

The Effect of Different Doses of Intramuscular Xylazine HCl Administration on Intraocular Pressure in Rabbits

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Abstract

This study was aimed to determine the effects of intramuscular Xylazine HCl administration on intraocular pressure (IOP) in rabbits at 5 mg/kg (XYL-5) and 10 mg/kg (XYL-10) doses. IOP measurements were recorded at baseline (T₋₁), and at 5 (T₅), 10 (T₁₀), 15 (T₁₅), 20 (T₂₀), 30 (T₃₀), 45 (T₄₅) and 60 (T₆₀) minutes following Xylazine HCl administration. IOP values were significantly decreased at T₁₅ in group XYL-5 (8.37±1.45 mm Hg) and at T₅ in group XYL-10 (8.00±1.13 mm Hg). In conclusion, intramuscular Xylazine HCl significantly reduced IOP in rabbits at the latest after 15 minutes of administration, regardless of the doses used in this study.

Keywords: Intraocular pressure, New Zealand White rabbit, Xylazine HCl

Farklı Dozlarda Uygulanan Ksilazin HCl'ün Tavşanlarda İntraoküler Basınç Üzerine Etkisi

Özet

Bu çalışmada tavşanlarda 5 mg/kg (XYL-5) ve 10 mg/kg (XYL-10) dozlarında uygulanan Ksilazin HCl'ün intraoküler basınç üzerine etkilerinin belirlenmesi amaçlandı. İntraoküler basınç ölçümleri Ksilazin HCl uygulamasını takiben bazal (T₋₁), 5 (T₅), 10 (T₁₀), 15 (T₁₅), 20 (T₂₀), 30 (T₃₀), 45 (T₄₅) ve 60 (T₆₀) dakikalarda yapıldı. Grup XYL-5'te T₁₅ (8.37±1.45 mm Hg) ve grup XYL-10'da T₅'te (8.00±1.13 mm Hg) önemli derecede IOP ölçümlerinin azaldığı belirlendi. Sonuç olarak, doza bakılmaksızın Ksilazin HCl, uygulamadan en geç 15 dakika sonra Beyaz Yeni Zelanda tavşanlarında intraoküler basıncı düşürdü.

Anahtar sözcükler: Beyaz Yeni Zelanda tavşanı, İntraoküler basınç, Ksilazin HCl

INTRODUCTION

Xylazine HCl is an alpha-2 adrenoceptor drug that has muscle relaxant, sedative and analgesic properties and commonly combined with ketamine for routine procedures ^[1]. It is used as a premedicant to prevent side effects (e.g, respiratory depression) associated with ketamine administration ^[2,3]. Alpha-2 adrenoceptor drugs decrease intracellular cyclic adenosine monophosphate levels and results with less production of aqueous humor and increased uveoscleral outflow ^[4].

Maintaining intraocular pressure (IOP) at certain level is an important aspect for experimental studies especially in ocular surgery ^[5]. Because sudden increase in IOP may provoke complications such as vitreal hemorrhage or retinal decollement, IOP alterations should be minimized

during the anesthesia ^[6]. Previous study has reported that topical and intraarterial administration of Xylazine HCl decreases IOP in rabbits, cats and monkeys ^[7]. Moreover, intravenous Xylazine HCl administration causes a decrease in IOP in horses ^[8]. It has shown that intramuscular (im) administration of 10mg/kg Xylazine HCl and 50 mg/kg Ketamine HCl combination results with lower IOP values in rabbits ^[6]. However, no significant alterations were observed in IOP after anesthesia achieved with the im combination of 5 mg/kg Xylazine HCl and 35 mg/kg Ketamine in rabbits ^[9].

Even though Xylazine HCl may be used alone for minor procedures in animals, to date no study has evaluated the im administration of Xylazine HCl alone on IOP in rabbits. For this reason, this study was aimed to detect the effects of 5 mg/kg and 10 mg/kg doses of Xylazine HCl administration on IOP in rabbits.



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MATERIAL and METHOD

Atatürk University Local Board of Ethics Committee for Animal Experiments has approved the study protocol of this research (HADYEK decision no: 2015/188).

Eight, adult male, New Zealand White rabbits weighing 2.2-3.5 kg were used in this study. They were housed in individual cages with food and water *ad libitum*. The humidity ranged between 40 and 60%. A uniform temperature of $22\pm 2^\circ\text{C}$ was maintained throughout with a 12:12 h 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 and they underwent a 14 days acclimation period. Food and water were not withdrawn before administration, and animals were weighed prior to experiment.

Animals received each drug treatment in random order in a crossover study, with a minimum interval of one week between treatments. All rabbits in group of XYL-5 received im 5 mg/kg Xylazine HCl (2% Rompun, Bayer, Istanbul, Turkey), and those in group of XYL-10 received im 10 mg/kg Xylazine HCl. The doses used in this study were selected based on previous studies [6,9]. All injections were performed to *quadriceps femoris* muscle by the same person who was unaware of the experimental design.

Handling of rabbit and calibration of tonometer were accomplished as previous report [10]. IOP was measured with a rebound tonometer (Tonovet, Icare, Vantaa, Finland). Anesthetic eye drops were not used during the measurements. IOP was recorded at the same time of the day (at 9:00 to 11:00) at baseline (T_{-1}), and at 5 (T_5), 10 (T_{10}), 15 (T_{15}), 20 (T_{20}), 30 (T_{30}), 45 (T_{45}) and 60 (T_{60}) min following Xylazine HCl administration. Measurements were discontinued until the use of im 0.70 mg/kg Atipamezole (Antisedan, Pfizer, Istanbul, Turkey) administration.

