,12	71,08 ± 25,38 *	62,69 ± 18,07	60,74 ± 17,39	62,84 ± 14,99	64,36 ± 15,96 *
Total bilirubin (mg/dL)	0.6	0,45 ± 0,18	0,36 ± 0,15	0,33 ± 0,10	0,25 ± 0,08 *	0,26 ± 0,07 *	0,24 ± 0,11 *	0,25 ± 0,10 *
	0.8	0,33 ± 0,19	0,30 ± 0,13	0,30 ± 0,22	0,21 ± 0,13	0,17 ± 0,06 *	0,14 ± 0,05 *	0,13 ± 0,04 *
Cholesterol (mg/dL)	0.6	77,01 ± 17,31	81,18 ± 14,92	89,95 ± 22,68 *	85,02 ± 15,14 *	79,12 ± 13,88	80,07 ± 16,74	78,00 ± 14,91
	0.8	74,36 ± 12,28	78,88 ± 13,36	86,48 ± 13,09 *	93,32 ± 12,11 *§	86,47 ± 9,89 *	82,09 ± 10,45 *	80,74 ± 11,33
Creatinine (mg/dL)	0.6	0,82 ± 0,13	0,39 ± 0,12 *	0,28 ± 0,09 *	0,78 ± 0,10	0,85 ± 0,08	0,85 ± 0,08	0,85 ± 0,08
	0.8	0,83 ± 0,12	0,23 ± 0,14 *§	0,04 ± 0,13 *§	0,37 ± 0,18 *§	0,69 ± 0,25 §	0,87 ± 0,19	0,88 ± 0,13
GGT (UI/L)	0.6	17,92 ± 5,46	14,80 ± 7,86	11,31 ± 5,30	19,99 ± 6,82	20,18 ± 6,44	21,36 ± 5,55	19,25 ± 6,79
	0.8	19,21 ± 5,78	17,07 ± 14,25	9,79 ± 10,92 *	14,98 ± 8,85	17,60 ± 6,77	19,33 ± 5,84	19,52 ± 5,94
Glucose (mg/dL)	0.6	27,07 ± 14,96	40,27 ± 15,88 *	46,57 ± 15,08 *	39,52 ± 11,38	39,97 ± 15,55	43,34 ± 14,67 *	48,91 ± 11,97 *
	0.8	30,80 ± 14,67	52,93 ± 12,70 *	63,98 ± 21,37 *§	63,21 ± 14,14 *§	49,97 ± 14,11 *	49,61 ± 11,28 *	57,79 ± 15,28 *
Globulin (g/L)	0.6	40,92 ± 1,37	47,05 ± 5,91	49,89 ± 4,58 *	43,10 ± 3,83	42,47 ± 3,53	41,56 ± 3,53	40,91 ± 3,68
	0.8	40,05 ± 5,72	48,33 ± 15,50 *	56,69 ± 18,40 *§	49,54 ± 13,46 *§	40,93 ± 7,33	39,52 ± 6,52	38,74 ± 5,92
Total protein (g/L)	0.6	65,20 ± 3,66	73,14 ± 6,35	78,09 ± 9,05 *	68,09 ± 5,74	67,15 ± 3,18	66,02 ± 3,62	64,91 ± 3,69
	0.8	62,92 ± 6,18	76,28 ± 18,90 *	86,46 ± 25,19 *	77,37 ± 16,68 *	64,78 ± 8,88	62,63 ± 7,61	62,09 ± 5,97
Triglycerides (mg/dL)	0.6	22,66 ± 8,11	397,67 ± 34,45 *	624,29 ± 84,55 *	218,18 ± 109,00 *	65,42 ± 82,63	38,11 ± 51,92	27,95 ± 31,99
	0.8	19,66 ± 4,69	547,79 ± 108,51 *§	843,15 ± 73,09 *§	468,78 ± 99,78 *§	166,48 ± 76,62 *§	67,28 ± 39,05	37,13 ± 17,09
Urea (mg/dL)	0.6	20,62 ± 4,95	22,04 ± 6,08	22,72 ± 6,72	22,39 ± 5,88	23,40 ± 4,90	23,33 ± 5,71	24,07 ± 6,12
	0.8	20,45 ± 3,10	21,22 ± 2,92	21,47 ± 4,23	21,21 ± 3,85	21,92 ± 3,91	23,14 ± 4,08	23,19 ± 3,98

