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INTERACTION OF XYLAZINE WITH GALLAMINE OR TOLAZOLINE ON THE NEUROMUSCULAR JUNCTION OF ANAESTHETISED DOGS

Ibrahim M. El-Ashmawy, Ahmed I. Bayomi* and Abd El-Hasseib Fayed**

Departments of Pharmacology, Surgery and Physiology**, Faculty of Veterinary Medicine, Alexandria University, Egypt*

ABSTRACT

Xylazine was tested on the neuromuscular transmission in anaesthetised dogs. In addition, its interactions with gallamine and tolazoline on the upper lip muscles of anaesthetised dogs have been studied. Xylazine inhibited neuromuscular transmission. Furthermore, xylazine potentiated the neuromuscular blocking action of gallamine. Pretreatment with tolazoline, prevented the depressant effect of xylazine on the neuromuscular transmission. At the same time, xylazine significantly prolonged the duration of anaesthesia caused by thiopental sodium in dogs. It could be concluded that xylazine inhibited neuromuscular transmission centrally via its action of the ∝-2 adrenoceptors and its effect was potentiated with gallamine and prevented with tolazoline.

INTRODUCTION

Xylazine is a well known sedative in veterinary practice. When xylazine is injected alone or concurrently with other anaesthetics, it produces sedation, analgesia and muscle relaxation via its action on the central nervous system[1-4].

Meanwhile, xylazine induces central muscle relaxation leading to general muscle relaxation which supplements the state of sleep and freedom of pain. This effect is based on inhibition of the interneural transmission impluses[5].

Obviously, minor surgery and ceasareans are accomplished after administration of xylazine and local anaesthetics[6]. However, yohimbine and atipamezole effectively reverses the sedative effects of xylazine[7,8].

There is no available data about the effect of xylazine on the neuromuscular transmission in dogs and its interaction with drugs commonly used during anaesthesia as muscle relaxants.

The present work was undertaken to study the duration of action of xylazine in dogs. The effect of pretreatment with the competitive neuromuscular blocker (gallamine) or the antihypertensive drug (tolazoline) on the neuromuscular blockade induced by xylazine was also investigated.

EXPERIMENTAL

Materials :

Xylazine (Bayer, Leverkusen, Germany), gallamine triethiodide (Flaxedil, Alex. Chemical Co., Egypt) tolazoline (Sigma, Chemical Co. U.S.A), thiopental sodium (Bio chemie), neostigmine bromide (Sigma) and heparine (Nile Co., Egypt) were used in this study and dissolved in saline solution.

The upper lip muscles preparation:

The preparation was performed according to the method described before[9], fifteen dogs of both sex weighing from 10-15 kg. (b.wt.) were anaesthetised using thiopental sodium

(10 mg/kg b.wt.) i.v. in the saphenous vein of the leg). The dogs were divided into three groups of 5. The 1st group was injected with xylazine 1 mg/kg (b.wt., i.v.), the 2nd group was injected with 2 mg/kg b.wt. and the 3rd group injected with 3 mg/kg (b.wt).

The trachea was cannulated and ventillation was controlled when required using AMBU apparatus consisting of a self inflating valve and rebreathing valve. The dog was placed in a lateral recumbency position. The area of the cheek was surgically prepared. A transverse incision was made in the skin of the facial crest (about 1-2 cm) under the lateral canthus of the eye to expose the dorsal buccal branch of the facial nerve. The nerve was freed from its surrounding connective tissue. A strong thread was passed through the upper lip of the operated side by means of a surgical needle and tied upon it. The thread was passed across two pullies to be connected to the lever. The nerve was electrically stimulated every 10 seconds interval by supramaximal single shocks of 1 msec. duration with a B. Braun stimulator. Tracings were recorded on smoked paper on a B. Braun kymograph using side writing spring lever.

After tracing the normal contractions of the upper lip facial nerve preparation, xylazine or gallamine alone was injected into the cannulated saphenous vein and the premedication with gallamine or tolazoline prior to xylazine were recorded. The recovery index (the time required for recovery between 25% and 75% of the control value) was studied as described earlier[10].

