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Emesis inducida por administración de ácido tranexámico en gatos

Emesis induced by tranexamic acid administration in cats

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Palabras claves:
Ácido tranexamico, emesis inducida, gatos.

Resumen

Introducción: aunque se ha cuestionado la eficacia de utilizar eméticos para la descontaminación en casos de intoxicación en seres humanos, en medicina veterinaria, se ha observado que la exposición a sustancias como productos farmacéuticos, cebollas, chocolates, tabaco, insecticidas, pesticidas, y otros elementos extraños que puedan ser eliminados por vómito sin causar daño, podría beneficiarse significativamente mediante la emesis inducida en un periodo de tiempo adecuado. En el presente estudio, se evaluó la eficacia del ácido tranexámico en la inducción del vómito en gatos seleccionados al azar y en óptimo estado de salud. Se llevaron a cabo una monitorización cuidadosa de los efectos del fármaco con el objetivo de lograr la emesis de manera controlada. **Objetivo.** El objetivo de la presente investigación fue evaluar la eficacia con dos experimentos: el uno incrementando las dosis con repeticiones de cinco minutos entre dosis y el otro con una sola dosis hasta obtener la emesis. **Metodología**. Esta investigación tuvo un enfoque cuantitativo experimental de tipo descriptivo donde 10 gatos fueron expuestos a dos experimentos en el primero (T1), se aplicaron tres dosis de 10mg/kg, 20mg/kg y 30mg/kg, con intervalos de 5 minutos para valorar la dosis efectiva. En el segundo experimento (T2), se realizó exposición a una sola dosis con intervalos de una semana para la siguiente dosis y así determinar a qué dosis (única) presenta la emesis. **Resultados:** El 90% de los gatos tuvo la emesis inducida en un periodo de no más 230 segundos y con un máximo de tres eventos por gato. **Conclusión:** El ácido tranexámico demostró ser eficaz en inducir el vómito, observándose que la emesis se produjo con el aumento de la dosis del fármaco, alcanzando este efecto incluso con una sola dosis de 40 mg/kg. **Área de estudio:** Medicina Veterinaria.

Keywords:
Tranexamic acid, induced emesis, cats.

Abstract

Introduction: although the effectiveness of using emetics for decontamination in cases of poisoning in humans has been questioned, in veterinary medicine, it has been observed that exposure to substances such as pharmaceuticals, onions, chocolates, tobacco, insecticides, pesticides, and other foreign elements that can be eliminated by vomiting without causing

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harm, could benefit significantly by induced emesis in an adequate period of time. In the present study, the efficacy of tranexamic acid in inducing vomiting was evaluated in randomly selected cats in optimal health. Careful monitoring of drug effects was carried out with the aim of achieving emesis in a controlled manner. Aim. The objective of the present investigation was to evaluate the efficacy with two experiments: one increasing the doses with repetitions of five minutes between doses and the other with a single dose until emesis was obtained. Methodology. This research had a descriptive quantitative experimental approach where 10 cats were exposed to two experiments in the first (T1), three doses of 10 mg/kg, 20 mg/kg and 30 mg/kg were applied, with intervals of 5 minutes to assess the effective dose. In the second experiment (T2), exposure to a single dose was carried out with one-week intervals for the next dose to determine at which (single) dose emesis occurs. Results: 90% of the cats had induced emesis in a period of no more than 230 seconds and with a maximum of three events per cat. Conclusion: Tranexamic acid proved to be effective in inducing vomiting, observing that emesis occurred with an increase in the dose of the drug, reaching this effect even with a single dose of 40 mg/kg. Study area: Veterinary Medicine.

Introduction

In everyday life, both dogs and cats can face potentially dangerous situations when ingesting objects that, when passing down the esophagus, become trapped in the stomach or intestine due to their size (1). This scenario leads to the diagnosis of a gastrointestinal foreign body, often manifesting with symptoms such as vomiting, lack of appetite and lethargy. Urgent treatment is essential, involving medication and removal of the object by surgery or endoscopy to prevent obstructions or perforations of the digestive tract, which could prove fatal (2).

When the foreign object is small enough and is located in the stomach, it is possible to induce vomiting to facilitate its expulsion along with the stomach contents. However, if there are still doubts about the nature or location of the object, techniques such as gastroscopy or surgery are used for its removal. Gastroscopy, performed after anesthesia

of the animal, allows the location and removal of the foreign body using a flexible endoscope and special forceps, avoiding the need to open the abdomen, provided that the shape and size of the object allow it (2).

In dogs, tranexamic acid has been used at a dose of 50 mg/kg to induce controlled vomiting. In cats, it has been used at a dose of 15 mg/kg to control bleeding during surgery. This study seeks to develop a safe tool for induced emesis, not only in cases of foreign bodies, but also in the elimination of unwanted food boluses (3).

