Surgery

Note

Effect of medetomidine on tear flow measured by Schirmer tear test

1 in normal pigs

Teppei Kanda\textsuperscript{1, 2)*, Ayumu Kajiyama\textsuperscript{2), Waka Morimitsu\textsuperscript{2), Yukiko Nishino\textsuperscript{2), Yutaro Oishi\textsuperscript{2}, Yuki Shimizu\textsuperscript{1, 2), Noritaka Maeta\textsuperscript{1), Kayo Furumoto\textsuperscript{2), Yoshi Itoh\textsuperscript{1), Toshinori Furukawa\textsuperscript{1})

1) Faculty of Veterinary Medicine, Okayama University of Science, 1-3 Ikoinooka, Imabari, Ehime, 794-8555, Japan
2) Department of Comparative Animal Science, College of Life Science, Kurashiki University of Science and the Arts, 2640 Nishinoura, Tsurajima-cho, Kurashiki, Okayama, 712-8505, Japan

* Correspondence to: Kanda T., Faculty of Veterinary Medicine, Okayama University of Science, 1-3 Ikoinooka, Imabari, Ehime, 794-8555, Japan
Email: t-kanda@vet.ous.ac.jp

Running head: MEDETOMIDINE EFFECT ON TEAR FLOW IN PIG
ABSTRACT

Medetomidine, an $\alpha_2$-adrenoceptor agonist, was reported to decrease tear flow in some species. However, there are no reports about the effect of medetomidine on tear flow in pigs. The purpose of this study was to elucidate it. The study was performed in 10 clinically normal female Landrace pigs aged 3 months. Tear flow was measured by the Schirmer tear test (STT) I before (baseline) and 15 and 30 min after intramuscular administration of 80 $\mu$g/kg medetomidine. Compared to the STT I value at baseline, the value decreased significantly at 30 min after administration in both the left and right eyes. In pigs treated with medetomidine, an artificial tear solution or ophthalmic gel should be applied to protect the ocular surface.

KEY WORDS: $\alpha_2$-adrenoceptor, medetomidine, pig, Schirmer tear test, tear
Medetomidine, an $\alpha_2$-adrenoceptor agonist, is widely used as a sedative or analgesic drug in veterinary medicine. However, some studies reported that $\alpha_2$-adrenoceptor agonists such as medetomidine and xylazine decreased tear flow in dogs and cats [4, 6, 7, 14]. Tears contribute to the immune system of the ocular surface and the metabolic processes on the cornea, which is avascular tissue. Tears provide a smooth optical surface by lubricating the nictitating membrane, conjunctiva, and cornea [8]. Insufficiency of tears damages the ocular surface tissue including the cornea and, at worst, might damage the vision. Animals with such changes, depending on the degree of change, experience irritation or pain on the ocular surface [2, 12, 16]. Although, medetomidine is often administered to pigs as a sedative agent [9–11, 13, 18], there are no reports of concerns about the effects of the administration of the drug on tear flow. In this study, we hypothesized that medetomidine would decrease tear flow in pigs, as it has been reported to cause in other species, and aimed to prove the hypotheses.

Ten clinically normal female Landrace pigs aged 3 months were included in the study. All pigs were sedated to perform computed tomography (CT) examination for another study. The mean (± standard deviation [SD]) body weight of the animals was 39.7 ± 5.3 kg (range, 32.7–47.2 kg). Body condition score was 3/5 in all the pigs examined. Physical and ophthalmologic examinations including observation of the globe and eyelids, assessment of corneal and eyelid reflexes, vision testing, assessment of direct and indirect pupillary light reflexes, slit lamp biomicroscopy, and intraocular pressure measurement, performed before the experiments revealed no abnormalities. On the basis of the results of the examinations, all pigs were diagnosed as American Society of Anesthesiologist physical status 1 [1]. This study was designed as a prospective and experimental trial, and was conducted in line with the
"Guidelines for Proper Conduct of Animal Experiments” reported by the Science Council of Japan [15]. All procedures in this study were approved by the Animal Care and Use Committee of Kurashiki University of Science and the Arts (Approval number, 23-27).

The pigs were administered 80 µg/kg medetomidine (Domitor, Nippon Zenyaku Kogyo, Fukushima, Japan) intramuscularly in the neck, after which the pigs were restrained using a sling and moved into the CT room. To achieve appropriate intramuscular injection, a 19-gauge 1 ½" needle was selected for drug administration. Tear flow was measured in both left and right eyes by the Schirmer tear test (STT) I using STT strips (ColorBar Schirmer tear test, EagleVision, TN, USA) before (baseline) and 15 and 30 min after drug administration while being restrained. During the interval between each measurement, the animals’ eyelids were kept closed with adhesive tape. After the measurements, we confirmed there were no complications including ocular damage. No reversal treatment with an α2-adrenoceptor antagonist such as atipamezole was performed.