Statistical analysis of the obtained data were performed by standard method[11].

RESULTS

Xylazine 1mg, 2 mg and 3 mg mg/kg. (b.wt.) reduced the indirectly elicited muscle twitches by 12.00 ± 0.60, 19.00 ± 1.30 and 33.62±1.75 percent, respectively compared with the controls (Fig. 1).

The interaction of xylazine (3 mg/kg b.wt.) with gallamine (0.7 mg/kg b.wt) and tolazoline (1 mg/kg b.wt.) was tested. It was found that the injection of xylazine and gallamine resulted in potentiation and prolongation of the inhibitory effect of gallamine on the neuromuscular transmission (Fig. 2 & 3). The maximum inhibition of neuromuscular transmission with xylazine (3 mg/kg), gallamine (0.7 mg/kg) and xylazine plus gallamine was 33.62±1.75, 37.90±3.52 and 68.69±4.28 percent respectively.

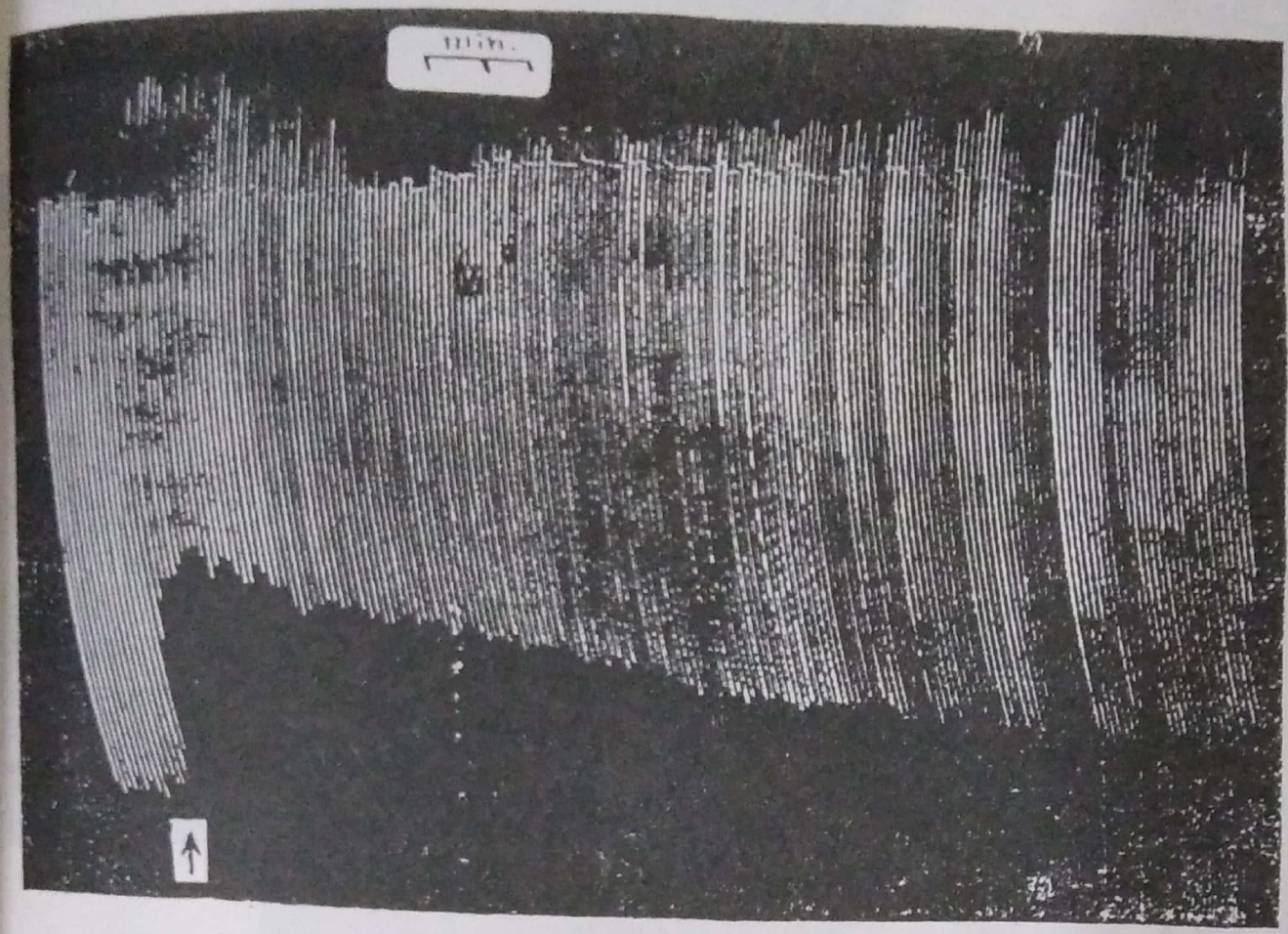
The recovery index was 10.0±0.07, 6.16 ± 0.07 and 21.12 ± 0.57 minutes, respectively.