(\*) Indicates a significant difference from the baseline, while (§) shows a difference regarding the infusion dosage

**Table 3** Oxidative stress parameters in calves under continuous propofol infusion in the rates of 0.6 mg/kg/minute and 0.8 mg/kg/minute

Variable	Propofol infusion rate	Baseline	TP30min	TP1h	TP2h	TP3h	TP4h	TP5h
Uric acid (mg/dL)	0.6	1,11 ± 0,11	3,24 ± 0,61	4,63 ± 0,75 *	1,92 ± 0,48	1,32 ± 0,25	1,25 ± 0,15	1,16 ± 0,14
	0.8	1,07 ± 0,19	7,40 ± 5,69 *§	11,54 ± 7,76 *§	6,41 ± 4,81 *§	2,19 ± 1,54	1,43 ± 0,57	1,18 ± 0,23
TAC (mmol/L)	0.6	0,67 ± 0,06	0,81 ± 0,10 *	0,87 ± 0,07 *	0,77 ± 0,05 *	0,70 ± 0,04	0,69 ± 0,06	0,69 ± 0,04
	0.8	0,68 ± 0,08	0,81 ± 0,02 *	0,86 ± 0,08 *	0,72 ± 0,11 *	0,62 ± 0,04 §	0,66 ± 0,05	0,64 ± 0,03
TOC (µmol/L)	0.6	7,78 ± 2,42	13,02 ± 6,81	18,01 ± 11,42	15,59 ± 6,33	13,85 ± 9,83	11,47 ± 3,16	7,38 ± 3,30
	0.8	7,63 ± 3,49	7,86 ± 5,94	10,10 ± 8,97	24,61 ± 25,54 *	17,17 ± 11,96	10,47 ± 6,74	7,45 ± 4,86
TBARS (µmol/L)	0.6	3,44 ± 2,10	8,55 ± 6,78	11,42 ± 6,70 *	4,64 ± 2,25	5,08 ± 2,93	2,92 ± 2,99	4,26 ± 2,70
	0.8	4,50 ± 3,06	7,29 ± 4,42	12,35 ± 5,83 *	14,95 ± 7,34 *§	9,83 ± 2,18	8,70 ± 3,43	6,57 ± 5,46

(\*) Indicates a significant difference from the baseline, while (§) shows a difference regarding the infusion dosage

of that, lipid peroxidation was bigger in the rate of 0.8 mg/kg/minute than in 0.6 mg/kg/min in TP2h. As for the TOC,

only the infusion rate of 0.8 mg/kg/minute caused a significant increase in TP2h (Table 3).

## Discussion

Until the present moment, no studies have evaluated the effect of anesthetic protocol based on anesthesia induction and maintenance only with propofol in bovine hematological, biochemical and oxidative stress parameters. However, Deschk et al. (2016) evaluated the bispectral index (BIS) and hemodynamic parameters in calves anesthetized over the same rates of propofol administered in the present study and found no BIS variables alterations, as well no clinically significant hemodynamic alterations, attesting the safety of the rates infused. The present study complements the previous study and showed a significant influence of propofol on biochemical and hematological parameters, with differences between dosages, in addition to emphasizing its action on oxidative stress parameters.

