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Effects of Dexamethasone and Metoclopramide on Emesis in Cats Sedated With Xylazine Hydrochloride

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Abstract: Xylazine hydrochloride is a sedative available for use in small animals. While xylazine produces sedation, it has undesirable actions. Emesis frequently is reported after administration of xylazine hydrochloride in cats and dogs, which may distress an animal and also increase the risk of aspiration pneumonia. The present study was conducted to compare the antiemetic effects of dexamethasone and metaclopramide on xylazine-induced emesis on cats. Six adult mixed-breed cats were used for the study. The antiemetic effects of dexamethasone and metoclopramide given IM 1 hour before IM administration of xylazine were evaluated. Standard dose of xylazine (2 mg/kg, IM) intramuscular injection in saline group evoked nausea and emesis incidence of 85% and 75%, respectively. Dexamethasone and metoclopramide reduced nausea and emesis induced by xylazine significantly ($p<0.05$). The results of the present study indicate that Dexamethasone and metoclopramide significantly reduces the frequency of emetic episodes induced by xylazine. Dexamethasone and Metoclopramide may be used as a prophylactic anti-emetic in cats treated with xylazine hydrochloride.

Key words: Xylazine Hydrochloride · Dexamethasone · Metoclopramide · Anti-Emetic · Cat

INTRODUCTION

Pets frequently resists restraint, due to either its nature or the procedure to be performed and thus requires sedation and analgesia. Xylazine hydrochloride is a sedative available for use in small animals in the circumstances such as radiography, ultrasonography, catheterization and skin biopsy. This drug also can be used for oral examination, minor laceration repair, wound debridement, bandage placement, ear canal examination and cleaning, either. From clinical experience, the maximum dose of xylazine recommended for sedation of dogs and cats is 1-2.2 mg/kg of intramuscular (IM) injection. While xylazine produces sedation, it has undesirable actions that may be of little consequence if the animal is healthy. These actions include muscle relaxation, anxiolysis, cardiovascular effects, respiratory effects, gastrointestinal effects, renal effects and hormonal effects. Emesis frequently is reported after administration of xylazine hydrochloride in cats and dogs, which may distress an animal and also increase the risk of aspiration pneumonia. Xylazine has been shown to evoke vomiting through its actions on the emetic chemoreceptor trigger zone (CTZ) of the area postrema [1, 2]. It has been shown that, both in cats [1, 3] and dogs [4, 5], the emetic action of xylazine injected intramuscularly is mediated through α2-adrenoceptors, because this effect of xylazine is prevented only by α2-adrenoceptor antagonists, such as yohimbine, tolazoline and phentolamine [1, 3]. On the other hand, Ho *et al.* have suggested that glucocorticoids, such as dexamethasone, may be involved in the control of vomiting induced by xylazine acting on the area postrema [6]. Dexamethasone is a glucocorticoid that is effective in preventing chemotherapy-induced emesis in humans [7, 8], cats [9], dogs [10], ferrets [11] and pigeons [12]. Centrally acting drugs are more effective than peripherally acting drugs. metoclopramide inhibits the chemoreceptor trigger zone and increases gastric tone and peristalsis, both of which inhibit emesis [13].

The present study was conducted to compare the antiemetic effects of dexamethasone and metaclopramide on xylazine-induced emesis on cats.

MATERIALS AND METHODS

Animals: Healthy adult mixed-breed cats (3 males and 3 females) weighing median, 2.7 ± 1.2 kg, were used for the study. Prior to the experiment they were sheltered individually in stainless-steel cages in a controlled room. All cats in each experiment were fed commercial dry food and water *ad libitum* and fasted for 12 hrs before the emetic experiment.

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Protocol: The antiemetic effects of dexamethasone and metoclopramide given IM 1 hour before IM administration of xylazine were evaluated. Antiemetic drugs were injected in the semitendinous muscle of one leg. All cats were subjected to the same procedures and each treatment was performed at a 1 week interval. On the first day, the cats were given saline solution (0.1 ml/kg of body weight, IM) and on days 7, 14 and 21, they were given dexamethasone (Aburaihan Co, Iran) (4 mg/kg b.wt, IM) and metoclopramide (Osveh Co, Iran) (0.4 mg/kg b.wt,IM). Immediately after these injections, the cats were fed 100- 150 g commercially produced dry food. One hour later, each cat was administered xylazine (Alfasan, Germany) (2 mg/kg b.wt, IM) in the semitendinous muscle of the other leg. The dosage was chosen on the basis of the effective dose to induce sedation on cats. The cats were observed until the end of the sedative effect. During this period, the time until the onset of the first emetic episode and the frequency of emesis were determined. Emesis was scored as an "all or none" response; separate episodes of emesis were considered when the interval between bouts of vomiting exceeded 10 seconds. During the observation period after the injection of xylazine, the number of emetic episodes was counted. The time until the onset of the first emetic episode was recorded.

Statistical Analysis: Results are expressed as mean ± SD Multiple comparisons were performed by Paired studeut T-test. In all analyses, the level of significance was set to ($P<0.05$).

