



Comparative Study Between IV and IM Co-administration of Xylazine with Ketamine on Some Physiological Parameters in Dogs



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CLINICAL anesthetic trial was conducted on 12 local dogs in different age, sex and body weight. The aim of study is to investigate the comparative effect of ketamine and xylazine combination injected either IM or IV on the anesthetic (induction times, duration of anesthesia and recovery time) and physiological parameters on the dogs. They were divided into two groups (G-I and G-II) randomly. All dogs were administered with atropine sulphate (0.04mg/kg BW, IM) 5 minutes before anesthetic protocol, ketamine+xylazine (10mg/kg+1mg/kg) respectively, was administered IM in G-I and IV in G-II. Clinical findings including inductions, duration and recovery period of anesthesia, HR, RR, RT, SPO₂, SBP, DBP and MAP were recorded before and during anesthesia. The study shows that there were no significant differences between G-I and G-II in physiological parameters of ketamine and xylazine anesthesia in dogs except induction, duration and recovery of anesthesia was longer in G-I than G-II. In conclusion, the results demonstrated that the combination of ketamine+xylazine can be a special satisfactory anesthetic protocol for excellent induction, good muscle relaxant and smooth recovery in dogs.

Keyword: Ketamine, Xylazine, Intravenously, Intramuscularly, Dogs.

Introduction

The combinations of ketamine, xylazine and atropine are widely used by anesthetists in our country due to the limited number of other anesthetic drugs available in the local market. Because of the high lipid solubility of ketamine, it has been shown to have analgesic properties which are attributable to direct antagonism of the N-methyl-D-aspartate receptors; it has an extremely fast distribution within the tissues [1-3]. By applying ketamine alone in preventing the postoperative pain showed ineffectiveness [4-6, 3]. However, for preventing the side effects such as hallucination, muscle rigidity, seizures/

convulsions and excitation, xylazine is commonly combined with adrenoceptor agonists (3, 7, 8). Xylazine is also used to initiate and prolong the duration of the general anesthesia, in addition showing the myorelaxant, sedative and analgesic effect at the time used as a premedicant [3, 8, 9]. The combination of xylazine hydrochloride with ketamine hydrochloride may be producing an easy induction with cataleptic state of recovery [8, 10]. The popularity of ketamine-xylazine (KX) combination is used mainly because of its supplemental effects (that is, muscle relaxation, analgesic properties, and sedation) [8, 11]. Although the combination of KX provides relatively safe anesthesia, this anesthetic

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combination has demonstrated variability in providing a surgical plane of anesthesia in dogs [12, 13].

Atropine is mainly used as premedication with xylazine hydrochloride to reduce or prevent bradycardia that caused by administration of α_2 -agonist in dogs and also atropine decrease potential muscle spasm gastrointestinal secretion and motility, respiratory secretion, salivation and also decrease lacrimation throughout anesthesia [14- 16].

Material and Methods

The study was carried out on 12 dogs of the same age group, breed and different body weight; all dogs were examined for physical examination and medical history which found healthy with no congenital or acquired abnormality at the Veterinary Medicine and Clinic Department in the Veterinary Medicine College at the University of Duhok. Ivermectin mg/kg was prescribed intramuscularly which was repeated 14 days in all dogs. Before sedation, all animals were allowed access to water for 4 hours while access to food was stopped for 12 hours. All dogs were divided into two groups six dogs for Group I and six for Group II depending on the anesthetic drugs given. The atropine 0.04 mg/kg body weight was administered to both groups 5 minutes before induction of anesthesia and then ketamine HCL 15 mg/kg and xylazine HCL 1mg/kg were mixed in a single syringe and injected intramuscularly to group I and intravenously to group II [17].

When animals get into anesthesia all differences were recorded. The dogs were placed on a padded table and positioned at sternal recumbency. Heart rate, respiratory rate, rectal temperature, hemoglobin oxygen saturation (SPO₂) and blood pressure including systole, diastole and mean arterial pressure were taken by electronic monitor (CE New Vet Veterinary Vital Signs ICU Patient Monitor/Chinese) before drug administration and repeated every 10 minutes

during anesthesia. All physical discomfort sign of dogs (urination, defecation, vomiting and convulsion) were taken during anesthesia. The induction time was calculated from the injection of ketamine and xylazine to the vanishing of the pedal reflex, while the anesthesia duration was calculated as the period between the disappearance and return of the pedal reflex. The Recovery period was measured from the time between the return of the pedal reflex and the time the animal could walk itself.