Only the propofol infusion rate of 0.6 mg/kg/minute caused a significant increase of HCT and hemoglobin. Alves et al. (2003) also observed an increase in both parameters in calves induced by propofol and kept under inhalation anesthesia with isoflurane but, as in the present study, the values remained within normality for the bovine species (Meyer and Harvey 2004). Such feature can be justified by the transitory blood cell liberation by splenic contraction, caused by the catecholamines liberated due to excitatory stimuli or stress (Stewart and McKenzie 2002; Serra et al. 2018) or by propofol, as showed by O'Brien et al. (2004) and Wilson et al. (2004) in dogs induced by propofol. In addition to that, RBC can also be altered by prolonged water fasting (Jones and Allison 2007) and by circadian fluctuations (Braun et al. 2015). Therefore, the maintenance of blood parameters within the reference values indicates that propofol does not compromise tissue oxygenation.

Leukocytosis was highlighted mainly due to neutrophilia in both dosages administered, being more noticeable in the rate of 0.6 mg/kg/minute. On the other hand, Sato et al. (2016) observed a reduction in WBC count and neutrophil concentration reduction in dogs induced and kept under propofol anesthesia in the rate of 26.4 mg/kg/hour. In calves, neutrophils are the predominant white-cells in blood and its count can increase as a response to excitatory stimulus, characterizing physiological leukocytosis (Jones and Allison 2007), or even due to splenic contraction, as aforementioned. In addition to that, Sato et al. (2016) showed that propofol administration significantly reduces neutrophil adherence ability, a relevant cause of neutrophilia that also happens due to excitement (Jones and Allison 2007).

Lymphocyte reduction was observed with an increase of eosinophils in the rate of 0.8 and an increase of platelets in the rate of 0.6 mg/kg/minute. Costa et al. (2013) observed

lymphocytes, eosinophils and platelets stability in dogs kept under continuous propofol infusion in the rate of 0.7 mg/kg/minute. The significant increase of platelets and the increase of eosinophils can also be explained by the splenic contraction (Thrall et al. 2012). Only the animals kept under the 0.8 mg/kg/minute rate presented a noticeable decrease in the lymphocytes count. Stressing stimuli can result in a stress leukogram, characterized by neutrophilia and lymphopenia (Jones and Allison 2007). So, the observed lymphopenia can be a consequence of stress, but other studies would be required to evaluate the influence of higher infusion propofol rates over lymphocytes.

There was an increase of TPP in both rates, but only the infusion rate of 0.6 mg/kg/minute promoted a significant increase in this parameter. An increase in the concentration of triglycerides promoted by propofol, to be discussed further, causes a bigger light refraction and can increase the measurement of TPP by the refractometer, similarly to what happens in the spectrophotometric biochemical analysis (Kazmierczak 2013; Oliveira et al. 2020a) and, according to what has been observed in the azotemia (Legendre et al. 2017) and lipemia in dogs (Oliveira et al. 2020b).

Triglycerides values presented a significant increase in both infusion rates and, additionally, there was a considerable difference between the rates, with 0.8 mg/kg/minute showing bigger values than the rate of 0.6 mg/kg/minute. According to Pogliani and Birgel Junior (2007), the reference values of triglycerides for Holstein calves from 6 to 12 months old varies between 19.26 and 27.97 mg/dL. Hypertriglyceridemia may have been induced by propofol that, being a lipid emulsion, when administered for long periods of time or big dosages can increase the blood triglycerides concentration and cause lipemia (Backer et al. 2005; Bowdle et al. 2014). Mainali et al. (2017) concluded that propofol intravenous infusion was responsible for 7.4% of the causes of the lipemia indicators' index increase in patients from another medical center. On the other hand, the incidence of lipemia associated with propofol is not commonly related in veterinary medicine, yet lipemia associated with hemolysis in cats kept under multiple administrations of propofol are well described (Gall et al. 2013). The gathering of lipoprotein particles leads to the sample turbidity and interferes in the spectrophotometric biochemical determination by a physical feature, increasing light absorption (Kazmierczak 2013). However, in spite of such fact, there is no literature which correlates the triglycerides levels with the turbidity of bovine blood samples as there is for dogs (Bauer 2004).