RESULTS

Standard dose of xylazine (2 mg/kg b.wt, IM) intramuscular injection in saline group evoked nausea and emesis incidence of 85% and 75%, respectively. All cats vomited most of the food they were fed. Dexamethasone and metoclopramide reduced nausea and emesis induced

Table 1: Effects on incidence and episode of nausea and emesis premedicated with Dexamethasone, metoclopramide or saline in cats sedated with xylazine hydrochloride

Groups	Nausea unset	Nausea episodes	Emesis unset	Emesis episodes
Normal Saline				
Total	6	18	6	9
Average	1	3	1	1.5
Total %	75%	85.7%	66.7%	75%
Dexamethasone				
Total	2	5	1	1
Average	33%	50%	17%	17%
Total %	25%*	14.3%*	11.1%*	8.3%*
Metoclopramide				
Total	0	0	2	2
Average	0%	0%	33%	33%
Total %	0%*	0%*	22.2%*	16.7*

*in each Column, shows significant differences ($p<0.05$)

Table 2: Effects on time of nausea and emesis premedicated with dexamethasone, metoclopramide, acepromazine or saline in cats sedated with xylazine hydrochloride

Groups	First nausea average time	Nausea average time	First emesis average time	Emesis average time
Normal Saline				
Average (min)	20.50	36.63	44.50	54.16
Standard deviation	13.91	15.77	30.09	18.85
Min	4.00	19.00	6.00	30.00
Max	40.00	57.50	84.00	84.00
Dexamethasone				
Average	39.00	41.25	4.00*	4.00*
Standard deviation	12.72	9.54	-	-
Min	30.00	34.50	4.00	4.00
Max	48.00	48.00	4.00	4.00
Metoclopramide				
Average	-	-	4.11*	4.50*
Standard deviation	-	-	0.70	0.70
Min	-	-	4.00	4.00
MAX	-	-	5.00	5.00

*in each Column, shows significant differences ($p<0.05$)

by xylazine significantly ($p<0.05$) (Table 1). As presented in Table 2, first emesis and emesis average time were reduced by Dexamethasone and metoclopramide pre-treatment, significantly ($p<0.05$).

DISCUSSION

It was shown in the present study that a standard dose of xylazine (2 mg/kg b.wt, IM) induced vomiting in cats, even when pre-treated with saline, Dexamethasone or metoclopramide. However, vomiting was reduced in cats administered xylazine after pre- treatment with Dexamethasone and metoclopramide. These results were similar to the data obtained in a previous study on cats treated with xylazine [6]. In previous studies, antagonist of α1-adrenoceptors (prozasin or phenoxybenzamine), β1-adrenoceptors (propranolol), dopaminergic receptors (domperidone), muscarinic receptors (atropine), 5-hydroxytryptamine3 receptors, opioid receptors (naloxone) and histamine receptors (diphenhydramine) did not prevent xylazine induced vomiting [1, 3]. These results suggested that the emetic action of xylazine is mediated by central α2- adrenoceptors in cats. The α2-adrenoceptor antagonist, yohimbine, prevented vomiting induced by xylazine [3, 5]. The antagonism of this specific α2-adrenoceptor is effective against xylazine induced emesis, but it is also capable of antagonizing the sedative effect of xylazine [6]. It was first reported in 1981 that Dexamethasone is an effective antiemetic in cancer patients receiving chemotherapy [14]. Since then, several studies have documented that Dexamethasone is effective in preventing emesis caused by chemotherapy in humans [7, 8, 15], cats [9], dogs [10], ferrets [11, 16]. The exact mechanism by which Dexamethasone exerts antiemetic action is not known, but it may involve central inhibition of prostaglandin synthesis and/or a decrease in serotonin turnover in the central nervous system [8]. Anti-dopaminergic agents like metoclopramide have been widely used (and still are) as anti-emetics for the prevention of nausea and vomiting during radiotherapy [17], cancer chemotherapy [18, 19]. It has been shown in decerebrated cats sedated with xylazine that dexamethasone exerts its central anti-emetic action through an activation of the glucocorticoid receptors in the bilateral nucleus tractus solitarii (NTS) in the medulla and prevents xylazine- induced emesis through an activation of the α2 adrenoceptors in these cats [20]. Additionally, corticosteroids are thought to stabilize membranes and affect the blood-brain barrier permeability to reduce the influx of emetogenic substances to the central nervous system [11,16]. Xylazine reportedly induces vomiting via its action on the area postrema that is mediated by α2-adrenoceptor in cats [3,5]. Therefore the potential antiemetic mechanism of Dexamethasone may involve the emetic pathway of the α2-adrenoceptor. There is evidence that glucocorticoid receptors and α2-adrenoceptors are abundant and coexist in the area postrema and nucleus of the solitary tract in the medulla oblongata [21]. It is established that these nuclei in the medulla oblongata have substantial neuronal activity in regulation of the emetic reflex. The area postrema contains a chemoreceptive trigger zone that can be activated by endogenous or exogenous agents released into the circulation from the periphery [22]. Dexamethasone may therefore exert its antiemetic action through these nuclei. Further studies are required to elucidate the precise mechanisms of the antiemetic effect of Dexamethasone. In conclusion, the results of the present study indicate that xylazine-induced vomiting was reduced by pre-treatment with Dexamethasone (4 mg/kg, IM) which however did not change the time until the onset of the first emetic episodes and did not disturb the sedative effect.

In conclusion, the results of the present study indicate that Dexamethasone and metoclopramide significantly reduces the frequency of emetic episodes induced by xylazine. Dexamethasone and Metoclopramide may be used as a prophylactic anti-emetic in cats treated with xylazine hydrochloride.

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