On the other hand, the pretreatment with tolazoline significantly blocks the depressant effect of xylazine previously recorded on the neuromuscular transmission (Fig.4). At the same time, xylazine prolonged the duration of anaesthesia produced by thiopental sodium from 17.25 ± 11 to 66.25 ± 5.54 min.

DISCUSSION

The present work was performed to demonstrate the effect of xylazine on the neuromuscular transmission in dogs, and its interaction with the competitive neuromuscular gallamine. At the same time, the influence of xylazine on the duration of anaesthesia produced by thiopental sodium in dogs was also investigated.

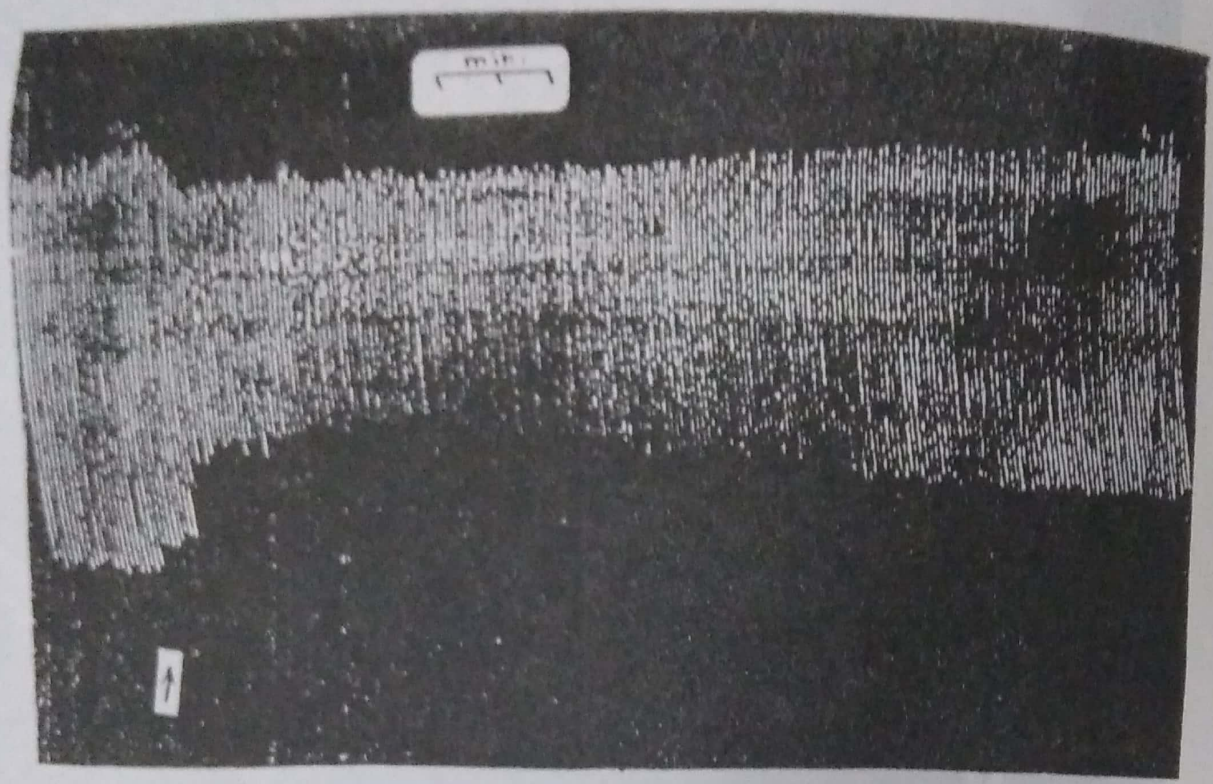
Xylazine given i.v. induced a dose-dependent transient partial neuromuscular blockade. It was observed that dogs were more resistant to xylazine than other animals as the dose of 0.05 to 0.1 mg/kg (i.v) was very effective in cattle, while the effective dose in horse was 0.5 to 1.0 mg/kg (b.wt., i.v) and produced its effect in 1 to 2 minutes (6). However,in this study, the administration of 1 mg/kg (b.wt., i.v) produced a very slight neuromuscular blockade in dogs.