All statistical analyses were performed using statistical software (GraphPad Prism 7, GraphPad Software, CA, USA). The Friedman test for repeated measures was used to evaluate the time of each treatment. The Dunn test was used to compare the baseline value with the mean value at each time point, when a significant difference was detected by the Friedman test. Differences between the left and right eyes at each time point were examined using the Wilcoxon matched-pairs signed-rank test. STT I data are reported as mean ± SD. Significance for all statistical analyses was set at $P < 0.05$.

There were no significant differences in the STT I value at each time point.
between the left and right eyes ($P = 0.38, 0.43, \text{ and } 0.65 \text{ at } 0, 15, \text{ and } 30 \text{ min, respectively, after administration}$. Compared to baseline values (left, 14.7 ± 3.1 mm/min; right, 15.6 ± 3.1 mm/min), STT I values decreased significantly at 30 min after medetomidine administration (left, 4.4 ± 2.6 mm/min, $P < 0.05$; right, 4.7 ± 2.8 mm/min, $P < 0.05$) in both the left and right eyes (Fig. 1). At 15 min after administration, STT I value showed tendency of decrease, but the decrease was not statistically significant in either eye (left, 10.1 ± 5.6 mm/min, $P = 0.28$; right, 9.2 ± 4.8 mm/min, $P = 0.06$).

STT values before medetomidine administration in this study were in agreement with the reference value (mean ± SD, 15.6 ± 3.7 mm/min; range 10–22 mm/min) reported previously [17]. Similar to that reported previously, there were no significant differences between the left and right eyes in this study. In the previous study, the STT value for juvenile pigs (age, < 6 months; body weight, 12–15 kg) was significantly lower than the value for adult pigs (age, 1–1.5 years; body weight, 120–200 kg). A comparison of the results of the present study with the mean values reported previously showed that the mean STT I value of the tested pigs (age, 3 months; body weight, 32.7–47.2 kg) was higher than the mean STT I value of the juvenile pigs (mean ± SD, 12.6 ± 2.0 mm/min), and was lower than that of the adult pigs (mean ± SD, 18.7 ± 2.1 mm/min) [17]. These results were consistent with the idea that STT values increase with an increase in body weight and age, as reported in dogs and pigs [3, 17]. Differences in the STT I value between male and female pigs were not investigated in the present study because previously sex was reported not to affect STT I values in pigs [17].

STT I values in pigs treated with medetomidine decreased significantly at 30
min after administration. Similar changes were observed in dogs and cats previously [6, 7]. These findings suggested that the medetomidine-induced decrease in tear flow measured by STT I was involved with the common mechanism in some mammal species. In our previous study, not only medetomidine but also xylazine decreased STT I values in dogs and cats [6, 7]. While medetomidine has affinity for both α2-adrenoceptor and imidazoline receptor, xylazine has no affinity for the imidazoline receptor [5]. Furthermore, atipamezole, an α2-adrenoceptor antagonist, was reported to reverse the medetomidine-induced decrease in STT I value in dogs [14]. Thus, it was suggested that the decrease in tear flow measured by STT I in pigs treated with medetomidine was also mediated by α2-adrenoceptors, similar to that in dogs and cats. However, such mechanisms involving the α2-adrenoceptor have not yet been elucidated in any species.

In the present study, the dose of medetomidine tested was 80 µg/kg. Furthermore, the observation time was limited up to 30 min after administration. These limitations of the study did not allow a discussion of dose dependence of medetomidine’s effect on tear flow in pigs.

As mentioned above, decreased tear flow might be one of the causes of damage to the ocular surface including the cornea, which is involved in pain or irritation in animals. It could damage the vision at worst. When pigs are sedated or anesthetized with medetomidine at the dose reported in the present study, an artificial tear solution or ophthalmic gel should be applied to protect the ocular surface in addition to careful observation.

REFERENCES


15. Science Council of Japan. 2006. Guidelines for Proper Conduct of


FIGURE LEGENDS

Fig. 1. Changes in STT I values before (baseline) and after medetomidine administration. Each bar represents STT I values for the left (black colored) and right eyes (grey colored). Data are expressed as the mean ± SD (n = 10). * P < 0.05 compared with the baseline value in each eye.
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