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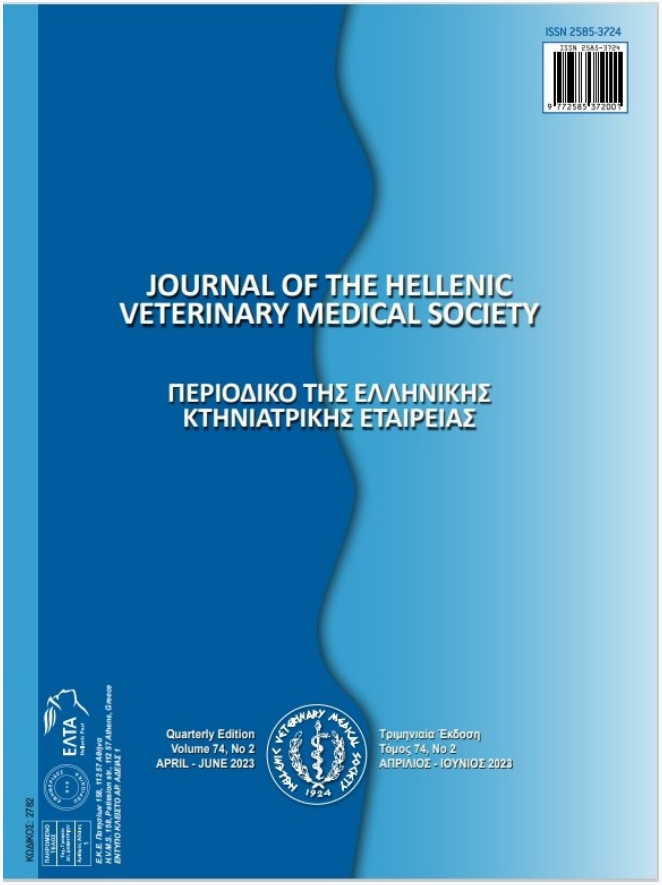

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Effect of Butorphanol with and without Medetomidine on Intraocular Pressure in Cats

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ABSTRACT: This study aimed to determine the effects of intramuscular administration of butorphanol with and without medetomidine on intraocular pressure (IOP) in cats. Sixteen clinically healthy cats were randomly allocated into two groups of 8 animals. In the butorphanol group, cats received 0.2mg/kg butorphanol, whereas in the butorphanol-medetomidine group, cats received a mixture of 0.05mg/kg medetomidine and 0.1mg/kg butorphanol in the same syringe. All injections were performed intramuscularly. IOP values were recorded before treatment (T0) and following the treatment at 10 (T10), 20 (T20), 30 (T30), and 40 min (T40) in both groups. The administration of butorphanol with and without medetomidine did not cause statistically significant changes in IOP values. The IOP did not change over time ($p = 0.41$). The mean values of IOP in butorphanol, and butorphanol-medetomidine groups were 20.00 ± 2.29 and 20.38 ± 2.35 mm Hg, respectively. In conclusion, intramuscular administration of butorphanol with or without medetomidine had no significant effect on IOP in cats.

***Keywords*:** Butorphanol; cat; intraocular pressure; medetomidine; sedation.

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INTRODUCTION

Intraocular pressure (IOP) is described as the pressure of eye contents against the eye's fibrous layer (Murphy, 1985). IOP may alter in a variety of ways, including changes in the relative volumes of aqueous humor, extraocular muscle tone, choroidal blood and vitreous humor (Duncalf, 1975). Maintenance of normal IOP is essential in patients with glaucoma or penetrating eye injuries (Murphy, 1985).

Sedation in cats is mainly accomplished with tranquilizers, sedatives, and analgesics. Benefits of sedation include less physical restraint, decreased stress, safer airway management, and rapid recovery (Robertson et al., 2018). However, sedative drugs may cause changes in IOP (Pierce-Tomlin et al., 2020).

Medetomidine is a commonly used sedative drug, which provides reliable dose-dependent sedation in cats (Lamont et al., 2001). A previous study reported that intramuscular administration of medetomidine did not affect IOP values in cats (Malmasi and Ghaffari, 2016). Butorphanol is a partial agonist for the k-opioid receptor, and a partial agonist and antagonist for the μ-opioid receptor (Gharagozlou et al., 2006). It is mainly used in cats for analgesia and short-term sedation (Simon and Steagall, 2017). Different results have been obtained in studies of butorphanol's effect on IOP in dogs (Douet et al., 2018; Mrazova et al., 2018). The combination of medetomidine and butorphanol administration in dogs has been reported to cause changes in IOP (Rauser et al., 2012). However, it is not known whether only butorphanol or in combination with medetomidine would affect IOP in cats. Thus, this study was aimed to determine the effects of butorphanol with and without medetomidine on IOP in cats.