Deepness of sedation and anesthetic effects of the drug were evaluated, the nociceptive stimulus was applied and findings were recorded. By inspecting the tail and ear movements the myorelaxant effects of the drugs were recorded. After the animals were recovering the signs of recovery (initial move, sternal recumbency and walking time) were taken till they started to walk. Following the study none of the food and water was given orally for 3 hours. Data were reported as mean and standard deviation. The paired t-test was applied for comparisons within the group to detect the difference in physiological parameters, induction, and duration of anesthesia and recovery time.

Results

The induction time, duration of anesthesia and recovery of the two groups were shown in (table 1). In both groups the induction was smooth (free from struggling). The induction time of anesthesia was showed significantly longer in group I (3.96 ± 2.35) than in group II (0.23 ± 0.1). The mean recovery time from anesthesia in G-I and G-II was 30 ± 7.97 and 28.25 ± 5.6 minutes respectively as in Table (1). The qualities of recovery in the two groups were smooth with no struggling and excitement.

The eyes of all animals were found open during anesthesia. Dogs have different movements when recovering from anesthesia. One by tail moving,

TABLE 1. Induction time, duration time and recovery period in poppies under the effects of anesthetic agents in both groups.

Groups	Induction (minutes)	Duration (minutes)	Recovery (minutes)
G-I	$3.96 \pm 2.35^*$	41.2 ± 6.2	30 ± 7.97
G-II	0.23 ± 0.1	30.2 ± 8.6	28.25 ± 5.6

*= Denotes statistically significant change with $p < 0.05$ as compared between two groups. Values were given as mean \pm SD.

some by ear moving and some by head moving recovery from the anesthesia. Vomiting and shivering were not found during anesthesia and waking from anesthesia.

Reflexes did not change throughout the anesthesia. It is found that good anesthetic status was determined in the all of dogs by applying a nociceptor stimulus during anesthesia.

The mean duration of anesthesia was 41.2 ± 6.2 and 30.2 ± 8.6 in both group I and group II respectively. As the result showed that the duration of anesthesia was been longer in G-I than in G-II, but there was no statistically significant ($P < 0.05$) difference between group I and group II in their duration of anesthesia.

The mean HR increased significantly after induction of anesthesia and at 10, 20, 30 and 40 minutes of anesthesia in both groups compared to 0-time and there was no statistical significant difference (by paired t-test) between the two groups in increasing the mean HR. The RR decreased significantly in G-I at 10-40 min compared with time 0 also in G-II decreased at 5-30 min. following anesthetic induction. In both groups rectal temperature was slightly elevated insignificantly at ($p < 0.05$), Only at minute 20 and at minutes 10-20 there was a significant decrease in SPO₂ in G-I and G-II, respectively.

There was a significant decrease in systolic blood pressure at 10, 20 and 30 min of anesthesia and in diastolic blood pressure only at 20 min of anesthesia in G-I compared at time 0. Whereas significant decrease in diastolic blood pressure was found only at min 30 of anesthesia in G-II compared at time 0. Also significant decrease in

MAP was seen at 20, 30 and 40 min. of anesthesia in G-I compared to G-II which no significant changes were found regarding to the MAP.

Discussion

The combination of xylazine HCL and ketamine HCL has been used to control many domestic and wild carnivores [18-22]. A rapid-acting general anesthetic of ketamine is inducing an anesthetic state characterized by profound analgesia, no muscle relaxant with normal pharyngeal-laryngeal reflexes, stimulation of cardiorespiratory and sometimes a transient and minimal respiratory depression [17, 23]. The ketamine+xylazine combination may result in a smooth induction and recovery with the pressor and cataleptic action of ketamine HCL being prevented by the myorelaxant, depressor and sedative effects of xylazine HCL [20, 22, 8].

The induction was seen faster in dogs of group II and the duration of anesthesia and recovery period were longer in group I. In the present study, the induction time of the ketamine+xylazine combination was relatively 3.96 ± 2.35 faster than the studies by Neshgash et al., who revealed 9.67 ± 1.211 minutes and Sindak et al., who revealed 8.3 minutes after intramuscular administration by xylazine HCL 1mg/kg and ketamine HCL 10mg/kg body weight [16, 22]. The fastest duration of action was obtained in the group I which might be due to the high distribution of ketamine+xylazine throughout the body, as they are well lipid soluble and can be distributed into muscular tissue and adipose tissues according to Azizpour and Hassani [24]. What do you mean by species variation we only worked on dogs.

TABLE 2. Mean physiological values determined in dogs before and after injection with xylazine (1 mg/kg, i.m.) and ketamine (10 mg/kg, i.m.)