Most biochemical analytes underwent significant changes during this peak of hypertriglyceridemia caused by the continuous infusion of propofol. Total cholesterol had a statistically significant increase in relation to the baseline in both rates of infusion, in addition to that the

rate of 0.8 mg/kg/minute presented values superior than the rate of 0.6 mg/kg/minute. Albumin, globulin and total protein levels had a statistically significant increase, being also highlighted in *in vitro* tests of lipemic bovine serum (Jacobs et al. 1992), as well as in *in vivo* and *in vitro* tests of canine lipemic serum (Oliveira et al. 2020a). The significant reduction of total bilirubin levels contradicts the increase of the studied substance in *in vitro* testing of lipemic bovine serum (Jacobs et al. 1992) and the maintenance of human lipemic serum (Calmarza and Cordero 2011), but is compatible to *in vitro* and *in vivo* tests in dogs (Oliveira et al. 2020a). The significative increase in the glucose levels was also shown in *in vitro* bovine and dogs' tests an in *in vivo* tests of dogs with lipemic serums (Jacobs et al. 1992; Oliveira et al. 2020a). The observed alterations are probably a result of the direct interference of the turbidity of the sample caused by lipemia, which increases the light absorption and promotes a false elevation in biochemical endpoint determinations (Jacobs et al. 1992; Johnson 2005).

Creatinine levels reduced with both infusion rates, being more evident in the rate of 0.8 mg/kg/minute. While Jacobs et al. (1992) and Calmarza and Cordeiro (2011) also related a reduction of the serum levels of creatinine, Oliveira et al. (2020a) did not observe relevant alterations of this substance in canine lipemic samples. The final values observed in the present study were higher than baseline, but still below the ones referenced in the species (Meyer & Harvey 2004). The amount of creatinine depends on the muscle mass and its reduction may be related to muscle loss, so it is relevant to correlate it with urea (Mohri et al. 2007). In the present study, urea was not affected by the different infusion rates nor lipemia, similarly to what happens with lipemia in dogs (Oliveira et al. 2020a) and bovines (Jacobs et al. 1992). Considering that there was no alteration in the measurement of urea, it is possible that the observed alterations in creatinine levels are related to different concentrations of triglycerides, induced by propofol emulsion.

AST activity increased in both infusion rates, but did not present clinical significance because remained within normal for the species (Meyer & Harvey, 2004). This increase in enzyme activity is compatible with the ones found in lipemic bovine serum tests (Jacobs et al. 1992) and lipemic serum in dogs (Oliveira et al., 2020a). In contrast, GGT activity significantly reduced under the infusion rate of 0.8 mg/kg/minute, while other studies did not observe alterations on GGT activity (Jacobs et al. 1992; Calmarza and Cordero 2011), others have observed a significant interference and an enzyme activity increase proportional to the lipemia level (Oliveira et al., 2020a). *In vitro* lipemia underestimates GGT high levels and overestimates its low levels (Likhodii et al. 2007), which explains the divergences among different studies. Because of that, it is possible to confirm that the light

absorption increase, caused by lipemia, is capable of interfering in the enzyme detection.

Uric acid levels increased significantly in both infusion rates, however the increase was more noticeable in the infusion rate of 0.8 mg/kg/minute for presenting a significant difference if compared to the rate of 0.6 mg/kg/minute. Calmarza and Cordero (2011) found a little significant reduction in the amount of urate in the *in vivo* lipemic samples, while Bonatto et al. (2021) and Likhodii et al. (2007) observed that *in vitro* lipemia tends to overestimate urate levels. It would be expected that there was an increase of uric acid levels due to propofol antioxidant action (Murphy et al. 1992). Plasma concentration of uric acid is 10 times bigger than other non-enzymatic antioxidants, which makes it constitute approximately 33.1% of the TAC (Erel 2004). So, the measurement of uric acid is important because of the great participation of this substance in the composition of the TAC and its increase could contribute with the propofol antioxidant action described in literature.

