



Pretreatment of Cats with Vitamin B6 Reduces Vomiting Episodes Following Xylazine Administration

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Abstract

Objective- Vomiting is a common problem of administration of xylazine in cats. This study was conducted to evaluate prophylactic antiemetic efficacy of vitamin B6 in sedated cats with xylazine.

Design- Experimental study

Animals- Eight adult cats (from both genders) were selected.

Procedures- All the cats were administered with intramuscular injection of normal saline or four increasing dosages of vitamin B6 (5, 10, 20 and 40mg/kg) an hour prior to administration of xylazine with one week intervals. All the cats were monitored after injection of xylazine for thirty min to record the onset of first emesis, frequency of emetic episodes and the onset of recumbency.

Results- Frequency of emetic episodes significantly decreased with each mentioned dosage of vitamin B6.

Conclusions and Clinical Relevance- This study showed that pretreatment of cats with vitamin B6 may reduce episodes of xylazine induced emesis without compromising its sedative effect.

Key Words- cat, sedation, vitamin B₆, vomiting, xylazine.

Introduction

Xylazine is a commonly administered medication in small animals. It is an alpha₂-agonist with sedative, analgesic and muscle relaxant properties that makes it a good choice for performing many procedures, such as radiography, ultrasonography, catheterization, and biopsy.¹ However, vomiting frequently is reported after xylazine administration in cats²⁻⁷ and dogs^{8,9}, which may distress an animal and also increase the risk of getting aspiration pneumonia.¹⁰ Antagonists of alpha₂-adrenoceptors such as yohimbine, tolazoline, and phentolamine are effective against xylazine induced emesis, but they also antagonize the sedative effects of xylazine.^{5,6,9,11,12}

Vitamin B6 is a water-soluble B complex vitamin that is an essential coenzyme in the metabolism of amino acids, carbohydrates, and lipids.¹³ It has been shown that vitamin B6 is an effective therapy for nausea and vomiting of pregnancy in humans.¹⁴⁻¹⁶ Vitamin B6 is also commonly used as first-line therapy for patients who experienced nausea and vomiting

during or after chemotherapy,¹⁷ and its safety has been proved when used in appropriate dose.^{18,19} Vitamin B6 in high doses may complications such as ataxia and severe peripheral sensory nervous system dysfunction. In a study of toxicity of vitamin B6 in mice, no clinical or pathological changes have been observed following intravenous injection of 100 mg/kg/day of vitamin B₆ for 14 days.²⁰

In this study, premeditative antiemetic efficacy of vitamin B6 was assessed in xylazine induced emesis in cats. The effect of vitamin B6 was also verified on sedative efficacy of xylazine in these animals.

Materials and methods

Animals

Eight healthy adult domestic short hair cats of either sex (4 males and 4 females), weighting between 2.6 and 4 kg (median, 3.5 kg), were used for the study. All cats were immunized subcutaneously with 1 m/ rabies vaccine (Rabisin-R, Merial, France) and 1 m/ of a killed trivalent feline rhinotracheitis- calici and Panleukopenia vaccine (Fel-O-Vax® PCT, Fort Dodge Animal Health, Fort Dodge, IA, U.S.A.). They were acclimatized in individual cages placing in an air-ventilated room with temperature controlled at 21 ± 2°C for one week prior to study. All the cats were fed a commercially available food and water *ad libitum* and fasted during the night

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before each experiment. The protocol of this study was approved by institutional animal research committee.

Procedure

The antiemetic effect of four dosages (5, 10, 20 and 40 mg/kg) of vitamin B6 (Pyridoxine HCl, 300 mg/ 3 ml, Darou Pakhsh Co., Tehran, Iran) and saline (0.9% NaCl) solution intramuscularly (IM) an hour before IM injection of xylazine (Xylazine HCl, 2%, Alfasan, Netherlands) was evaluated. All cats were subjected to the same procedures, and each treatment was conducted at one-week intervals. Cats were initially administered with intramuscular injection of normal saline (0.056 ml/kg of body weight) on day 0 (control treatment). Vitamin B6 (pH adjusted) was injected in four increasing doses (5, 10, 20 and 40 mg/kg) on days 7, 14, 21 and 28, respectively. After injection of saline solution or each dosage of vitamin B6, cats were fed with 150g of commercial food. An hour later, the dose of 0.66 mg/kg of xylazine which was diluted in sterile normal saline to reach an injection volume of 0.2 ml was injected intramuscularly to the animals. Selection of xylazine dose is based on the effectiveness of xylazine to induce emesis in 95% of cats.^{2,3} All the cats were observed for thirty min after injection of xylazine to record onset of the first emetic episode, frequency of emetic episodes and the onset of recumbency.

