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The Effects of Propofol and Sevoflurane Anaesthesia on Lipid Peroxidation and the Antioxidant System in Angora Goats

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ABTSRACT
The present study was aimed at the determination of the effects of propofol and sevoflurane administration on blood malondialdehyde (MDA) levels and certain antioxidant parameters in goats. The study was conducted on 7 healthy Angora goats. Blood samples were taken from all of the animals prior to the administration of propofol, following the induction of anaesthesia, and 15, 30, 60 and 120 minutes and 24 hours after sevoflurane administration. The collected blood samples were used to measure plasma MDA, vitamin A and β-carotene, vitamin E levels and erythrocyte superoxide dismutase (SOD) and catalase (CAT) and glutathione peroxidase (GPx) activities. In the Angora goats, which were anaesthetized with propofol and sevoflurane, neither plasma MDA, vitamin A and β-carotene, vitamin E levels, nor erythrocyte SOD and CAT activities displayed any statistically significant difference during and after anaesthesia. In result, it was determined that propofol and sevoflurane anaesthesia did not induce any adverse effect on blood MDA levels or the antioxidant parameters investigated in the Angora goat.

Keywords: Angora goat, Antioxidant status, Lipid peroxidation, Propofol, Sevoflurane.

INTRODUCTION

In the last decade, research has continued on the development of anaesthetics that can be used safely in veterinary medicine. Propofol and sevoflurane are among the most frequently investigated anaesthetics in the past few years (Koc and Saritas, 2004; Topal, 2005; Brioni et al., 2017). The use of inhalation anaesthetics is highly preferred in animals (Natalini, 2001). Generally, the primary criterion for the selection of an anaesthetic agent is interested about its non-toxicity for internal organs and tissues (Dundee, 1988). It has been demonstrated in several studies that certain intravenous anaesthetic agents cause tissue damage by increasing the production of reactive oxygen species (ROS) (Fassoulaki et al., 1986; Murphy et al., 1993; Okutomi, 1995; Abidova, 2002).

Normally, ROS are generated as a result of metabolic reactions and physiological processes, and once generated; they may trigger adverse reactions in the organism (Halliwell and Gutteridge, 2000). Reactive oxygen species lead to lipid peroxidation (LPO) due to their effect on unsaturated fatty acids found in the cell membrane, thus, they cause damage to the structure and functions of the cell (Akkus, 1995). The organism is equipped with antioxidant systems, comprising several vitamins (A, C, E) and enzymes, including SOD, CAT and GPx, which protect the cell against the adverse effects of free radicals, and therefore, against LPO (Oz and Kurtoglu, 2002).

Propofol has ROS scavenger effects that protects the cell membrane against LPO. This effects attributed to the chemical structure of propofol. In fact propofol is an alkylphenol with a phenolic hydroxyl group, similar to vitamin E (Hans et al., 1996). On the other hand sevoflurane, a halogenated inhalation anaesthetic with a low degree of metabolism (Smith et al., 1996), enhance ROS production by its metabolism (Kharasch, 1995) and by altering mitochondrial bioenergetics (Yesilkaya et al., 1998; Sedlic et al., 2009).

In previous studies conducted in humans and different animal species, it has been reported that both propofol (Yamaguchi et al., 2000; Allaouchiche et. al., 2001; Kudo et al., 2001; Mercan, 2004; Lee and Kim, 2012; Tomsic et al., 2018) and sevoflurane (Allaouchiche et. al., 2001; Yurdakoc et al., 2008; Tomsic et al., 2018) have effect on oxidative stress. However, to the authors' knowledge, there is no literature report indicating propofol or sevoflurane's effect on LPO and the antioxidant system in goats. In recent years, propofol and sevoflurane have found common use in small ruminants. In this respect, the present study was aimed at the determination of the effects of propofol and sevoflurane on LPO and the antioxidant system in goats.

MATERIALS AND METHODS

Seven adult female Angora goats, which were confirmed to be healthy by anamnesis, physical examination and complete blood cell count, and which weighed 34-50 kg (39.5 kg±4.36 kg), constituted the material of the study. This research was initiated upon its approval (Document No. 10/04) by the Local Ethics Board for Experimental Animals of Kirikkkale University. For the induction of anaesthesia, the animals were administered with propofol (Propofol 1%, Fresenius Kabi, Sweden) in bolus form at a dose of 5.00 ± 0.6 mg/kg by intravenous route. In order to prevent the development of ruminal tympany (bloating), gastric decompression was employed by the insertion of an orogastric tube. The animals were positioned in right lateral recumbency and were administered with 1-3% sevoflurane (Sevorane Liquid, ABBOTT Laboratories Ltd., United Kingdom) in100% oxygen (O_2) for 1 hour. The amount of fresh O_2 entering the system was adjusted to a level of 3 l/min. The adequacy of the depth of anaesthesia was monitored throughout the trial by assessing the palpebral reflex, and the response of the ani-

mal to tail clamping and the clamping of the interdigital web of pads using Kocher's forceps. If the depth of anaesthesia was found to be inadequate, then the concentration of sevoflurane was increased to 5%, and upon the confirmation of the accomplishment of an adequate depth of anaesthesia the concentration of sevoflurane was decreased to 3%.