Supporting this result, the TAC increased in both rates, nevertheless the infusion rate of 0.8 mg/kg/minute showed a worse performance if compared to the infusion rate of 0.6. Erbas et al. (2015) also observed a statistically relevant increase of the TAC in post-operative dogs kept under continuous propofol infusion in increasing dosages up to the 6 mg/kg/minute rate. Braz et al. (2015) showed that the anesthesia maintenance with propofol in the concentrations of 3.0 and 5.0 µg/mL raised the concentrations of antioxidant components such as uric acid and γ-tocopherol and, consequently, elevated the TAC. Additionally, during *in vitro* tests done in multiple healthy mice tissues, propofol improves antioxidant capacity through the increase of the glutathione system (De La Cruz et al. 1998a). The measurement of the TAC is a cheaper, easier and more sensitive technique to evaluate the antioxidant capacity (Erel 2004), however, there is no individual analysis in the antioxidant system's components.

Even with an increased TAC, there was an increase of TOC in the infusion rate of 0.8 mg/kg/minute. Braz et al. (2015) observed that propofol did not induce oxidative damage in DNA and Erbas et al. (2015) concluded that the total oxidative state was smaller, despite not being statistically relevant, in comparison to the baseline of the dogs kept under anesthesia with continuous infusion of propofol. As lipemia effect over the TOC was not yet determined, especially in bovines, there is no way to affirm that such effect occurs because of oxidation or if it is influenced by the spectrophotometric measurement.

However, considering that lipid peroxidation can be a consequence of the increased amount of oxidative substances and that a lipid peroxidation increase was observed in both infusion dosages, being more evident in the infusion rate of 0.8 mg/kg/minute, we cannot discard the possibility

of an anesthesia contribution to oxidative stress in calves, even with an increased TAC. De La Cruz et al. (1998a) emphasized a dose-dependent inhibition of TBARS formation by in vitro propofol studies. Additionally, De La Cruz et al. (1998b) noticed that in vitro propofol promoted a 47% reduction in the TBARS levels in mice brains that suffered from anoxia and reoxygenation injuries. It is also important not to discard the possibility of lipemia interference over the determination of lipid peroxidation. Such a marker has an ideal absorbance in 545 nm (Hunter et al. 1985) and, according to Nikolac (2014), lipoproteins effectively affect methods that utilize waves in the lengths between 300 and 700 nm. Because of that, it is necessary to also consider the lipemia influence over the increase of TBARS levels.

As limitations of the study, the absence of randomization for the choice of the infusion rate and the short time interval between the two anesthetic procedures can be mentioned. The main hematological changes observed occurred at the infusion rate of 0.6 mg/kg/minute and considering that these animals were not used to the type of handling and containment employed, it is possible to assume that such changes may be also due to excitation or stress and that they are not exclusively caused by the propofol, as there was no dose dependent outcome. Further studies could help to identify changes resulting from propofol or other conditions, such as those induced by handling animals. Another important factor to be considered and which has been extensively discussed is the interference that propofol-induced lipemia can cause in biochemical analyzes, which could also alter oxidative stress parameters (Bonatto et al. 2021). As this influence of lipemia could not be avoided, even these analyzes must be interpreted with caution.

## Conclusion

Anesthesia maintenance with propofol caused discreet alterations on CBC and biochemical parameters in calves, in addition to inducing the increase of the TAC with an increase in uric acid levels. When put together, such effects confirmed the safety of this drug in anesthesia and maintenance of calves.

**Authors' contributions** The study conception and design were performed by Maurício Deschk, Paulo Cesar Ciarlini, Paulo Sérgio Patto dos Santos and Breno Fernando Martins de Almeida. Material preparation, data collection and analysis were performed by Luis Gustavo Narciso, Jefferson Filgueira Alcindo, Maurício Deschk and Breno Fernando Martins de Almeida. The first draft of the manuscript was written by Pedro Paulo Arcanjo Lima and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

**Funding** The authors are grateful to the State of São Paulo Research Support Foundation (FAPESP) for its financial support (Proc. 2010/11948-7 and 2010/19568-9).

**Availability of data and material** The datasets generated during and analyzed during the current study are available from the corresponding author on reasonable request.

