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SHORT COMMUNICATION

# Effects of medetomidine and xylazine on intraocular pressure and pupil size in healthy Beagle dogs

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## Abstract

**Objective** To determine the effects of intramuscular (IM) administration of medetomidine and xylazine on intraocular pressure (IOP) and pupil size in normal dogs.

**Study design** Prospective, randomized, experimental, crossover trial.

**Animals** Five healthy, purpose-bred Beagle dogs.

**Methods** Each dog was administered 11 IM injections of, respectively: physiological saline; medetomidine at doses of 5, 10, 20, 40 and 80 μg $kg^{-1}$, and xylazine at doses of 0.5, 1.0, 2.0, 4.0 and 8.0 mg $kg^{-1}$. Injections were administered at least 1 week apart. IOP and pupil size were measured at baseline (before treatment) and at 0.25, 0.50, 0.75, 1, 2, 3, 4, 5, 6, 7, 8 and 24 hours post-injection.

**Results** A significant decrease in IOP was observed at 6 hours after 80 μg $kg^{-1}$ medetomidine compared with values at 0.25 and 0.50 hours, although there were no significant changes in IOP from baseline. In dogs treated with 8.0 mg $kg^{-1}$ xylazine, significant reductions in IOP were observed at 4 and 5 hours compared with that at 0.25 hours after administration. In dogs treated with 5, 10, 20 and 40 μg $kg^{-1}$ medetomidine and 0.5, 1.0 and 2.0 mg $kg^{-1}$ xylazine, there were no significant changes in IOP. Pupil size did not change significantly after any of the medetomidine or xylazine treatments compared with the baseline value.

**Conclusions and clinical relevance** Low or moderate doses of medetomidine or xylazine did not induce significant changes in IOP or pupil size. In contrast, high doses of medetomidine or xylazine induced significant changes up to 8 hours after treatment, but values remained within the normal canine physiological range. The results of this study suggest a lack of significant change in IOP and pupil size in healthy dogs administered low or moderate doses of xylazine or medetomidine.

***Keywords*** dog, intraocular pressure, medetomidine, pupil size, xylazine.

## Introduction

Ocular effects of $\alpha_2$-adrenoceptor agonists in dogs have been reported (Verbruggen et al. 2000; Artigas et al. 2012; Rauser et al. 2012). One study found that intravenous (IV) administration of 1500 μg $m^{-2}$ medetomidine had no effect on intraocular pressure (IOP) (Verbruggen et al. 2000), whereas another found that a combination of 300 μg $m^{-2}$ medetomidine and 6.0 mg $m^{-2}$ butorphanol IV induced a transient increase in IOP

(Rauser et al. 2012). IV administration of 5 μg $kg^{-1}$ dexmedetomidine, the dextrorotatory enantiomer of medetomidine, also reduced IOP significantly in dogs (Artigas et al. 2012). The validity of such comparisons is limited, however, by interstudy variability with regard to drug doses, treatment combinations and the duration of observations. Another important factor that can affect IOP is pupil size, which is affected by the administration of $\alpha_2$-adrenoceptor agonists. Miosis is known to reduce IOP by increasing the outflow of aqueous humor (Gelatt & Brooks 1999). Further studies are necessary to investigate the changes in IOP over time induced by sedation protocols involving different doses of medetomidine and xylazine.

The aim of this prospective study was to investigate the effects of different doses of medetomidine and xylazine, respectively, on IOP and pupil size in healthy dogs. It was hypothesized that medetomidine and xylazine would each induce transient increments in IOP, followed by reductions, in healthy dogs at the higher doses tested. It was further hypothesized that the administration of each drug would be associated with reductions in pupil size.

## Materials and methods

### Animals

All procedures were carried out with the approval of the Institutional Animal Care and Use Committee of Kurashiki University of Science and the Arts, Kurashiki, Japan. Five healthy, purpose-bred, male Beagle dogs, with a mean ± standard deviation (SD) age of 6.6 ± 0.8 years and a mean ± SD weight of 14.3 ± 3.5 kg were used in this study. The dogs were maintained under uniform conditions in the authors' laboratory at the animal institution. Routine physical and ophthalmic examinations, which consisted of observations of the globe and eyelid, vision testing, direct and indirect pupillary light reflex testing, slit-lamp biomicroscopy, direct ophthalmoscopy, Schirmer's tear test, and IOP measurements were performed prior to the start of the study and indicated no abnormalities. All dogs were evaluated as being of American Society of Anesthesiologists (ASA) class I physical status.

### Study protocol

Each dog was administered 11 intramuscular (IM) injections of 2 mL volume into the semimembranosus muscle throughout the experiment. Injections consisted of, respectively: physiological saline solution; 5, 10, 20, 40 and 80 μg $kg^{-1}$ of medetomidine hydrochloride (0.1%; Domitor; Nippon Zenyaku Kogyo Co. Ltd, Japan), and 0.5, 1.0, 2.0, 4.0 and 8.0 mg $kg^{-1}$ of xylazine hydrochloride (2.0%; Celactar; Bayer Yakuhin Ltd, Japan). All injections were separated by intervals of at least 1 week, and the order in which they were administered was determined using a randomized Latin square crossover design. For the sake of clarity, these treatments are subsequently referred to as control, MED-5, MED-10, MED-20, MED-40, MED-80, XYL-0.5, XYL-1, XYL-2, XYL-4 and XYL-8, respectively. All dogs were acclimated to the experiment room and fasted for 12 hours before treatment. The schedule of room illumination remained consistent throughout the study.

Intraocular pressure and pupil size were measured at baseline (before treatment), and at 0.25, 0.50, 0.75, 1, 2, 3, 4, 5, 6, 7, 8 and 24 hours after each injection. After the 8 hour measurements, dogs were kept in the experiment room regardless of whether they were still sedated and were not subjected to any treatment, including reversal treatment.

### Measurements

Intraocular pressure was measured in the left eye using rebound tonometry (Tono Vet; Icare Finland Oy, Finland). Prior to each measurement, the tonometer was calibrated and a new probe was attached. IOP measurements were obtained while the dog was positioned in right lateral recumbency, with the head maintained in a relaxed manner at the level of the thorax. Pupil diameter was measured using Haab's pupillometer (Muranaka Medical Instruments Co. Ltd, Japan).

### Statistical analysis

All data were analyzed using GraphPad Prism Version 6.0 (GraphPad Software, Inc., CA, USA). Friedman's test for repeated measures was used to evaluate the time effect in each treatment. When a significant difference was found using Friedman's test, Dunn's test was used to compare the baseline mean with the mean at a particular timepoint. The level of significance in all tests was set at $p < 0.05$.