Effect of Sedation with Xylazine-Ketamine on Intraocular Pressure in Laboratory Rabbits

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Purpose
Xylazine HCl and ketamine are often used in combination for sedation and anesthesia in rabbits.¹ Studies have shown that xylazine causes a decrease in intraocular pressure (IOP) in multiple species,² while ketamine causes an increase in IOP.³ However, the effect of systemic xylazine combined with ketamine on IOP in rabbits has not been reported. The purpose of this study was to determine the effect of intravenous (IV) and intramuscular (IM) administration of xylazine-ketamine on IOP in laboratory rabbits.

Methods
Twenty female New Zealand white rabbits approximately 15 weeks old and weighing approximately 2.5 kg (range 2.42-2.89 kg) were used. Rabbits underwent a complete ophthalmic examination, including slit lamp biomicroscopy and indirect ophthalmoscopy, prior to enrollment in the study. All rabbits had clinically normal eyes.

Animals were assigned to two groups based on route of xylazine-ketamine sedation, either IV (Group 1) or IM (Group 2). Group 1 was administered the combined anesthesia with concentrations of 4.6 mg/mL xylazine and 15.4 mg/mL ketamine in a dose volume of 1 mL/kg. IOP measurements were obtained at baseline (prior to sedation) and at 5, 10, 20, and 25 minutes after administration of anesthesia. Group 2 was administered the combined anesthesia with concentrations of 10 mg/mL xylazine and 50 mg/mL ketamine in a dose volume of 1 mL/kg. IOP measurements were obtained at baseline (prior to sedation) and at 10, 20, 30, and 45 minutes after administration of anesthesia. Different time points were chosen based on time to effect and duration of anesthesia; IV administration has a much quicker onset of action and a much shorter duration than IM administration of the same drug.

Pressure readings were measured bilaterally using an applanation tonometer on the central cornea. Proparacaine HCl 0.5%, 1 drop, was delivered to each eye prior to IOP measurement. All measurements were obtained by the same examiner. The left eye was examined first, followed by the right.

Data for IOP measurements were interpreted using statistical analysis. One-way analysis of variance (ANOVA) combined with Dunnett’s multiple comparison procedure was used to compare IOP measured at baseline and at different time points. Student’s t-test was used to compare differences in IOP at 10 and 20 minutes between groups. Values were considered to be significantly different when p < 0.05.

Results

Group 1: IOP measurements at baseline and following IV xylazine-ketamine sedation (Table 1)

The mean IOP at baseline was 20.15 ± 2.24 mm Hg. IOP post-sedation was 18.75 ± 2.51 mm Hg at 5 min, 17.43 ± 2.45 mm Hg at 10 min, 16.05 ± 2.70 mm Hg at 20 min, and 15.60 ± 2.04 mm Hg at 25 min. With mean decreases from baseline of 1.40, 2.73, 4.10, and 4.55 mm Hg, respectively (Figure 1). Based on ANOVA, IOP measurements decreased significantly after IV administration from baseline values at 10, 20, and 25 min, but not at 5 min. The difference between IOP at 10 vs. 20 min was significant, but not 20 vs. 25 min.

Group 2: IOP measurements at baseline and following IM xylazine-ketamine sedation (Table 2)

The mean IOP at baseline was 19.03 ± 1.77 mm Hg. IOP post-sedation was 16.15 ± 2.19 mm Hg at 15 min, 17.3 ± 1.65 mm Hg at 20 min, 15.08 ± 2.09 mm Hg at 30 min, and 14.43 ± 1.76 mm Hg at 45 min, with mean decreases from baseline of 2.88, 3.30, 3.95, and 4.60 mm Hg, respectively (Figure 2). Compared with baseline values, IOP measurements decreased significantly after IM administration at all four time points. Based on ANOVA, the differences between IOP at 10 vs. 20 min, 20 vs. 30 min, and 30 vs. 45 min were not significant.

Comparison of IOP measurements between Groups 1 and 2: The difference between baseline mean IOP for Groups 1 and 2 was not significant. Student’s t-test was performed comparing the differences from baseline in each group at 10 and 20 min, and there was no significant difference between Groups 1 and 2.

Conclusions
IV and IM administration of xylazine-ketamine caused a statistically significant decrease in IOP in laboratory New Zealand White rabbits with clinically normal eyes. This response was maintained for at least 25 min after IV administration, and for at least 45 min after IM administration. At the common time points of 10 and 20 min for both dose routes, there was no significant difference in the decrease in IOP from baseline between those groups. When IOP is a biomarker of efficacy or adverse effect of an investigative drug or device, it is important to be aware that the combination of xylazine and ketamine reduces baseline IOP. In addition, xylazine-ketamine sedation and anesthesia is a good choice when it is desirable to avoid an increase in IOP in investigative studies or clinical situations in rabbits. Further studies are needed to investigate possible dose-dependence and the effect of varying the ratio of the two agents.

References