Emetic and sedative responses

Emesis was scored as an all-or-none response, and separate episodes of emesis were considered when the interval between bouts of vomiting exceeded 5 sec.²¹ The time from injection of xylazine to the onset of the first emetic episode (latency time of emesis) was recorded. During an observation period (thirty min), the number of episodes of emesis was also

counted. Premonitory signs of emesis such as salivation and licking were not considered an emetic response. Sedative response was recorded when a cat assumed sternal or lateral recumbency and was unable to stand.²² The time until onset of sedation after administration of xylazine was also recorded.

Statistical analysis

All data were reported as median (range). Differences among the episodes between the five trials analyzed using Friedman's nonparametric tests. *P* values less than 0.05 were considered significant. If Friedman's analysis demonstrated a significant difference, Wilcoxon's signed-rank test was performed for pairwise comparisons.

Results

Cats pretreated with saline solution (control treatment) showed 5.5 episodes of emesis (median) after xylazine injection. Number of episodes of emesis was 3.5, 3, 2.5, and 2 for vitamin B6 at dosages of 5, 10, 20, and 40 mg/kg, respectively. Pretreatment of cats with each dosage of vitamin B6 (5, 10, 20, and 40 mg/kg) significantly reduced the number of episodes of emesis induced by xylazine (Table 1).

The time until onset of the first emetic episode (latency time of emesis) and time until onset of sedation after administration of saline solution or 5, 10, 20, or 40 mg of vitamin B6/kg an hour prior to administration of xylazine are shown in Table 1. Pretreatment of cats with mentioned dosages did not significantly alter the time until first emetic episode after administration of xylazine. Prior treatment with vitamin B6 at any of these dosages did not also significantly alter time until onset of sedation after administration of xylazine.

Table 1- Values for administration of saline solution (0.056 ml/kg, IM) and different dosages of vitamin B6 one hour before injection of xylazine (0.66 mg/kg, IM) on the number of episodes of emesis, latency time of emesis and time until onset of sedation in eight cats. Results are presented as median.

Medications	Dosages	Episodes of emesis	Latency time of emesis (min)	Time until onset of sedation (min)
Normal Saline	0.056 ml/kg	5.5	6.5	15.5
Vitamin B6	5 mg/kg	3.5	4.5	10
Vitamin B6	10 mg/kg	3	5	12
Vitamin B6	20 mg/kg	2.5	4	10.5
Vitamin B6	40 mg/kg	2	4.5	8

Discussion

In the present study, the Friedman test showed that IM injection of vitamin B6 at dosages of 5, 10, 20 and 40 mg/kg an hour prior to IM injection of xylazine significantly reduces the number of emetic episodes in cats. Vitamin B6 in any of mentioned dosages couldn't affect latency time of emesis irrespective of B6-dosage. This observation may show that triggering time of vomiting (latency time) after xylazine injection in this animal was not affected with vitamin B6. The

exact mechanism of this conflict between efficacy of vitamin B6 on the latency time and episodes of vomiting is not completely clear.

Since vitamin B6 has antiemetic properties, it is used to treat nausea and vomiting of early pregnancy in humans.^{15,16,19} Despite considerable research effort, cause of nausea and vomiting of pregnancy and the mechanism(s) by which vitamin B6 can be effective in reducing nausea and vomiting is still unknown. In this content, it has been found that vitamin B6 treated patients undergoing radiation therapy show lower

vomiting than control group (21.1% vs. 28.8%).²³ Although vitamin B6 is a water-soluble vitamin, its overdose or long term use may have some side effects. We didn't see any side effect or adverse effect in any animal; therefore, its use as antiemetic may be safe.