Parameters	Time (minutes)					
	0	Induction	10	20	30	40
HR	145.4±39.5	187±51.8	182.6±49.3*	177.2±52.5*	180.4±59.9*	178.6±63.5*
RR	39.2±9.5	19.8±7.6	13.8±2.4*	14.2±2.5*	15±3*	23±9.6*
Temp.	39.2±0.2	39.6±0.4	39.7±0.3	39.6±0.4	39.8±0.4	39.7±0.5
SPO ₂	99±1.2	97.2±3.6	96.2±3.6	98.6±1.1*	97.8±1.1	97.6±2.6
SBP	162±34.6	145.4±34.2	126.6±27.6*	104±32.2*	95.8±36.4*	116.8±19.4
DBP	106.4±32.7	97.2±32.2	88±31.5	65.6±22.9*	59±22.9	71.4±14.7
MAP	120.4±23.5	120.6±36.3	101±33.5	79.4±25.5*	73±29.4*	91.6±14.9*

* $P < 0.05$; compared to baseline; ± SD.

TABLE 3. Mean physiological values determined in dogs before and after injection with xylazine (1 mg/kg, i.v.) and ketamine (10 mg/kg, i.v.).

Parameters	Time (minutes)				
	0	Induction	10	20	30
HR	128±17.3	165±23.4*	173.6±37.6*	176.4±34.7*	164±30*
RR	63.8±26.5	17.6±3.6*	21.6±10.5*	16±3.2*	21.8±5.9*
Temp.	39.4±0.3	39.7±0.2	39.5±0.3	39.5±0.2	39.7±0.3
SPO2	98.8±1.6	94.4±2.8	94±2.6*	94.4±2.9*	95.8±2.6
SBP	144±16.2	156±28.8	159±28.8	128.4±30.7	127.8±30.9
DBP	106±29.8	109±33.6	118.8±26.7	81±28.1	79±22.9*
MAP	116.6±21	129.8±29.8	132.4±26.7	103.8±26.6	100.2±21.6

* P < 0.05; compared to baseline; ± SD.

The duration of action of the ketamine+xylazine combination through Sindak et al., was relatively 14.05 minutes longer who reported 55.25 minutes and Emami et al. was relatively 30.4 minutes longer who reported 71.6±3.07 minutes when compared to the present study which is 41.2±6.2 minutes [22, 25]. The duration of action in the current study was relatively shorter 41.2 minutes than the studies by Neshgash et al. showed 59.17 minutes [16]. The recovery period in the xylazine+ketamine combination in the present study finding was 30±7.97 minutes (group I) and 28.25±5.6 minutes (group II) relatively shorter than the studies by Sindak et al. (2010) showed 73.15 minutes [22]. The recovery time of anesthesia in this study was prolonged when different to the studies by Neshgash et al., showed 13.83 minutes [16]. This difference in finding in this study from other studies might be due to differences in physiological status and breed of the dogs.

The excitement, convulsions and emetic signs were noticeable in 50% of dogs treated with the ketamine+xylazine combination by some researchers [22, 26, 27]. There were not any emetic signs and excitement shown in this study.

In healthy dogs premedicated with xylazine has been associated with an increase in mortality rate when differentiate from other preanesthetic protocols [22, 23, 17]. In this study there was no mortality recorded.

Diamond et al., and Kerr et al., have been observed that use of Xylazine caused bradycardia and followed by bradyarrhythmia and ketamine

administration result in increase and correct heart rate [28, 29]. There was significant decrease in the mean heart rate after 15-60 minutes of ketamine administration [30- 32]. Prolonged heart rate decrease to 120 min with ketamine and xylazine combination used in dogs found by the studies of Kul et al., and a 27% decrease in the heart rate at 45 min showed by Moens and Fargetton [30,33]. In the studies of Sindak et al., and Gebremedhin et al., showed that 1mg\kg of xylazine and 10mg\kg of ketamine started bradycardia at 30 min intra, the mean heart rate initiated to decrease from the injection but mainly significantly decreased at 30-45 min following induction [8, 22]. A contrast result was observed in the present study, which showed increase heart rate significantly at 10 min in group I and at 5 min in group II following anesthetic induction. This result may be due to premedication with atropine sulphate 0.04mg\kg, which commonly used with alpha2 agonists in dogs to treat bradycardia and arrhythmia caused by xylazine [14].

In the studies of Kolata and Rawlings, (1982) showed that combination of Ketamine+xylazine premedicated with atropine in dogs caused a rise in arterial pressure, left atrial pressure and peripheral resistance [34]. Ketamine has been shown to have analgesic properties which are attributable to direct antagonism of the N-methyl-D-aspartate receptors; stimulates cardiovascular system, it differs from most anesthetic agents it producing change in pressure of blood and it rises the concentration of catecholamine resulting rise in pressure of blood and cardiac output [35, 36]. When atropine is premedicated with xylazine, it

produced strong hypertension [37]. A different result was observed in the current study, that the ketamine+xylazine combination premedicated with atropine caused decrease in blood pressure after 10 minutes of anesthesia in both groups.