Each measurement of IOPs 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 IOP was assumed as the animal's IOP.

Statistical Analysis

All data were analyzed using the SPSS 19 (IBM Company, Version 19.0, SPSS Inc, USA, 2010) statistical package. Data are reported as means \pm SD. Prior to statistical analysis data were subjected to Kolmogorow-Smirnow test to assess normality. An independent samples t-test was used to determine pre-treatment differences between groups. Post-treatment differences within each treatment group were evaluated using a paired samples t-test. A P-value of <0.05 was considered statistically significant.

RESULTS

The mean values of IOP at all time intervals are shown in Table 1. All data were expressed as mm Hg. The mean T_{-1} values of IOP in group XYL-5 and XYL-10 were 10.25 ± 2.54 and 10.62 ± 2.04 mm Hg, respectively. There were significant differences ($P<0.05$) observed between groups at T_{45} and T_{60} values. However, the differences in IOPs at the other predefined time (T_5 , T_{10} , T_{15} , T_{20} , T_{30}) points were not statistically significant.

IOP values were significantly decreased at T_{15} in group XYL-5 (8.37 ± 1.45 mm Hg) and at T_5 in group XYL-10 (8.00 ± 1.13 mm Hg). The lowest IOP values were obtained at T_{60} in both groups. These were 8.12 ± 1.40 mm Hg in group XYL-5 and 5.93 ± 0.77 mm Hg in group XYL-10.

DISCUSSION

This study is the first report on the IOP alterations following different doses of im Xylazine HCl administration. The im Xylazine HCl significantly reduced IOP in rabbits at the latest after 15 min of administration, regardless of the doses used in this study.

Rabbits are commonly preferred in ocular experiments because of their large size of the eye, easy handling and meekness [11]. Normal IOP measurements using rebound tonometer in rabbits are ranged between 9.51 ± 2.62 mm Hg [10]. In the current study, the mean IOP of baseline values for all rabbits were within the reference values. The IOP can vary throughout the day and environmental factors may

Table 1. Mean and SD of intraocular pressure values during the predefined time points in two groups. Group XYL-5 received im 5 mg/kg Xylazine HCl, Group XYL-10 received im 10 mg/kg Xylazine HCl

Tablo 1. İki grubun tanımlanan zamanlarda intraoküler basınç ortalamaları ve standart sapma değerleri. Grup XYL-5'deki deneklere im 5 mg/kg Xylazine HCl, Grup XYL-10'daki deneklere im 10 mg/kg Xylazine HCl uygulanmıştır

Groups	Predefined Time Points							
	T_{-1}	T_5	T_{10}	T_{15}	T_{20}	T_{30}	T_{45}	T_{60}
XYL-5	10.25 ± 2.54	9.25 ± 1.44	8.81 ± 1.69	$8.37\pm 1.45^*$	$8.12\pm 1.12^*$	$8.15\pm 1.70^*$	$8.62\pm 1.15^{*a}$	$8.12\pm 1.40^{*a}$
XYL-10	10.62 ± 2.04	$8.00\pm 1.13^*$	$8.31\pm 1.18^*$	$8.25\pm 1.95^*$	$7.65\pm 1.23^*$	$8.31\pm 1.66^*$	$6.40\pm 1.18^{*b}$	$5.93\pm 0.77^{*b}$

* Indicates significant differences within the groups ($P<0.05$); ^{a,b} indicates significant differences between the groups; T_{-1} Baseline value

alter the measurements ^[12,13]. Based on these premises, IOP measurements of rabbits were recorded at the same time of the day and after two weeks of acclimatization period.

Previous study has reported that Xylazine HCl at the dose of 1 or 2 mg/kg do not cause any significant changes in IOP, whereas 4 or 8 mg/kg doses of Xylazine HCl administration results in lower IOP values in dogs ^[14]. In the present study significant decrease in IOP was observed 15 min after im administration of 5 mg/kg Xylazine HCl (T₁₅). Moreover, 10 mg/kg doses of xylazine used in this study reduced IOP 5 min after administration (T₅) in comparison with the baseline value (T₋₁). In the current study, no significant decrease on IOP was observed between groups at all time intervals with the exception of T₄₅ and T₆₀. Xylazine HCl at 10 mg/kg dose used in the present study more reduced IOP at 45 and 60 min, compared with at the dose of 5 mg/kg. A limitation to the present study is the rabbits that enrolled having healthy eyes. Effects of Xylazine HCl administration on IOP involving rabbits with ocular diseases is a worthy topic for future study.

It has been stated that reduced blood pressure results with lower IOP values ^[15]. Similarly in this study, Xylazine HCl administration causes reduced IOP in rabbits possibly due to xylazine-induced bradycardia ^[1].

In conclusion, im Xylazine HCl at 5 mg/kg or 10 mg/kg doses reduced IOP in rabbits. Comparison of two pre-anesthetic regimen suggests Xylazine HCl at 10 mg/kg is preferred over 5 mg/kg in rabbits that require lower intraocular pressure for procedures that lasts more than 45 min. Because present study was carried out in only eight rabbits, additional studies involving larger numbers of rabbits are needed to confirm our results.

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