**Code availability** Not applicable.

## Declarations

**Conflicts of Interest/Competing interests** The authors have no conflicts of interest to declare that are relevant to the content of this article.

**Ethics Approval** All applicable international, national, and/or institutional guidelines for the care and use of calves were strictly followed. This article does not contain any studies with human participants performed by any of the authors. The study was approved by the Ethics Committee of Animal Usage in Animal Experimentation (CEEA) of the School of Veterinary Medicine at the Araçatuba Campus of São Paulo State University (Unesp), under procedural number FOA-9416/10.

**Consent to Participate** All authors contributed to the study conception and design. All authors read and approved the final manuscript.

**Consent for Publication** All authors gave their consent for research publication.

## References

- Alves GES, Hartsfield SM, Carroll GL, Santos DAML, Zhang S, Tsolis RM, Bäumlér AJ, Adams LG, Santos RL (2003) Emprego do propofol, isoflurano e morfina para a anestesia geral de longa duração em bezerros. *Arq Bras Med Veterinária e Zootec* 55:41–420. <https://doi.org/10.1590/s0102-09352003000400005>
- Backer MT, Naguib M, Warltier DC (2005) Propofol: the challenges of formulation. *Am Soc Anesthesiol* 103:860–876. <https://doi.org/10.1097/00000542-200510000-00026>
- Bauer JE (2004) Lipoprotein-mediated transport of dietary and synthesized lipids and lipid abnormalities of dog and cats. *J Am Vet Med Assoc* 224:668–675. <https://doi.org/10.2460/javma.2004.224.668>
- Bonatto NCM, Oliveira PL, Mancebo AM et al (2021) Postprandial lipemia causes oxidative stress in dogs. *Res Vet Sci* 136:277–286. <https://doi.org/10.1016/j.rvsc.2021.03.008>
- Bowdle A, Richebe P, Lee L et al (2014) Hypertriglyceridemia, lipemia, and elevated liver enzymes associated with prolonged propofol anesthesia for craniotomy. *Ther Drug Monit* 36:556–559. <https://doi.org/10.1097/FTD.0000000000000073>
- Braun JP, Bourghès-Abella N, Geffré A et al (2015) The preanalytic phase in veterinary clinical pathology. *Vet Clin Pathol* 44:8–25. <https://doi.org/10.1111/vcp.12206>
- Braz MG, Braz LG, Freire CMM, Lucio LMC, Braz JRC, Tang G, Salvadori DMF, Yeum KJ, Amornytin S (2015) Isoflurane and propofol contribute to increasing the antioxidant status of patients during minor elective surgery a randomized clinical study. *Med (United States)* 94:1–9. <https://doi.org/10.1097/MD.00000000000001266>
- Brohan J, Goudra BG (2017) The role of GABA receptor agonists in anesthesia and sedation. *CNS Drugs* 31:845–856. <https://doi.org/10.1007/s40263-017-0463-7>