Xylazine
(3 mg/kg)

Fig. (1): The effect of xylazine (3 mg/kg. i.v) on the indirectly elicited muscle twitches of the upper lip muscles of anaesthetised dogs. The nerve was stimulated by a square pulse wave of 6 volts and of 1 msec. duration repeated every 10 seconds interval. Time interval: 1 minute.

Note : Partial neuromuscular blockade induced by the drug.



gallamine
(0.7 mg/kg)

Fig. (2): The effect of gallamine (0.7 mg/kg. i.v) on the indirectly elicited muscle twitches of the upper lip muscles of dogs. The nerve was stimulated by a square pulse wave of 6 volts and of 1 msec.duration repeated every 10 seconds interval.

Time interval: 1 minute.

Note : Partial neuromuscular blockade induced by gallamine.

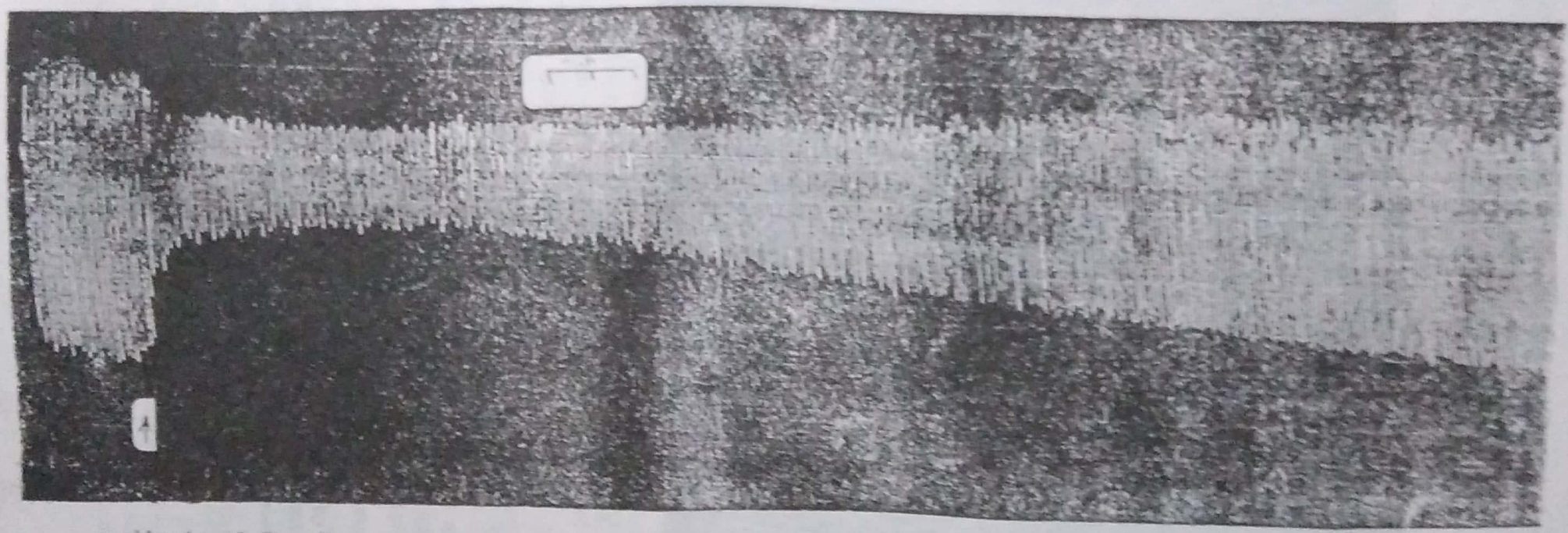
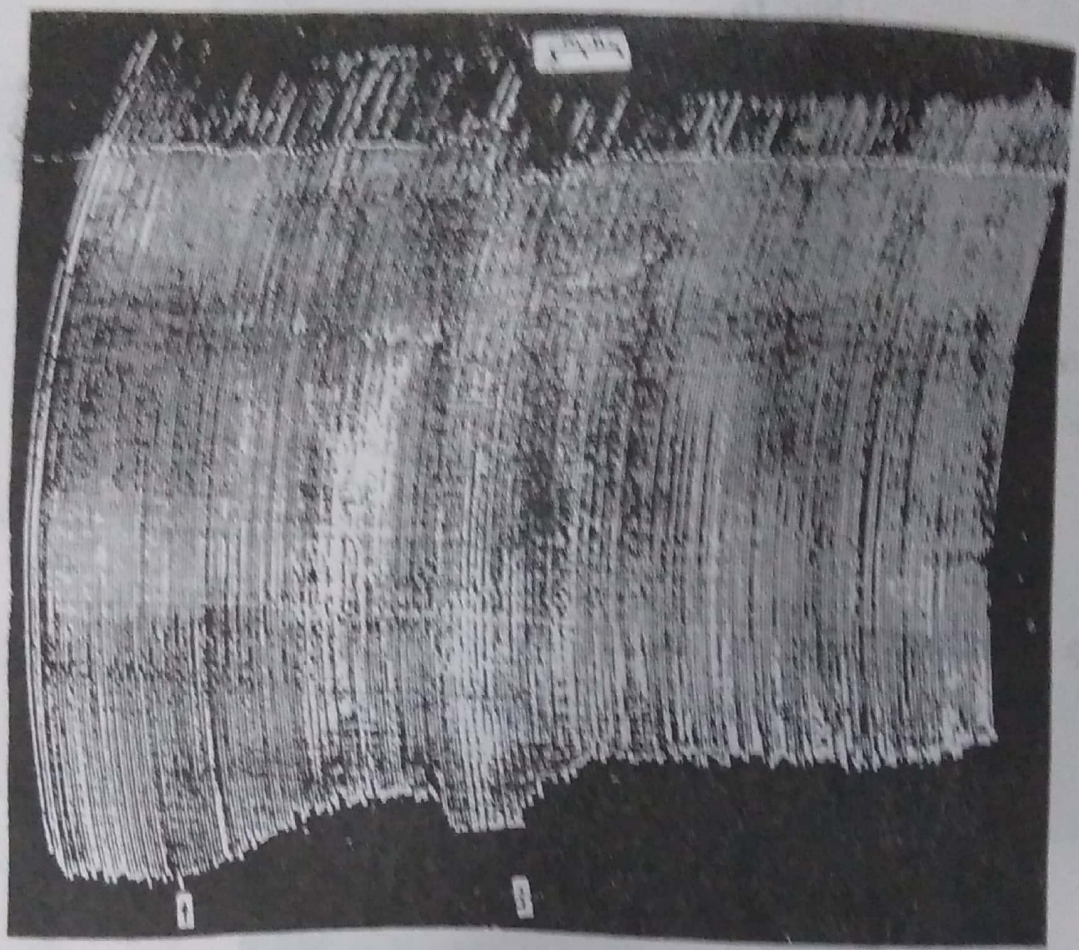


Fig. (3): The effect of prior administration of xylazine (3 mg/kg. b.wt., i.v.) on the response of the upper lip muscles to gallamine (0.7 mg/kg. b.wt., i.v.) in anaesthetised dogs.