Prior to premedication following the administration of propofol, and 15, 30, 60, 120 minutes and 24 hours after the administration of sevoflurane, 7 blood samples were taken from the jugular vein of each animal into lithium heparin-containing vacuum tubes. The blood samples were centrifuged at 3000 rpm and +4 °C for 10 minutes for the extraction of plasma and erythrocytes. The samples were stored at -80 ºC until analysed. Plasma MDA levels were measured as described by Moreno et al. (2003), vitamin A and β-carotene, vitamin E levels were determined spectrophotometrically (Shimadzu UV-1700, Japan) according to the method described by Suzuki and Katoh (1990), Martinek (1964), respectively. Erythrocytes were washed as described by Witterbourn et al. (1975), catalase (CAT) activity was measured in compliance with the method of Aebi (1983), and superoxide dismutase (SOD) activity was measured according to the method of Sun et al. (1988). Haemoglobin (Hb) levels were measured using the cyanomethaemoglobin method (Fairbanks and Klee, 1987).

Statistical Analyses

Differences between the groups were assessed by one-way analysis of variance (ANOVA), whilst the significance of the differences between the groups were determined by Tukey's test. Results were given in mean ± standard error. In statistical analyses, values of $P<0.05$ were considered significant. The statistical analyses of the data obtained were performed using the SPSS 15.0 software (SPSS Inc., Chicago, Illinois, USA).

RESULTS

The alterations determined in plasma MDA, vitamin A and β-carotene, vitamin E levels and erythrocyte SOD and CAT activities prior to and after propofol administration and 15, 30, 60, 120 minutes and 24 hours after sevoflurane administration in goats are shown in Table 1. It was observed that, following the administration of propofol, plasma MDA levels decreased in goats. Furthermore, compared to the levels measured both prior to and after the administration of propofol, plasma MDA levels, which were observed to have increased 15 minutes after the administration of sevoflurane, decreased in the following minutes. However, these increases and decreases were statistically insignificant ($P>0.05$). In the goats administered with propofol, a statistically insignificant increase was determined in erythrocyte SOD and CAT activities in comparison to the period prior to anaesthesia. On the other hand, following the administration of sevoflurane, statistically insignificant irregular increases and decreases were observed in SOD activity, whilst irregular decreases were determined in CAT activity ($P>0.05$).

Furthermore, following the administration of propofol and sevoflurane, statistically insignificant irregular increases and decreases were observed in plasma vitamin A and beta-carotene, vitamin E levels, in comparison to the period prior to anaesthesia.

Table 1. Levels of MDA, β-carotene and vitamin A (n=7), vitamin E (n=6) in plasma and SOD and CAT activities in erythrocytes in Ankara goats treated with propofol and sevoflurane anaesthesia - (n=7).

PARAMETERS	Prior to administration of Propofol	After the administration of Propofol	Sevoflurane 15.MIN	Sevoflurane 30. MIN	Sevoflurane 60.MIN	Sevoflurane 120. MIN	Sevoflurane 24. H	P
MDA (mmol/L)	1.96 ± 0.29	1.40 ± 0.14	1.83 ± 0.24	1.41 ± 0.17	1.42 ± 0.13	1.51 ± 0.19	1.63 ± 0.31	NS
SOD (U/g-Hb)	273.34 ± 90.38	274.50 ±95.89	251.33 ± 79.16	258.41 ± 90.26	270.71±92.09	270.33±79.43	235.57±92.19	NS
CAT (k/g-Hb)	36.51 ± 9.32	38.24 ± 10.08	34.66 ± 5.02	33.13 ± 4.49	38.11 ± 6.93	29.39 ± 5.01	33.45 ± 10.44	NS
β-carotene (mg/dl)	11.01 ±0.79	11.46 ± 1.68	7.43 ± 1.06	10.30 ± 0.93	9.82 ± 1.00	8.45 ± 1.18	7.75 ± 0.52	NS
Vitamin A (mg/dl)	56.15 ± 5.34	59.37 ± 9.21	50.04 ± 8.60	60.38 ± 8.51	48.19 ± 7.49	50.96 ± 10.38	46.66 ± 7.64	NS
Vitamin E (mg/dl)	0.41 ± 0.06	0.53 ± 0.09	0.43 ± 0.09	0.35 ± 0.03	0.39 ± 0.04	0.38 ± 0.1	0.43 ± 0.07	NS

NS: not significant

DISCUSSION

Some anaesthetics, apart from inhibiting the functions of leukocytes, prevent the generation of ROS and thereby, exhibit antioxidant effect (Gunaydin and Celebi, 2003). The most significant product of LPO is MDA. Research conducted in humans (Ansley et al., 1999) and animals (Allaouchiche et al., 2001) have shown that, propofol, when administered as an anaesthetic agent, increases the antioxidant capacity of erythrocytes and decreases plasma MDA levels. Similar to the research referred to above, the present study demonstrated that plasma MDA levels decreased after the administration of propofol, yet, these decreases were found to be statistically insignificant.