- Cagnardi P, Zonca A, Gallo M et al (2009) Pharmacokinetics of propofol in calves undergoing abdominal surgery. *Vet Res Commun* 33:177–179. <https://doi.org/10.1007/s11259-009-9281-9>
- Calmarza P, Cordero J (2011) Original issue: special article responsible writing in science Lipemia interferences in routine clinical biochemical tests, pp 160–166
- Costa PF, Nunes N, Belmonte EA et al (2013) Hematologic changes in propofol-anesthetized dogs with or without tramadol administration. *Arq Bras Med Vet e Zootec* 65:1306–1312. <https://doi.org/10.1590/S0102-09352013000500007>
- De La Cruz JP, Sedeño G, Carmona JA, De La Cuesta FS (1998a) The in vitro effects of propofol on tissular oxidative stress in the rat. *Anesth Analg* 87:1141–1146. <https://doi.org/10.1213/00000539-199811000-00031>
- De La Cruz JP, Villalobos MA, Sedeño G, Sánchez De La Cuesta F (1998b) Effect of propofol on oxidative stress in an in vitro model of anoxia-reoxygenation in the rat brain. *Brain Res* 800:136–144. [https://doi.org/10.1016/S0006-8993\(98\)00516-2](https://doi.org/10.1016/S0006-8993(98)00516-2)
- Deschk M, Wagatsuma JT, Araújo MA et al (2016) Continuous infusion of propofol in calves: Bispectral index and hemodynamic effects. *Vet Anaesth Analg* 43:309–315. <https://doi.org/10.1111/vaa.12302>
- Erbas M, Demiraran Y, AkYildirim H et al (2015) Comparison of effects on the oxidant/antioxidant system of sevoflurane, desflurane and propofol infusion during general anesthesia. *Brazilian J Anesthesiol (English Ed)* 65:68–72. <https://doi.org/10.1016/j.bjane.2014.05.004>
- Erel O (2004) A novel automated direct measurement method for total antioxidant capacity using a new generation, more stable ABTS radical cation. *Clin Biochem* 37:277–285. <https://doi.org/10.1016/j.clinbiochem.2003.11.015>
- Erel O (2005) A new automated colorimetric method for measuring total oxidant status. *Clin Biochem* 38:1103–1111. <https://doi.org/10.1016/j.clinbiochem.2005.08.008>
- Feitosa FLF (2014) Semiologia de recém-nascidos ruminantes e equídeos. In: Feitosa FLF (ed) *Semiologia veterinária: a arte do diagnóstico*. 3rd Edn, Roca, pp 69–95
- Gall GO, Gehrcke MI, Tamanho RB et al (2013) Indução anestésica com nanoemulsão ou emulsão lipídica de propofol durante dias consecutivos em gatas. *Cienc Rural* 43:2011–2017. <https://doi.org/10.1590/S0103-84782013001100015>
- Grimm KA et al (eds) (2015). *Veterinary anesthesia and analgesia: the fifth edition of Lumb & Jones*. Wiley
- Guo XN, Ma X (2020) The effects of propofol on autophagy. *DNA Cell Biol* 39:197–209. <https://doi.org/10.1089/dna.2019.4745>
- Hunter MIS, Nlemadim BC, Davidson DLW (1985) Lipid peroxidation products and antioxidant proteins in plasma and cerebrospinal fluid from multiple sclerosis patients. *Neurochem Res* 10:1645–1652. <https://doi.org/10.1007/bf00988606>
- Jacobs RM, Lumsden JH, Grift E (1992) Effects of bilirubinemia, hemolysis, and lipemia on clinical chemistry analytes in bovine, canine, equine, and feline sera. *Can Vet J* 33:605–608
- Jain NC (1986) *Schalm's Veterinary Hematology*, 4th edn. Lea and Febiger, Philadelphia
- Johnson MC (2005) Hyperlipidemia disorders in dogs. *Compend Contin Educ Pract Vet* 27:361–370
- Jones ML, Allison RW (2007) Evaluation of the ruminant complete blood cell count. *Vet Clin North Am - Food Anim Pract* 23:377–402. <https://doi.org/10.1016/j.cvfa.2007.07.002>
- Kazmierczak SC (2013) Hemolysis, lipemia, and high bilirubin. effect on laboratory tests. *Accurate results clin lab a guid to error detect correct* 372:53–62. <https://doi.org/10.1016/B978-0-12-415783-5.00005-0>