Xylazine, an alpha 2-adrenoceptor agonist, induces emesis in cats. It is well established that the alpha 2-adrenoceptors are present in the Area Postrema (AP),²⁴ and the AP is essential for xylazine induced emesis.³ Colby *et al.* reported that ablation of AP of the medulla oblongata results in elimination of xylazine induced emesis in cats, but doesn't affect the general sedative effect of the standard dose (0.66 mg/kg) of the medicine. They concluded that xylazine acts on the chemoreceptor trigger zone (CTZ) of the area postrema to induce emesis.³

Several medicines have been studied to control xylazine induced emesis in cats; for instance, dexamethasone^{1,25}, maropitant²⁶, metoclopramide²⁷, promethazine²⁸ and ondansetron²⁹. It has been shown that all these medicines may effectively inhibit xylazine induced emesis in cats from different mechanisms. Maropitant, a neurokinin-1 (NK-1) receptor antagonist, prevents xylazine-induced emesis in central nervous system.²⁶ In this respect, it has been shown that the antiemetic effect of dexamethasone on xylazine induced emesis is mediated through activation of the glucocorticoid receptors in the bilateral nucleus tractus solitarii (NTS).³⁰ It could be postulated that all the mentioned antiemetics like metoclopramide, dexamethasone and maropitant, don't pass antiemetic efficacy against xylazine induced emesis by inhibiting alpha 2-adrenoceptors. They may inhibit dopamine, serotonin (5-HT₃), corticosteroids and NK-1 receptors in the bilateral NTS of medulla oblongata to elicit this antiemetic effect.²⁷ The consequence of efficacy of mentioned antiemetics on xylazine induced emesis may mean that control of vomiting can be achieved through the precise targeting of the key neurotransmitter receptors, located in the NTS.³¹

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On the other hand, it has been shown that baclofen, a selective GABA_B (gamma-amino butyric acid) receptor agonist, significantly suppresses the morphine induced retching or vomiting in ferrets, indicating the involvement of GABA_B receptors in emetic control pathway.³² In this line, it has been mentioned that vitamin B6 administration can increase central production of GABA.³³ The main role of vitamin B6 in the nervous system comes from the fact that the putative neurotransmitters, dopamine, norepinephrine, serotonin, GABA and taurine, are synthesized by vitamin B6-dependent enzymes.³⁴ It could be concluded that vitamin B6 indirectly affects CTZ of xylazine injected cats by increasing the content of GABA in central nervous system. As GABA receptors are abundant in the area postrema of the cat,³⁵ vitamin B6 may exert its antiemetic action indirectly on vomiting center in medulla oblongata and block vomiting pathways via stimulating GABA receptors of the area postrema. Probably, vitamin B6 may have just a role on the synthesis of GABA neurotransmitters and does not prevent xylazine induced emesis by antagonizing the alpha 2-adrenoceptors. However, further studies are required to consider exact mechanism of action of vitamin B6 in reducing nausea and vomiting in xylazine injected cats.

The results of the present study indicate that pretreatment of cats with vitamin B6 (5, 10, 20 and 40 mg/kg) before injecting xylazine (IM) may reduce episodes of emesis without any significant change in the time needed for sedation of cats after administration of xylazine. Vitamin B6 may be used as a prophylactic antiemetic in cats treated with xylazine.

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چکیده

درمان پیش گیرانه با ویتامین ب۶، استفراغ ناشی از تجویز زایلازین در گربه ها را کاهش می دهد

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هدف - استفراغ یکی از مشکلات معمول تجویز زایلازین در گربه ها است. این مطالعه به منظور ارزیابی اثر پیش گیرانه ضد استفراغی ویتامین ب۶ در گربه های تسکین یافته با زایلازین صورت گرفت.

طرح - مطالعه تجربی

حیوانات - تعداد هشت گربه بالغ (از هر دو جنس) انتخاب گردید.

روش کار - تمامی گربه ها یک ساعت قبل از تجویز زایلازین، نرمال سالین و ویتامین ب۶ (با دوز های ۵، ۱۰، ۲۰ و ۴۰ میلی گرم بر کیلوگرم عضلانی و به فواصل یک هفته) دریافت نمودند. تمامی گربه ها پس از تجویز زایلازین به مدت ۳۰ دقیقه برای ثبت زمان اولین استفراغ، تعداد استفراغ ها و زمان آرامبخشی پایش گردیدند.

نتایج - تعداد استفراغ ها با تمامی دوزهای مورد اشاره ویتامین ب۶ به طور معنی داری کاهش پیدا کرد.

نتیجه گیری - این مطالعه نشان داد که درمان پیشگیرانه با ویتامین ب۶ می تواند تعداد استفراغهای ناشی از تجویز زایلازین در گربه ها را بدون اینکه تاثیری در مدت زمان اثر آرامبخشی آن داشته باشد به طور معنی داری کاهش دهد.

کلیدواژگان - گربه، تسکین، ویتامین ب۶، استفراغ، زایلازین.

