Influence of Atropine Premedication on Cardiac rate in Donkeys injected with Xylazine and Xylazine-Ketamine combination

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SUMMARY

The study was carried out in four groups of 5 donkeys each to evaluate the influence of atropine sulphate premedication on cardiac rate in donkeys injected with xylazine and xylazine-ketamine combination. Where atropine was given, it was injected subcutaneously at a dosage of 0.1 mg/kg. Xylazine hydrochloride (2.0 mg/kg) and the drug combination of xylazine (2.0 mg/kg) - ketamine hydrochloride (4.4 mg/kg) were injected intramuscularly. Where the drug combination xylazine - ketamine was given, the two drugs were mixed together and given in the same syringe.

Group 1 animals were injected with xylazine , group 2 with atropine and xylazine, group 3 with xylazine and ketamine and group 4 with atropine-xylazine-ketamine. Xylazine and atropine-xylazine caused a transient decrease in mean heart rate rates in group 1 and 2 animals. Xylazine-ketamine and atropine-xylazine-ketamine caused a transient decline in mean heart rates in group 3 and 4 animals in the first five minutes following their injection followed by a transient rise and then a decline over the rest of the 2-hour monitoring period. However, all these changes were not statistically significant ($P > 0.05$). The baseline mean heart rates in atropine premedicated groups were significantly higher ($P < 0.05$) than in the unpremedicated groups . This difference persisted for 2 hours. The potential for atropine to overstimulate heart rates leading to myocardial hypoxia exists and it should not indiscriminately be used prior to every anaesthesia.

INTRODUCTION

Atropine sulphate, an anticholinergic drug, is routinely used by many veterinary practitioners as part of a preanaesthetic regimen to prevent excessive upper airway secretions and to prevent either reflexly or pharmacologically increased vagotonia, with resultant bradycardia (Muir, 1978). However, use of anticholinergics in routine equine anaesthesia is not recommended because their potential advantages including decreased salivation and maintenance of higher heart rates do not outweigh their potential disadvantages which include postoperative ileus (Ducharme *et al*, 1983) and increased myocardial oxygen consumption (Hubbell *et al*, 1984). Studies on possible deleterious effects of atropine including type of airway secretions produced, ventricular excitability and predisposition to cardiac dysrrhythmias have been carried out (Muir, 1978; Averill *et al*, 1959; Kolman *et al*, 1975; Kolman *et al*, 1976). Detailed review on the effects of anticholinergic drugs on the cardiovascular system can be found in the literature (Mirakhur, 1979).

Xylazine hydrochloride, a drug noted for its sedative-analgesic properties in the horse has been associated with decreased heart rate and a high incidence of second-degree atrioventricular (AV) block after an intravenous administration in the horse (Muir *et al*, 1977). The second-degree atrioventricular block could be obviated by the administration of atropine sulphate (Kerr *et al*, 1972). Ketamine hydrochloride, a dissociative anaesthetic drug which produces tachycardia in various animal species when given alone provides reasonably stable cardiopulmonary function when given in conjunction with xylazine in the horse (Muir *et al*, 1977; Hall *et al*, 1981) and donkey (Mogoa, 1990).

This paper presents the results of a study carried out to evaluate the influence of atropine premedication on cardiac rate in donkeys given xylazine and xylazine-ketamine combination.

MATERIALS AND METHODS

A total of twenty healthy donkeys of both sexes, aged between 2 and 11 years and weighing between 80 and 200 kg were used in this study. They were randomly assigned into four groups of five animals each. Water and food were provided *ad libitum*. The donkeys were fasted for 18 hours before commencement of the trial.

The time when either xylazine or the combination was injected was designated as time zero. The donkeys which were premedicated with atropine sulphate were injected with the drug subcutaneously in the neck twenty five minutes before time zero. All the other injections were made intramuscularly into the lateral muscles of the neck. Where the drug combination xylazine-ketamine was given, the two

were mixed in the same syringe. The group treatments were as follows:

Group 1 : xylazine hydrochloride (Rompun-Bayer) at 2.0 mg/kg body weight.
Group 2 : atropine sulphate (Bimeda Chemicals) at 0.1 mg/kg then xylazine hydrochloride at 2.0 mg/kg body weight.

Group 3 : xylazine hydrochloride at 2.0 mg/kg and ketamine hydrochloride (Ketalar-Parke Davis) at 4.4 mg/kg body weight.

Group 4 : atropine sulphate at 0.1 mg/kg then xylazine hydrochloride at 2.0 mg/kg and ketamine hydrochloride at 4.4 mg/kg body weight.

The cardiac rate was determined by auscultation of the heart and counting the number of heart beats over a one minute period. This was done just prior to injection of either xylazine or xylazine-ketamine (time zero) to obtain baseline values and every 5 minutes there-after for 2 hours.

Data Management

The results were analysed using analysis of variance and covariance with repeated measures and the significance level was set at $P < 0.05$. Where a significant F ratio (variance ratio) was obtained, the Student's *t*-test was used to compare the means between the groups. The results are given as Means ± standard deviation.