MATERIALS AND METHODS

Animals

Atatürk University Local Board of Ethics Committee for Animal Experiments was approved the study (decision no: 2018/39). The inform consent was obtained from the owners of each animal.

Sixteen male cats weighing between 2.3 and 4.3 kg (3.2 ± 0.6) and ranging in age from one to 2 years (1.4 ± 0.2) were used. Clinical examination and blood analysis of the cats were performed before the experiment. Cats, status ASA (American Society of Anesthesiologists) 1-2, were included in the study. A direct ophthalmoscopy (Aesculap AC-635 C, Braun, Germany), corneal pachymetry (Reichert, USA) and tonometry (Tonovet, Icare, Finland) were used prior to the study to ensure the clinical situation of the eyes. The eye examinations and measurements were carried out by the same person, who was unaware of the administered drugs. All the cats were fasted for 6 hours before premedication. Cats were randomly allocated into two treatment groups. In the group of butorphanol, cats received 0.2mg/kg butorphanol (Butomidor, Richter Pharma AG, Austria), while in the group of butorphanol-medetomidine, cats received a mixture of 0.05mg/kg medetomidine (Domitor, Orion Pharma, Finland) and 0.1mg/kg butorphanol in the same syringe. All injections were performed intramuscularly.

Measurements

One drop of proparacaine (Alcaine 0.5% Alcon, Belgium) was applied to each eye 5 minutes before the measurement of the Central Corneal Thickness (CCT). Moisture on the pachymeter probe was wiped off with a dry cotton swab after each measurement. The CCT of left and right eyes for each cat were randomly collected once before the treatment protocol. The mean CCT value of both eyes was evaluated as the animal's CCT.

Intraocular pressure measurement of cats was performed at sternal position without any pressure on the neck and head. Local anaesthetic eye drops were not applied before IOP measurements. All measurements were carried out between 9 and 10 am. The IOPs were measured before treatment (T0; baseline) and after the treatment at the time points 10, 20, 30, and 40 min (T10, T20, T30, and T40).

Statistical Analysis

Power calculation was performed to determine sample size. At least 8 cats for each group were needed to succeed a study power of 80% with an error of 0.05. Statistical analysis was performed using SPSS 19 statistical program (IBM Company, version 19.0, SPSS Inc., USA, 2010). Data are reported as mean ± SD. The one-sample Kolmogorov-Smirnov test was used to test normality. IOP values for the right and left eyes were compared by paired samples t-test. A repeated measure of ANOVA was used to compare within-group changes and the differences between the two groups. Statistically significant level was set as $p < 0.05$.

RESULTS

No complications associated with anaesthesia

were observed throughout the experiment. The mean CCT was 599.63 ± 9.11 μm. In both groups, there was no statistically significant difference between the mean IOP values of the left (20.02 ± 0.78) and right (20.38 ± 0.98) eyes at all-time points (p=0.94). For this reason, the mean IOP values of both eyes were recorded as a mean value at each time point.

The mean baseline (T0) values of IOP in butorphanol and butorphanol-medetomidine groups were 20.00 ± 1.69 and 19.75 ± 2.92 mm Hg, respectively, and no statistically significant differences (p=0.75) were observed between groups (Figure 1). There were no significantly differences between groups at all-time points. The IOP did not change over time (p = 0.41). The mean values of IOP in butorphanol and butorphanol-medetomidine groups were 20.00 ± 2.29 and 20.38 ± 2.35 mm Hg, respectively, and these were not statistically significantly different (p = 0.93).