There are multiple reports indicating the interaction of anaesthetic agents with ROS (Allaouchiche et al., 2001; Yurdakoc et al., 2008; Kamiloglu et al., 2009). Allauchiche et.al. (2001), reported that sevoflurane did not induce a chemical reaction sequence leading to the generation of free oxygen radicals. Anaesthetics have been known to generate free radicals by effecting intracellular cytochrome p450, peroxisomes and mitochondrial enzymatic systems (Stephen et al., 1997). Tomsic et al. (2018), found that administration of propofol or propofol and sevoflurane had no significant effect on oxidative stress in dogs with early stage myxomatous mitral valve degeneration MMVD. In terms of oxidative stress, both protocols may be equally safely used in dogs with early stage MMVD. In agreement with the report of Yarsan et al. (2010), indicating that inhalation anaesthetics do not affect blood parameters of LPO in dogs. Contrary to the results of our study, in one study evaluating the oxidant effects of desflurane, sevoflurane and propofol in porcine, plasma MDA concentrations were significantly lower in pigs exposed to propofol, whereas no significant changes were observed after sevoflurane exposure (Allaouchiche et al., 2001). The present study demonstrated that sevoflurane and propofol administration did not alter MDA levels in Angora goats.

Superoxide dismutase, an antioxidant enzyme, catalyses the conversion of superoxide, which is capable of causing cell damage, into hydrogen peroxide and oxygen. On the other hand, the enzyme CAT has peroxidase activity and breaks down hydrogen peroxide into O_2 and water (Oz and Kurtoglu, 2002). In a study conducted in swine, it was determined that propofol and sevoflurane administration did not cause any alteration in plasma SOD activity (Allaouchiche et al., 2001). Furthermore, it has been reported by Ansley et al. (1998) and Gunaydin and Celebi, (2003) that propofol does not affect erythrocyte SOD and CAT activities. In agreement with the above mentioned literature reports, it was ascertained in the present study that, following the administration of propofol, neither SOD nor CAT activity was altered in goats. Tomsic et. al. (2018), reported that propofol or propofol and sevoflurane didn't effect erythrocyte SOD activities in dogs. Similarly, sevoflurane, which is a volatile anaesthethic, did not have any effect on the activity of these enzymes.

Carotenoids, which act as precursors of vitamin A, prevent the generation of free radicals by inhibiting the production of singlet oxygen, an intermediate product of LPO (Oz and Kurtoglu, 2002; Dundar and Aslan, 2000). In a study conducted by Naziroglu and Gunay (1999), on enflurane anaesthesia in dogs, it was determined that serum vitamin A and β-carotene levels decreased. In the present study, it was observed that plasma vitamin A and β-carotene levels didn't change following the administration of propofol when compared to prior to administration of propofol. In the further stages of the present study, statistically insignificant decreases were observed in vitamin A and β-carotene levels as a result of sevoflurane administration, in agreement with the findings reported by Naziroglu and Gunay (1999). Vitamin E is the most abundant lipid-soluble antioxidant in biological membranes by scavenging free radicals (Liebler, 1993). Berit et al. (2009), reported that propofol administration didn't change vitamin E levels in human. This may be related to the fact that antioxidant effect of propofol has structural similarity to α-tocopherol (Murphy et al., 1993; Corcoran et al., 2004). In contrast to Berit et al. (2009), it was reported that vitamin E levels were significantly decreased in inhalated sheep (Lalonde et al., 1997). In the present study, Vitamin E levels were insignificantly increased following to administration of propofol.

It is considered that, in cases associated with the risk of the development of ischaemia- reperfusion damage during anaesthesia, the use of anaesthetic agents with antioxidant property would be advantageous in veterinary practice (Gunaydin and Celebi, 2003). The findings obtained in the present study demonstrated that, in goats, the use of propofol and sevoflurane as anaesthetics led to statistically insignificant decreases in plasma MDA and vitamin A levels and did not have any effect on erythrocyte SOD and CAT activities. In conclusion, it was ascertained that, although to a limited extent, propofol had antioxidant property in goats, whilst sevoflurane did not induce any negative effect on lipid peroxidation and the antioxidant system.

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