Time interval : 1 minute.



tolazoline (1mg/kg.i.v.)

xylazine (3 mg/kg.i.v.)

Fig. (4): The effect of prior administration of tolazoline (1 mg/kg., b.wt., i.v.) on the response of the upper lip muscles to xylazine (3 mg/kg., b.wt., i.v.) in anaesthetised dogs.

Time interval : 1 minute.

Xylazine may have a local anaesthetic activity and this property may enhance the previously recorded neuromuscular blockade induced by xylazine (is a point of research).This inhibitory effect of xylazine on the neuromuscular transmission might be attributed to its ∝ 2-adrenoceptor agonist activity. It was suggested that the neuromuscular effect of xylazine on isolated rat diaphragm and chick biventor muscles was neither depolarizing nor competitive in nature[12]. Moreover, previous work reported that the centrally active ∝ 2-adrenoceptor agonists cause sedation and decrease in locomotor activity[13,14]. Furthermore, it has been reported that yohimbine (∝2-adrenoceptor antagonist) blocks sedation and depression of motor activity induced by xylazine, clonidine and 2-aminotetralines in rats, mice and dogs[15-17]. It has been found that the injection of tolazoline i.v. enabled camels immobilized with xylazine to stand within 12 mins. compared with one hour or more without tolazoline[5]. Moreover, it has been reported that yohimbine reduced the time to stand of the sheep to xylazine from 95 to 2.8 mins[18].The potentiation of the neuro- muscular blockade by local anaesthetics has been confirmed by many workers[19,20]. Local anaesthetics inhibit the acetylcholine release by a prejunctional effect and cause a membrane stabilization as well as a decrease response to indirect and direct stimulation[21]. The local anaesthetics enhance desensitization of acetylcholine receptor and antagonise the action of calmodulin[22,23].

In the present study, the prior administration of tolazoline (∝1 and ∝2-adrenoceptors antagonist) significantly reduced the inhibitory effect of xylazine on the neuromuscular transmission. These results show that xylazine significantly augmented and potentiated the neuromuscular blockade induced by the competitive muscle relaxant gallamine.

The present findings show that xylazine significantly prolonged the duration of anaesthesia of thiopental sodium in dogs. This coordinated with other authors previously[24-26] reported that xylazine prolonged the anaesthetic effect of chloral hydrate as well as the combination of xylazine-ketamine induced surgical anaesthesia in rats for up to 2 hours without regidity.

The prolongation of neuromuscular blockade induced by a combination of xylazine and gallamine might be of clinical importance.

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تداخل الزيلازين مع الجلامين والتولازولين على الاتصال العصبى العضلى فى الكلاب المخدرة

ابراهيم محمد العشماوى - احمد بيومى* - عبد الحسيب فايد**

أقسام الفارماكولوجى والجراحة والفسيولوجى***

بكلية الطب البيطرى - جامعة الاسكندرية - مصر

فى هذا البحث احدث الزيلازين تثبيطا جزئيا فى الانتفاضات العضلية الناشئة نتيجة للتنبيه العصبى لعضلات الشفة العليا فى الكلاب المخدرة بالثيوبنتال. كما انه زاد من التأثير المثبط للجلامين على الاتصال العصبى لعضلات الشفة العليا فى الكلاب. وعلى العكس ادى اعطاء التولازولين الى تقليل التأثير المثبط للزيلازين على الاتصال العصبى العضلى فى الكلاب. وفى نفس الوقت اطال الزيلازين من فترة تخدير الكلاب بالثيوبنتال صوديوم. يستخلص من ذلك ان للزيلازين تأثيرا مثبطا على الاتصال العصبى العضلى مركزيا من خلال تأثيره على مستقبلات الفا وأن هذا التأثير زاد بالتدخل مع الجلامين وقل مع اضافة التولازولين.