- Legendre KP, Leissing M, Le Donne V et al (2017) The effect of urea on refractometric total protein measurement in dogs and cats with azotemia. *Vet Clin Pathol* 46:138–142. <https://doi.org/10.1111/vcp.12464>
- Likhodii SS, Martens P, Mah W et al (2007) Effect of interferences on the general chemistry assays of the Abbott Architect® c8000 System. In: *American Association for Clinical Chemistry Annual Meeting*. pp 1–2
- Mainali S, Davis SR, Krasowski MD (2017) Frequency and causes of lipemia interference of clinical chemistry laboratory tests. *Pract Lab Med* 8:1–9. <https://doi.org/10.1016/j.plabm.2017.02.001>
- Meyer DJ, Harvey JW (2004) *Veterinary Laboratory Medicine: interpretation and Diagnosis*, 3rd edn. Saunders, Philadelphia
- Mohri M, Sharif K, Eidi S (2007) Hematology and serum biochemistry of Holstein dairy calves: age related changes and comparison with blood composition in adults. *Res Vet Sci* 83:30–39. <https://doi.org/10.1016/j.rvsc.2006.10.017>
- Murphy PG, Myers DS, Davies MJ et al (1992) The antioxidant potential of propofol (2,6-diisopropylphenol). *Br J Anaesth* 68:613–618. <https://doi.org/10.1093/bja/68.6.613>
- Nikolac N (2014) Lipemia: causes, interference mechanisms, detection and management. *Biochem. Medica* 24:57–67. <https://doi.org/10.11613/BM.2014.008>
- O'Brien RT, Waller KR, Osgood TL (2004) Sonographic features of drug-induced splenic congestion. *Vet Radiol Ultrasound* 45:225–227. <https://doi.org/10.1111/j.1740-8261.2004.04039.x>
- de Oliveira PL, Souza SL, Bonatto NCM et al (2020a) Effect of food intake on complete blood count of healthy dogs. *Rev Agrar Acad* 3:105–116. <https://doi.org/10.32406/v3n62020/105-116/agrariacad>
- Oliveira PL, Bonatto NCM, Bosculo MRM et al (2020b) Effect of post-prandial lipemia on canine biochemical parameters. *Comp Clin Path* 29:763–775. <https://doi.org/10.1007/s00580-020-03130-y>
- Pogliani FC, Birgel Junior E (2007) Valores de referência do lipidograma de bovinos da raça holandesa, criados no Estado de São Paulo. *Brazilian J Vet Res Anim Sci* 44:373. <https://doi.org/10.11606/issn.1678-4456.bjvras.2007.26621>
- Riebold TW (2007) Ruminants. In: Tranquilli WJ, Thurmon JC, Grimm KA (eds) *Lumb & Jones' veterinary anesthesia and analgesia*, 4th edn. Blackwell, Ames, pp 731–746
- Sato R, Aoki T, Kobayashi S et al (2016) The modulating effects of propofol and its lipid carrier on canine neutrophil functions. *J Vet Med Sci* 78:1825–1829. <https://doi.org/10.1292/jvms.16-0025>
- Serra M, Wolkers CPB, Urbinati EC (2018) Physiological indicators of animal welfare. *Rev Bras Zootecias* 19:70–96. <https://doi.org/10.34019/2596-3325.2018.v19.24726>
- Stewart IB, McKenzie DC (2002) The human spleen during physiological stress. *Sport Med* 32:361–369. <https://doi.org/10.2165/00007256-200232060-00002>
- Thrall MA, Weiser G, Allison RW, Campbell TW (eds) (2012) *Veterinary hematology and clinical chemistry*. Wiley
- Vasileiou I, Kalimeris K, Nomikos T et al (2012) Propofol prevents lung injury following intestinal ischemia-reperfusion. *J Surg Res* 172:146–152. <https://doi.org/10.1016/j.jss.2010.07.034>
- Visvabharathy L, Xayarath B, Weinberg G et al (2015) Propofol increases host susceptibility to microbial infection by reducing subpopulations of mature immune effector cells at sites of infection. *PLoS ONE* 10:1–19. <https://doi.org/10.1371/journal.pone.0138043>
- Walsh CT (2018) Propofol: Milk of Amnesia. *Cell* 175:10–13. <https://doi.org/10.1016/j.cell.2018.08.031>
- Wilson DV, Evans AT, Carpenter RE, Mullineaux DR (2004) The effect of four anesthetic protocols on splenic size in dogs. *Vet Anaesth Analg* 31:102–108. <https://doi.org/10.1111/j.1467-2987.2004.00152.x>

**Publisher's note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.