



A Comparative Study Between of Effect of Tramadol and Xylazine as Premedication Those Followed by Ketamine Anesthesia in Dogs

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Abstract

The analgesic effects of Tramadol and Xylazine as a preanesthetic in followed by Ketamine in adult dogs. A twelve male was randomly divided in to three groups . first group serves as control group given normal saline, a second 4mg /kg B.W. i.m. of Tramadol and third group 1 mg/kg B.W. i.m. Xylazine premedication, was then administered intramuscular followed by Ketamine anesthesia at dose 5 mg/kg B.w.. The behavioral changes, the duration of surgical anesthesia, and biochemical parameters. Xylazine pretreatment significantly ($P<0.05$) increased the degree of sedation when compared with the control. The duration of surgical anesthesia was significantly ($P<0.05$) increased by Tramadol pretreatment when compared with control group. There were no significant ($P<0.05$) differences in biochemical tests total Protein, Creatinine, Alanine Transaminase ALT and Aspartate Transaminase AST among the groups. This result suggests that intrmuscular Tramadol at 4mg /kg is a useful preanesthetic agent for extending the surgical level of anesthesia in ketamine anesthesia in dogs.

Key word: Tramadol, Xylazine, Kitamine, Dog

دراسة مقارنة بين تأثير الترامادول و الزيلازين كمساعدات تخدير متبوعة باعطاء مخدر

الكيتامين في الكلاب

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الخلاصة:

التأثير المسكن للترامادول و الزيلازين عند استخدامه كأدوية مساعدة للتخدير العام بإستعمال الكيتامين في الكلاب البالغة .حيث قسم اثنا عشر من الذكور إلى ثلاثة مجامي. عشوائيا. وكانت المجموعة الأولى هي مجموعة السيطرة حيث حقنت بمحلول الملح الفسيولوجي، و المجموعة الثانية حقنت بالعضلة بالتزامدول بجرعة 4 ملغم/ كجم من وزن الجسم المجموعة الثالثة حقنت بالعضلة بالزيلازين بجرعة 1 ملغم/ كجم من وزن الجسم ، ومن ثم تلاها مخدر الكيتامين بجرعة 5 ملغ / كغ من وزن الجسم . و تم قياس التغيرات السلوكية، ومدة التخدير الجراحي، والقياسات البيوكيميائية، حيث وجد زيادة معنوية ($P<0.05$) في فترة النوم عند استخدام الزيلازين من مجموعة السيطرة و وجد ارتفاع معنوي ($P<0.05$) في مدة التخدير الجراحي بإستعمال الترامادول عن مجموعتي السيطرة و الزيلازين . و لم توجد اي اختلافات معنوية ($P<0.05$) بين المجاميع في الفحوصات الكيموحيوية البروتين الكلي و الكرياتين و انزيم الالانين ترانسامينيز و انزيم الاسبارتات ترانسامينيز . هذه النتائج اوضحت امكانية استعمال الترامادول كدواء مساعد في عملية التخدير مع مخدر الكيتامين في الكلاب بسبب الزيادة في مدة التخدير الجراحي.