DISCUSSION

Opioids are combined with α_2-adrenergic agonists to achieve more profound sedation (Reader et al., 2019; Selmi et al., 2003). The synergistic effect of both groups of agents minimizes the required dose of these drugs for sedation (Ossipov et al., 1990). The previous observations claim a decrease in IOP levels following opioid administration (Murphy, 1985; Duncalf, 1975). However, a recent study that used butorphanol in dogs has reported an increase in IOP values with the highest value as 22 mm Hg (Douet et al., 2018). The results of the current study indicate that butorphanol with or without medetomidine does not have a significant effect on IOP in cats. The reason for this finding is unclear, probably due to several factors that may influence IOP readings, such as scleral rigidity, extraocular muscle tone, choroidal blood volume or aqueous humor dynamics (Duncalf, 1975).

Because the IOP values for both groups were clinically in the normal range throughout the current study, it could be said that butorphanol with or without medetomidine may be used in cats safely where the IOP needs to be maintained at approximately 20 mmHg. Therefore, even though this study did not aim to detect the effect of medetomidine administration on IOP levels of cats, the insignificant difference in IOP recordings between groups showed that medetomidine did not affect IOP either. A similar result was observed in a previous study that used medetomidine in cats to evaluate the IOP levels (Malmasi and Ghaffari, 2016).

It has been stated that measuring CCT is an important examination to avoid underestimation of IOP (Gordon et al., 2002). Several studies in humans have shown the relationship between IOP and CCT (Kniestedt et al., 2005; Bron et al., 1999; Chatterjee et al., 1997). In the current study, an ultrasonic pachymeter was used to measure the CCT to ensure the situation of the eyes. The mean CCT value was 599.63±9.11 μm, and the results were consistent with previous reference (Yanmaz et al., 2016). The ultrasonic pachymeter gains popularity because of its easy

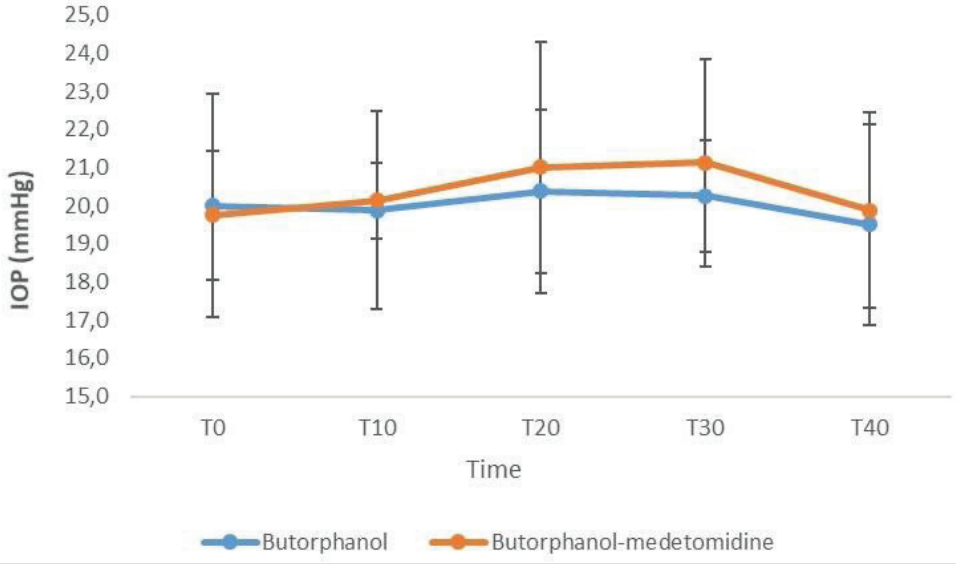

Figure 1. Mean ± SD intraocular pressure (IOP) in butorphanol and butorphanol-medetomidine groups at baseline T0, and T10, T20, T30, and T40 mins after the administration

use and rapid results (Telle et al., 2019). The main disadvantage of ultrasonic pachymeter is the necessity of corneal touching by the device's tip (Binnawi et al., 2019), which may cause an undesirable accident on the cornea.

The main limitation of the current study is the lack of including glaucomatous cats. Our groups consisted of healthy cats only, which raises the question whether our results could be valid to cats with eye diseases or aggressive ones. A previous study stated that the pharmacological effect of butorphanol is strongly associated with the animals' health condition (Douet et al., 2018), which might also affect IOP.

CONCLUSIONS

Intramuscular administration of butorphanol or butorphanol-medetomidine combination had no significant effect on the IOP of healthy cats. Further investigations may be needed to determine the effect of butorphanol administration on IOP values of cats with eye diseases.

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CONFLICT OF INTEREST

The authors do not have any potential conflicts of interest to declare.

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