Cardiopulmonary effects of the anesthesia by romifidine as a premedication, midazolam and ketamine induction and infusion in donkeys

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Abstract

The objective of this study was to determine the cardiopulmonary effects of romifidine 0.1 mg/kg as a premedication and anesthesia by intravenous injection of a mixture of midazolam 0.1 mg/kg and ketamine hydrochloride 2.2 mg/kg in the ten health She donkeys. The maintenance of anesthesia was performed by intravenous infusion of a mixture of the midazolam 0.065 mg/kg/hrs. and ketamine 6.6 mg/kg /hrs. clinical Parameters included respiratory rate and heart rate were measured at time zero (control data) and at 5, 10, 15, 20, 25, 30, 45, 60 and 90 minutes of this regime. The results revealed significant differences P>0.05 in the means of heart rate (beat/minutes) between zero and 5min 38.7 ± 0.76-36.7 ± 0.83 respectively with 10 min 42.3 ± 0.775 also respiratory rate (breath/minutes) similar to heart rate at zero and 5 min 19.1 ±0.348-21 ± 0.466 beat/min show significant differences P>0.05 with 10 min 25 ± 0.683 beat/min. The general anesthesia in this protocol was good and little effect on the cardiopulmonary in donkeys.

التأثيرات القلبية الرئوية للتخديرِ مِن قِبل الرومفدين كعلاج تمهيدي والميدازولام كيتامين للاستحداث والإدامة في الحمير

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الخلاصة

هدفت الدراسة الحالية تحديد التأثير القلبي الرئوي للتخدير العام الوريدي بحقن عقار رومفدين بجرعة 0.1 ملغم/ كغم كعلاج تمهيدي واستحداث التخدير العام بإعطاء مزيج الميدازولام بجرعة 0.1 ملغم/ كغم والكيتامين بجرعة 2.2 ملغم/ كغم من وزن الجسم والمحافظة على التخدير العام بواسطة التسريب الوريدي لمزيج الميدازولام بجرعة 0.065 ملغم/ كغم/ ساعة والكيتامين بجرعة 6.6 ملغم/ كغم/ ساعة. تم تسجيل معاير التنفس ومعدل ضربات القلب في الأوقات صفر (سيطرة)، 5، 10، 15، 20، 25، 30، 45، 60 و90 دقيقة. اظهرت نتائج معدلات دقات القلب وجود فرق معنوي بين الاوقات صفر و5 دقيقة مع الوقت 10 دقيقة وكذلك أظهرت نتائج معدل التنفس فرق معنوي بين الاوقات صفر و5 دقائق مع الوقت 10 دقائق. كان التخدير العام بواسطة هذا المزيج جيد مع تأثير قليل على التنفس والقلب في الحمير.

Introduction

The α-2-adrenoceptor agonists drugs have been recognized worldwide in veterinary medicine for their sedative, analgesic and muscle relaxation properties in large and small animals (1). The commonly used α_2-agonists in veterinary practice include xylazine, detomidine, medetomidine and romifidine. Romifidine is a recent α-2 adrenoceptor agonist marketed for use in horses (2). Romifidine has been available since 1985 (3). It has been used successfully for sedation, analgesia, and premedication in horses in several countries since 1988 (4) with effects similar to other α-2

adrenoreceptor agonists (5). The pharmacological actions of romifidine other than sedation are similar to all α-2 adrenoceptor agonists. Following I.V. administration there is bradycardia, a fall in cardiac output, and hypertension followed by lowered blood pressure (6, 7) The effects of α-2 adrenoceptor agonists include bradycardia arhythmia, atrioventricular block, transitory hypertension, followed by hypotension, increase of central venous pressure, reduction of systolic volume and cardiac output, increase of vascular resistance and respiratory depression, produced by reduction of respiratory rate and minute volume (8). Dysrhythmias characterized by heart block, premature ventricular depolarization and tachycardia have been noted with anticholinergic and α-2 agonist combinations, especially if the anticholinergic is administered concurrently rather than prior to the alpha2-agonist (9, 10). Midazolam is a short-acting benzodiazepine with hypnotic, anticonvulsant, muscle-relaxant and anxiolytic properties. In clinical practice, it is used for the induction of anesthesia (11). Midazolam induces hypotension when used in combination with narcotics, and during cardiopulmonary bypass (12). This hypotension is accompanied by a decreased systemic vascular resistance which is probably due to the direct vasodilation effect of midazolam (13, 14). Ketamine is a phencyclidine derivative that produces a dissociative state of anesthesia. Dissociative anaesthesia was characterized by dissociation between the thalamo-cortical and limbic system on the electroencephalogram (EEG) (15, 16). As a sympathomimetic drug, ketamine stimulates the cardiovascular system, which is characterized by increases in heart rate, mean aortic pressure, pulmonary arterial pressure, central venous pressure and cardiac output (17). Respiration rate is usually maintained or mildly increased, while alveolar ventilation can be transiently decreased, depending on the dose administered arterial blood gases are generally preserved when ketamine is used alone (18).