RESULTS

Table 1 shows the mean heart rates in beats per minute (± standard deviation) for the four groups of animals under the different regimens of treatment. Group 1 and 2 animals injected with xylazine and atropine-xylazine respectively showed a statistically insignificant ($P > 0.05$) decrease in mean heart rate in the first one hour following xylazine administration. This decrease was more marked in group 2 animals. Group 3 and 4 animals injected with xylazine-ketamine and atropine-xylazine-ketamine respectively showed a decrease in mean heart rate as compared to the baseline values in the first five minutes following injection of the drug combination. This was followed by a transient rise and then a decline in mean heart rates over the rest of the 2-hour monitoring period. However, all these changes were not statistically significant ($P > 0.05$).

The group 2 and 4 animals premedicated with atropine had significantly ($P < 0.05$) higher mean heart rates over the entire 2 hours as compared to unpremedicated animals in groups 1 and 3. Time zero mean heart rate for atropine-xylazine group was 98.4 ± 20.9 (xylazine group, 48.0 ± 9.4) and for the atropine-xylazine-ketamine group was 81.0 ± 14.6 (xylazine-ketamine group, 37.8 ± 10.0). At the end of the 2 hours, mean heart rate for the atropine-xylazine group was 71.4 ± 15.6 (xylazine group, 50.4 ± 10.8) and the atropine-xylazine-ketamine group mean was 66.8 ± 15.6 (xylazine-ketamine , 37.8 ± 7.8)

Table 1.
Mean heart rates (± standard deviation)at 10 minute intervals for the four groups of animals.

Group Time (Min)	Group1	Group2	Group3	Group4
0	48.0±9.4	98.4±20.9*	37.8±10.0	81.0±14.6*
10	46.8±7.8	84.0±27.5*	39.0±7.9	80.8±25.3*
20	46.8±9.8	82.0±27.6*	41.0±4.4	74.6±27.9*
30	46.8±9.8	78.2±30.6*	39.8±2.4	73.2±18.0*
40	45.6±10.8	81.0±22.8*	38.4±3.2	72.0±19.3*
50	45.6±10.8	73.2±28.4*	38.6±5.4	73.8±17.1*
60	45.6±10.8	70.4±27.9*	38.6±5.6	73.2±17.5*
70	47.6±13.4	69.8±24.9*	37.2±4.6	72.4±18.1*
80	50.8±11.0	72.6±20.1*	37.2±4.6	73.2±17.5*
90	49.2±10.7	72.4±16.9*	37.2±4.6	73.6±17.2*
100	48.0±9.4	71.8±16.2*	37.2±4.6	73.6±17.2*
110	49.2±10.7	71.4±15.6*	37.2±4.6	72.4±14.8*
120	50.4±10.8	71.4±15.6*	37.8±7.8	66.8±15.6*

* Significantly ($P < 0.05$) different from mean rates of the unpremedicated group at the same time.
Group 1- xylazine hydrochloride
Group 2- atropine sulphate + xylazine hydrochloride
Group 3- xylazine hydrochloride + ketamine hydrochloride
Group 4- atropine sulphate + xylazine hydrochloride + ketamine hydrochloride.

DISCUSSION

The changes in heart rate in donkeys injected with the various drugs and drug combinations as used in this study have been reported (Mogoa, 1990; Tantawy *et al*, 1979). Similar effects have been reported in horses (Clarke *et al*, 1969) and sheep (Byagagaire, 1982). Reduction in heart or pulse rate by xylazine is through intense vasoconstriction through an a-sympathomimetic effect (Knight, 1980) and its depressive effect on cardiac performance like other a_2-adrenergic agonists. Transient rise in heart rate seen with atropine-xylazine-ketamine is thought to be due to the superseding of the inhibitory action of xylazine by atropine and ketamine since atropine is vagolytic and ketamine is chronotropic. Elevation of heart rates following atropine premedication seen in this study has been reported in horses (Short *et al*, 1986)and dogs (Muir, 1978). Atropine competitively antagonises acetylcholine at the post-ganglionic effector sites causing parasympathetic blockade and resulting in tachycardia (Brown *et al*, 1993). This abolishes vagally mediated parasympathetic tone exposing the heart to increased sympathetic activity and development of dysrrhythmias (Muir, 1978). Although no heart rhythm disturbances were evaluated in this study, their occurrence following atropine premedication and in association with use of various sedatives and anaesthetic agents have been reported in other animal species (Muir, 1978; Short *et al*, 1986).

It is known that tachycardia from any cause promotes the efflux of potassium ions from and influx of calcium ions into the myocardial cells, further increasing cardiac irritability (Muir, 1978). Furthermore, slow heart rates (as caused by a $_2$- adrenoceptor agonists) as well as excessively rapid heart rates are known to increase myocardial oxygen demand, thereby decreasing cardiac reserve and prom oting the production of ventricular premature depolarizations despite increased coronary artery blood flow (Averill et al, 1959). Possibilities of developing myocardial hypoxia if heart rates were overstimulated in the presence of low normal oxygen levels with the spontaneous breathing of atmospheric air therefore do exist. Although atropine may be lifesaving in cases of profound sinus bradycardia with hypotension, its potential side effects dictate that it should not indiscriminately be used prior to every anaesthesia.

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