الكلمات المفتاحية : الترامادول , الزيلازين , الكيتامين , الكلب

Introduction

Tramadol is a centrally acting analgesic agent with activity at μ -opioid, adrenergic and 5-hydroxytryptamine (5-HT) receptors. Its analgesic effect is a result of its dual mechanism of action, that is, as a re-uptake inhibitor of norepinephrine and serotonin and agonist of the μ -opioid receptor [1,2]. Tramadol has been in clinical use for the relief of mild to moderate pain in human and veterinary medicine [3,4]. Tramadol is also used perioperatively in veterinary anesthesia as it significantly reduces the requirements of volatile anesthetics and opioid agents [5,6]. Although tramadol has relatively effective analgesic effects, a higher tramadol infusion rate was needed to reduce sevoflurane requirements in dogs [6]. Furthermore, recent results showed that tramadol exhibits different metabolic rates between species: tramadol is metabolized quickly to inactive metabolites in goats, horses and dogs [7,8,9,10]. A combination of Xylazine and ketamine is commonly used for animal anesthesia [11,12]. Ketamine is used as intramuscular general anesthetic. It appears to provide good somatic analgesia but poor visceral analgesia. Ketamine increases muscle tone and may cause rigidity, if administered alone, so it is usually combined with drugs Xylazine with good muscle relaxant properties as α_2 adrenoceptor agonists Xylazine HCl Injection (xylazine), a non-narcotic compound, is a sedative and analgesic as well as muscle relaxant. Its sedative and analgesic activity is related to central nervous system depression. Its muscle-relaxant effect is based on inhibition of the intraneural transmission of impulses in the central nervous system. The principal pharmacological activities develop within 10 to 15 minutes after intramuscular or subcutaneous injection, and within 3 to 5 minutes following intravenous administration. [13].

Materials and Methods

Animals

A total of twelve adult male dogs. All animals were considered clinically healthy based on physical examination, each dog was housed individually. The dogs were randomly divided into 3 groups the first group serve as control group administered normal saline, the second group administered 2 mg/ kg of Tramadol (Swiss pharma, Swiss), the third group administered 1 mg/kg Xylazine(RXV, India), all groups followed by Ketamine (Daksh pharma, India) anesthesia 5 mg/kg intramuscular. This study was approved by the faculty of Veterinary Medicine University of Kufa.

Behavioral parameters

Degree of sedation: The degree of sedation was assessed by a numerical sedation score (NSS) [14]. The NSS consists of a scale ranging from 0 to 3, with 0: no sedation; 1: mild sedation (less sedation but still active); 2: moderate sedation (drowsy, recumbent but can walk); and 3: intense sedation (very drowsy, unable to walk).

Duration of anesthesia

After ketamine injection to the time the dog showed loss of righting reflex (RR), head-up, positioning to a sternal recumbency position and walking movements were measured, and the mean values were presented. The time difference between head-up movement and walking was defined as the recovery time.

Duration of surgical anesthesia

The duration of surgical anesthesia was determined by pedal withdrawal reflex. After ketamine administration, the period in which the dog showed negative response to toe-web pinching test was defined as surgical anesthesia. .

Biochemical Analysis

Blood sample collect by plain tubes (Echo, Jordan) than separated serum in ependrof tube (Echo, Jordan) by centrifuge (Hinti, Germany) at 3000 p.r.m. for 15 min then measuring the blood parameters Total Protein, Creatinine, Alanine transaminase ALT and Aspartate transaminase AST by use chemical kits (CYAN, Belgium) with sime-automatic chemistry analyzer (CYAN, Belgium).

Statistical analysis

All data parameters were calculated as average to the baseline values, and were expressed as mean $\pm$ standard error. values were statistically analyzed by One-way ANOVA followed by correction were included to identify the statistical differences of behavioral changes (time to

loss of righting reflex, mean head-up time, mean sternal- recumbency time, mean walking time and total recovery time), numerical sedation score and the duration of surgical anesthesia. Values of $P < 0.05$ were considered significant.

Results

Behavioral parameters

Degree of sedation

Table (1) shows the effect of administration tramadol and xylazine on adult dogs. A resulted in a significant increase of and Degree of sedation when compared to control group respectively at 7.5 and 15 min after tramadol administration. Then xylazine significantly increased in Degree of sedation at 15 and 30 min after xylaxine administration (table. 1).

Table.1 The effect of tramadol and xylazine on degree of sedation

	Degree of sedation		
	7.5 min	15 min	30 min
Control	0	0	0
Tramadol & Kitamine	1	1	2
Xylazine & Ktamine	1	2*	3*

*Significant different from control group. $p, < 0.05$

Duration of anesthesia

Table (2) shows the effect of administration tramadol and xylazine on adult dogs Revealed that no variables of behavioral changes during anesthesia were significantly affected by pretreatment with different doses of tramadol more than xylazine (table. 2).