The result of this study in both groups which showed a significant reduce in respiratory rates were in agreement with the studies by Emami et al., following injection of xylazine and ketamine combination reported reduction in respiratory rate at 5-55 minutes and Sindak et al., at 20-45 minutes after injection of ketamine+xylazine resulted decrease in respiratory rates; Gebremedhin *et al.*, reported decrease in respiratory rate non-significantly at 10-45 minutes of xylazine+ketamine anesthesia [25, 22, 8]. On the other hand, a significant decreased in respiratory rate at minutes of 15-60 after induction with ketamine+xylazine found by Kul et al. (2000); also, the result of the studies by Demirkan et al., and Atalan et al., throughout the ketamine+xylazine anesthesia showed significant remained lower respiratory rate than the baseline [32, 27, 38]. This decrease of respiratory rate might be attributed to the depression of the respiratory center by the combination of ketamine+xylazine administration either intravenously or intramuscularly [8].

When patients breathe spontaneously in the absence of supplemental oxygen on the pulse oximetry is the useful method detects respiratory abnormalities (hypoxia and hypercapnia) [39]. The decrease of RR with low SPO₂ values seen in both groups at 10-20 minutes of anesthesia confirm hypoventilation (hypoxia and hypercapnia) caused by this protocol.

The increases non-significantly in body temperature after the xylazine+ketamine administration shown in the current study were contrary to the findings of Sindak *et al.*, and Gebremedhin *et al.*, reported depression in body temperature at 20-45 minutes of anesthesia with ketamine and xylazine [8, 22]. Other studies by Wyatt *et al.*, found no change in the temperature of the body following injection of 1mg/kg xylazine and 10mg/kg ketamine intramuscularly [12].

Conclusions

Ketamine alone is not used because it has poor muscle relaxation, tachycardia, innate analgesia and muscle stiffness. For that reason, ketamine is mainly used with alpha-2 agonist, benzodiazepine and phenothiazine to produce visceral analgesia

in the case of thoracoabdominal surgery, to provide muscle relaxation, to prevent convulsion and to prolong the action of anesthesia. This combination of ketamine+xylazine can be a very satisfactory anesthetic protocol for excellent induction, adequate muscle relaxant and smooth recovery and for surgical procedures it can be safe if used safely and appropriately in dogs. Nevertheless, further investigation on some other anesthetic combinations i.e. (glycopyrolate+xylazine+ketamine and medetomidin+ketamine) on local breeds of dogs and some other anesthetic combination can be used.

Conflict of interest statement

The authors have no conflicts of interest to declare.

We certify that we have NO affiliations with or involvement in any organization or entity with any financial interest.

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دراسة مقارنة بين الحقن الوريدي والعضلي المشترك للزلازين مع الكيتامين على بعض المتغيرات الفسيولوجية للكلاب

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تم إجراء تجربة التخدير السريري على ١٢ كلبًا محليًا من مختلف الأعمار والجنس ووزن الجسم. الهدف من الدراسة هو التحقيق في التأثير التوافقي لتوليفة الكيتامين والزيلازين المحقونة إما بالعضل أو الوريد على معايير التخدير (أوقات التحريض، مدة التخدير ووقت التعافي) والمعايير الفسيولوجية على الكلاب. تم تقسيمهم إلى مجموعتين (G-I و G-II) بشكل عشوائي. تم إعطاء كل الكلاب بكميات الأتروبين (٠,٠٤ مجم / كجم من وزن الجسم، عضليًا) قبل ٥ دقائق من بروتوكول التخدير، تم إعطاء الكيتامين + زيلازين (١٠ مجم / كجم + ١ مجم / كجم) على التوالي، عضليًا في G-I و وريديًا في G-II. تم تسجيل النتائج السريرية بما في ذلك التحريصات والمدة وفترة التعافي من التخدير، HR، RR، RT، SPO₂، SBP، DBP و MAP قبل وأثناء التخدير. أظهرت الدراسة أنه لا توجد فروق ذات دلالة إحصائية بين G-I و G-II في المتغيرات الفسيولوجية للكيتامين والزيلازين في الكلاب باستثناء التحريض والمدة واستعادة التخدير كان أطول في G-I منه في G-II. في الختام، أظهرت النتائج أن مزيج الكيتامين + الزيلازين يمكن أن يكون بروتوكول تخدير مرضي خاص لتحريض ممتاز، وإرخاء عضلي جيد، وتعافي سلس في الكلاب

الكلمات الدالة: الكيتامين، الزيلازين، الحقن الوريدي، الحقن العضلي، الكلاب.