Materials and Methods

Ten clinically healthy she donkeys weighing between 70- 100 kg aged 8-12 months was used in this study. Romifidine was used as a premedication drug (Sedivet® 1.0%Boehringer Ingelheim Vetmedica, Inc., Spain). Midazolam from Alsaad pharmaceuticals, Syria and ketamine from kepro pharmaceuticals, Holland. Was used to induction and maintained the anesthesia. The regime of general anesthesia was made by administration of: Romifidine Hydrochloride, midazolam mixed with Ketamine Hydrochloride. Romifidine at a dose of 0.1 mg/kg B.W. has been injected intravenously in the jugular vein as a premedication and after five minutes, a mixture of midazolam at a dose of 0.1 mg/kg B.W. and Ketamine at a dose of 2.2 mg/kg B.W. in the same syringe (19), had been injected intravenously. Fifteen minutes later an infusion of midazolam 10 mg mixed with ketamine 1000 mg in 500 ml normal saline was administrated to maintain the anesthesia, the rate of dripping was 100-110 drops per minute (20 drops equal to 1ml). The cardiopulmonary effect of this regime was evaluated by respiratory rate (breath/ min) and heart rate (beats/ minutes) (by Omni II Touch Screen). The Omni II Touch Screen is a patient monitor used to access the heart rate by the sensor consists of light emitting diodes (LEDs) that emit light in the red (660 nm) and infrared (940 nm) wavelengths and a photo detector that measures the amount of light that has been transmitted through tissues (20). The results were expressed as means (M) ± stander error (SE). Parametric data were analyzed by one ways Analysis of Variance (ANOVA) continued with Least Significant Difference (L.S.D.), and $P< 0.05$ was considered to be significant. Statistical Package for Social Sciences (SPSS) was used (21).

Results and Discussion

The respiratory rate described in table was gradually increased during the first five minutes (M ± SE were 19.1± 0.348 in zero time to 21.8± 0.466 in 5 min breath/min) followed the injection of romifidine, on the other hands the respiratory rate continue in the increase after the injection of midazolam/ketamine and slightly increased reaching 25±0.683 breath/ min at 15 min and stable above the base line to the end of the experimental time of study. The statistical analysis revealed that there were no significant differences at the level of ($P>0.05$) among the control (zero) time and 45, 60 and 90 minutes, but there were a significant differences ($P<0.05$) between control with 5, 10, 15, 20, 25 and 30 minutes. The increase in the respiratory rate may be attributed to the excitement of the animal during IV injection of pre-anesthetic drugs, and the increase more clearly 5 minute post-injection of midazolam- ketamine due to excitement phases of stage 1 and stage 2 of general anesthesia. While the stability of the respiratory rate within 15-90 minutes after administration of drugs may be due to the increased in the depth of general anesthesia of the romifidine, midazolam and ketamine. This pattern of respiratory rate disagree with the most researches, this may be due to difference in the doses used in our and their study which used (romifidine and midazolam) that showed decrease in respiratory rate which may attribute to depressive effect of both drugs. Freeman and England, (22) who described that alpha-2 agonist drug, causes respiratory depression by alpha-2 adrenergic probably mediated by adrenergic neuron in the medullary respiratory center. Also Domino *et al.,* (23) found that midazolam which causes respiratory depression due to depression of the CNS. Evaluation of heart rate revealed slowly decreased through the first five minutes (38.70 ± 0.760; 36.7± 0.830 beat/minutes) after the injection of romifidine, then thought 75 minutes of general anesthesia time by maintenance, the heart rate increased and stable above base line to the end of experiment and became (39.60±0.371) at 90 minutes. The statistical analysis revealed that significant differences at the level of ($P<0.05$) between 10min with the 5min, but show no significant deference between control time, 5, 10, 15, 20, 25, 30, 45, 60 and 90 min (Table1). The results agreed with the result of other researches which attributed to the effect of α-2 agonist drugs which causes decrease in the heart rate that was caused arrhythmogenic include sinoatrial block, first and second atrioventricular (AV) block, bradycardia, and sinus arrhythmia. Bradycardia occurred after administration of romifidine is thought to be resulted of increased vagal tone in response to depression and of barorreceptor stimulation in the carotid sinus in response to initial hypertension by the administration of an α-2 agonist drugs (24; 25, 26). After 10 minute, of the experiment, the heart rate increased because ketamine affect the cardiovascular stimulating properties, such as high blood pressure, tachycardia, and increased cardiac output, is primarily sympathomimetic actions as a result of stimulation of the central sympathetic nervous system (27). The heart rate slowly return to normal rate due to the reverse effects of the romifidine and midazolam by ketamine, this agree with other study, which indicated that direct effect of ketamine on the cardiovascular which cause increase the work over load of the heart and still can develop arrhythmias, as a minor sensible. Up take of the heart to catecholamine cause direct vasodilation of vascular smooth muscle lead to increase heart rate and mean arterial blood pressure (28, 29). The general anesthesia in this protocol was good and little effect on the cardiopulmonary in donkeys and can be used for anesthesia of donkeys.

Table (1) Effect of general anesthesia regime on cardiopulmonary in (10) donkeys

parameter	Time minutes									
	zero	5	10	15	20	25	30	45	60	90
Respiratory rate Breath/minute	19.1± 0.348 D	21± 0.466 C	25± 0.683 A	23.1± 1.100 B	22.6± 0.945 BC	22 ± 0.906 BC	21.± 0.819 C	20.7± 0.597 D	20.± 0.654 D	20.5± 0.428 D
Heart rate Beat/minute	38.7± 0.760 AB	36.7± 0.830 B	42.3± 0.775 A	40.6± 0.763 A	41± 0.894 A	40.7± 0.894 A	41.1± 0.504 A	41.6± 0.777 A	40.3± 0.650 AB	39.6± 0.371 AB

Value is expressed as M ± SE.

Different in the capital latters refer significant differences (P<0.05) between time.

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