Table. 2 The effect of tramadol and xylazine on duration of anesthesia

	Duration of anesthesia min
Control	30 ± 0.01
Tramadol & Kitamine	$120 \pm 0.05^*$
Xylazine & Ktamine	96 ± 0.023

*Significant different from control group. $p, < 0.05$

The duration of surgical anesthesia

Table (3) shows the effect of administration tramadol and xylazine on adult dogs. The revealed treatments were tramadol administration pretreatment significantly increased the duration of surgical anesthesia when compared to the Xylazine group (table. 3).

Table. 3 The effect of tramadol and xylazine on duration of surgical anesthesia

	Duration of surgical anesthesia min
Control	15 ± 0.02
Tramadol & Kitamine	75 ± 0.047*
Xylazine & Ktamine	58 ± 0.018

*Significant different from control group. $p, < 0.05$

Biochemical Analysis

Table (4) shows the effect of administration tramadol and xylazine on adult dogs. There have not any significant difference between groups in following biochemical parameters (table. 4)

Table. 4 The effect of tramadol and xylazine on biochemical Analysis

	Total Protein	Creatinine	AST	ALT
Control	7.5 ± 0.001	1.7 ± 0.02	109 ± 0.09	150 ± 0.07
Tramadol & Kitamine	5.22 ± 0.007	0.62 ± 0.04	102.1 ± 0.05	136.3 ± 0.08
Xylazine & Ktamine	6.38 ± 0.005	0.66 ± 0.02	114.4 ± 0.07	145 ± 0.01

Discussion

The results of present study show that premedication with 4mg/ kg of tramadol significantly increased the duration of surgical anesthesia of Xylazine and ketamine without affecting the parameters or delaying the recovery, undergoing soft tissue and orthopedic surgery provided effective post-operative analgesia [15], and 4mg/kg of tramadol had an analgesic potency comparable to that of 0.2mg/ kg of morphine [16]. In addition, constant rate infusion of tramadol also had minimum alveolar concentration MAC reducing effects in dogs [6]. In contrast, some results have indicated that pretreatment with a single bolus of tramadol for anesthesia was insufficient to obtain a significant level of enhanced surgical general anesthesia [17]

Recent pharmacokinetics results of tramadol in beagles suggested that lower plasma concentration levels were detected in dogs, and the metabolite is an important analgesic contributor of tramadol [18,19]. Prior to our experiment, effective enhancement only at the higher dose of tramadol could be related to the low level of metabolites in dogs as mentioned earlier. Furthermore, a rapid elimination rate of tramadol in dogs cannot be ruled out, The

higher dose of tramadol resulted in higher and more sustained tramadol plasma concentration [20], and tramadol itself seemed to have an analgesic effect in dogs [18]. in the early period of anesthesia, the effect of tramadol could be masked by Xylazine, but as the anesthetic time passed, the efficacy of tramadol as well as Xylazine could be attenuated. In this situation, the higher tramadol plasma concentration would contribute to the enhancement of anesthetic depth.

Tramadol administration. Previous results about the sedative effect of tramadol were controversial are less than Xylazine [16,18], but another study reported no marked sedation, The affected the anesthetic induction or behavioral changes during recovery, and the sedative effect of tramadol did not persist for long.

Tramadol premedication did not cause a clinically important sedation in dogs during the recovery period [6].

In the present study, variables of behavioral changes were not significantly affected by different doses of tramadol, although a dose-dependent delay was observed. That is, tramadol premedication did not affect the recovery time, and the higher dose of tramadol in the present study

prolonged the surgical anesthesia without hangover.

Conclusion

Tramadol premedication at a dose of 4mg/kg can significantly ($P < 0.05$) increase the duration of surgical anesthesia more than classical Xylazine and ketamine in dogs, without imparting significant changes to the biochemical parameters or recovery from anesthesia.

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