Introduction

Ketamine and propofol are frequently used anaesthetics in rabbits. Ketamine is commonly combined with other premedicants such as benzodiazepines or α2-adrenergic agonists. However, propofol is mainly used for anaesthesia induction [12].

Ketamine and propofol mixtures in the same syringe, known as ketofol, is commonly used in emergency department for short-term interventions [3]. It has been stated that ketofol results an increase in the depth of sedation and minimizes side effects compared to sole use of ketamine and propofol [5]. Moreover, negative effects of propofol on cardiovascular system can be precluded by using ketamine [6].

Studies have shown that ketamine causes an increase in intraocular pressure [7], whereas propofol results in decreased intraocular pressure [4]. The purpose of this study was to compare the effects of propofol, ketamine and ketofol on intraocular pressure in New Zealand white rabbits.

Materials and methods

ANIMALS

Atatürk University Local Board of Ethics Committee for Animal Experiments has approved the study protocol of this research (HADYEK decision no: 2013/139).

Eight, adult male, New Zealand white rabbits weighing 2.5–3.3 kg were used in this study. They were housed in individual cages with food and water ad libitum. Bedding material was not used. The humidity ranged between 40 and 60 %. A uniform temperature of 22 ± 2 °C was maintained throughout with a 12:12h light:dark cycle. The rabbits were screened for pre-existing ocular disorders and clinical assessment was performed to ensure adequate health status. All animals were determined to be free of corneal and conjunctival diseases. Rabbits underwent a minimum 14 days acclimation period prior to experiment. Food and water were not withdrawn before treatment. The left ear of each rabbit was clipped and the skin cleaned with alcohol, a 22 G catheter was placed in the marginal ear vein for anaesthetic injections.
KETOFOL ON INTRAOCULAR PRESSURE IN RABBITS

STUDY DESIGN

The animals were randomly assigned one of three different anaesthetic regimens. Treatment order was randomized, and each animal received all three anaesthetics with a minimum one week washout period. Required induction doses of anaesthetic drugs were selected based on previous studies [9, 17, 28]. All animals were received 0.6 mg/kg Xylazine (2% Rompun, Bayer, Istanbul, Turkey) administration for premedication. The three groups were 10 mg/kg propofol (1% propofol, Fresenius, Istanbul, Turkey), 6 mg/kg ketamine (10% Ketason, Interhas, Richter Pharma, Austria) and ketofol (2 mg/kg ketamine and 2 mg/kg propofol, mixed in the same syringe). All anaesthetics were administered by using intravenous catheterization until the loss of jaw tone and pedal withdrawal reflex. All anaesthetics were administered by the same anaesthetist who was unaware of the experimental design.

MEASUREMENTS

Handling of rabbit was accomplished using a towel with minimal head and neck restraint, and the measurements were taken after the calibration of tonometer in ‘p’ mode [24]. The intraocular pressure was measured with a rebound tonometer (Tonovet, Icare, Vantaa, Finland). Anaesthetic eye drops were not used during the measuresmements. The intraocular pressure was recorded at the same time of the day (at 8:00 to 9:00) at baseline, 15 minutes after xylazine administration, and at 2, 5, 10, 20 and 25 minutes following induction. Each measurement of intraocular pressure’s were taken by the same examiner who was unaware of performed medications. The left eye measurement was always performed prior to the right eye measurement. The mean of the left and right intraocular pressure was assumed as the animal’s intraocular pressure.

STATISTICAL ANALYSIS

All data were analyzed using the SPSS19 (IBM Company, Version 19.0, SPSS Inc, USA, 2010) statistical package. Data are reported as mean ± standard deviation. An independent samples t-test was used to determine pre-treatment differences between groups. To evaluate the differences in intraocular pressure between the three groups, a one-way ANOVA followed by Tukey’s multiple comparison test was performed. Differences in pre- and posttreatment values of intraocular pressure within the groups were compared with a paired t-test. A p-value of <0.05 was considered statistically significant.

Results

Induction of anaesthesia occurred without using additional injections in all groups. No complication was observed during anaesthesia. Recovery was smooth and uneventful in all rabbits. The mean values of intraocular pressure at all time intervals are shown in Table I. All data are expressed as mmHg. The mean baseline values of intraocular pressure in propofol, ketamine and ketofol group’s were 9.62 ± 2.04, 9.18 ± 3.48 and 10.75 ± 2.36 mm Hg, respectively, and no statistically significant differences were seen in intraocular pressure after xylazine administration in propofol, ketamine and ketofol group’s at all time intervals. The mean baseline value of intraocular pressure significantly decreased in propofol group (7.00 ± 1.13, 8.56 ± 2.29) and ketamine group (8.56 ± 2.29) following xylazine administration and remained lower levels till 25 minutes following induction. In ketofol group, however, the intraocular pressure was significantly reduced at 5 (7.00 ± 1.51), 10 (7.06 ± 0.90) and 20 (8.31 ± 0.79) minutes following induction.

Discussion

The large size of the eye and easy handling make rabbits more appropriate subjects for ocular experimental studies compared to dogs, rats or primates which are relatively non-economic and aggressive animals [15]. Stabilization of intraocular pressure during the anaesthesia is the main

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<td>Propofol</td>
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<td>-1 (Baseline value), 0 (15 minutes after xylazine administration), ** different superscripts in columns indicates significant differences between groups (P &lt; 0.05)</td>
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Table I: The mean (±SD) intraocular pressure values of rabbits during the predefined time points in propofol (10 mg/kg), ketamine (6 mg/kg) and ketofol (2 mg/kg ketamine+2 mg/kg propofol) group.
The intraocular pressure have a tendency to decrease following administration of anaesthetics, with the exception of ketamine which cause a contraction at the extraocular muscles and results with increase in intraocular pressure [13]. However, in the current study ketamine administration following premedication with xylazine decreased the intraocular pressure. This decrease may be induced by extraocular muscle relaxation effect of xylazine [14].

Use of propofol for induction of anaesthesia is known to reduce the intraocular pressure [26]. Similarly in this experiment, intraocular pressure decreased after induction of anaesthesia with propofol. This decrease can be related with extraocular muscle relaxation effect of xylazine and/or propofol [14, 23]. Although there are no studies showing the effect of propofol after the xylazine premedication, our data suggest that this combination could be preferred for ophthalmic procedures in New Zealand white rabbits.

Rapeport et al. have been stated that with the use of ketamine and propofol mixture, the dose of both anaesthetics is decreased [25]. Admixture of 2mg/kg propofol and 1mg/kg ketamine have been used in rabbits for anaesthesia induction [12]. In this study, however, 2 mg/kg ketamine and 2 mg/kg propofol were selected to obtain 1:1 combination of ketofol. Eventhough the aim of this research was not to determine the optimal ratio or dosage of ketofol admixture, based on our observations it could be said that combination of 2 mg/kg ketamine and 2 mg/kg propofol may be preferred in rabbits for anaesthesia induction. In ketofol group, intraocular pressure did not alter immediately following induction, but reducing in intraocular pressure were observed at 5, 10 and 20 minutes following induction. This could be related with negative interaction of both drugs, which resulted with late central nervous system effects on extraocular muscles.

Conclusion

Intravenous ketamine (2 mg/kg) and propofol (2 mg/kg) admixture in New Zealand white rabbits is reduced intraocular pressure compared to propofol and ketamine, alone. Ketofol may be an alternative agent for ophthalmic procedures. Intravenous xylazine premedication reduces intraocular pressure in New Zealand white rabbits.

Conflict of interest

Author's inform that there is no conflict of interest.

Acknowledgments

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References

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