The process of vomiting is a reflex that begins in the brain stem, where clusters of nuclei are found, including serotonergic (5HT) and adrenergic (alpha2) receptors. Neurokinergic (NK1) receptors in the adjacent nucleus of the solitary tract can stimulate the vomiting center. These receptors are activated indirectly by humoral pathways through chemoreceptors (CRTZ) or by pathways in the gastrointestinal tract, cerebral cortex, or vestibular system. The lack of a blood-brain membrane in the CRTZ prevents sampling of chemical stimuli in the blood, placing it in the area postrema in the floor of the fourth ventricle, where these stimuli are presented endogenously and exogenously (drugs, toxins, uremic or hepatoencephalic toxins). Although CRTZ possesses dopaminergic (D2), histaminergic (H1), adrenergic (alpha2), serotonergic (5HT3), cholinergic (M1), enkephalinergic (ENKu, o) and neurokinergic (NK1) receptors, there are differences between species that influence responses to emesis in dogs and cats. Apomorphine (D1 and D2 agonist) is very effective for induced emesis in canines, whereas in cats its emetic effect is almost null. In contrast, xylazine (alpha2 agonist) is highly effective in cats. Afferent vagal, sympathetic, vestibular and cerebrocortical pathways stimulate emesis, as well as stimuli from the gastrointestinal tract by releasing serotonin from enterochromaffin cells, which binds to 5HT3 receptors on afferent nerves in the dog or on the CRTZ in the cat. In the dog, vestibular stimulation feeds the CRTZ before activating the vomiting center, whereas in the cat, it probably acts directly on the vomiting center (4).

A study in dogs found that an intravenous dose of 50 mg/kg induced vomiting in all animals without causing adverse effects, whereas lower doses (20 to 40 mg/kg IV) were not consistently effective. Specific pharmacokinetic information for animals is not available (3).

In humans, tranexamic acid has a bioavailability of 45% after oral administration, reaching maximum concentrations at 3 hours. In dogs, tranexamic acid was found to be emetogenic, causing vomiting two minutes after administration. These vomits typically occurred once or twice, persisting for approximately 4 to 5 minutes. In a larger cohort of dogs, 85% experienced vomiting, with an average duration of 2.5 minutes and an average of 2 episodes of emesis (5).

Tranexamic acid lacks pharmacokinetic studies in cats or dogs. It helps control bleeding by inhibiting fibrin breakdown, reversibly binding lysine binding sites on plasminogen to prevent its binding to fibrin, thus stabilizing the clot. It is widely used to reduce bleeding in dogs and cats, as well as controlling hyperfibrinolysis due to Angiostrongylus vasorum infection (6). It has been shown to be effective and safe as an emetic in dogs due to its emetogenic effects, probably through NK1 receptors. It is thought to be able to antagonize GABA and glycine receptors, having a possible proconvulsant effect. No conclusive studies have been conducted on its emetic effect in felines (5).

In summary, tranexamic acid, known to prevent blood clot formation, has shown stimulating properties on smooth muscle contractions in the stomach (3,8). This makes it a potential option for inducing controlled emesis in cats. The justification for this study lies in the need for safe and effective options for the management of poisoning or foreign body ingestion in felines, situations that can frequently occur in domestic environments, putting the health and life of cats at risk. Although controlled induced emesis is a widely used technique to eliminate toxic substances or foreign bodies from the digestive system of animals, in the case of cats, the options available to perform this procedure safely and effectively are limited (3, 8, 9). This study evaluated the efficacy of three doses of tranexamic acid for induced emesis in cats, establishing the emetic effect of consecutive doses between 10 mg/kg and 30 mg/kg, as well as the effect of a single dose between 30 mg/kg and 60 mg/kg. Finally, the duration and frequency of emesis induced by the use of tranexamic acid in cats is examined.

Methodology

Animals: In this study, ten common domestic cats, aged between 1 and 8 years, in good health, with body weights in the range of 2.5 kg to 6 kg, were used. The cats were fed a regular diet of 2 to 3 meals per day. Each animal was housed individually in cages before and after drug administration.

The administration of tranexamic acid, which was present at a concentration of 10%, was carried out through a permeable catheter inserted intravenously into the cephalic vein.

Two experiments were carried out to induce vomiting. In the first experiment, it was based on the observation that cats can vomit approximately 5 minutes after administration of tranexamic acid (10). An initial dose of 10 mg/kg was implemented, followed by a second dose of 20 mg/kg after 5 minutes and finally an additional dose of 30 mg/kg.

For the second experiment, cats were exposed to a single dose of 30 mg/kg, waited one week, and then another dose of 40 mg/kg was applied, repeating this process until a dose of 60 mg/kg was reached.

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The choice of these doses was based on the Spearman Correlation Coefficient (rho), which evaluated the relationship between the dose and the occurrence of vomiting, the relationship between the dose and the animal's response time, as well as the relationship between the dose, time and frequency of vomiting.

Results

The total prevalence of cases in which the application of Tranexamic Acid in doses between 10 mg/kg and 60 mg/kg was 43.3%. In the first experiment in which the drug was applied in an ascending manner, positive events reached 33.3%, while in the second experiment positive cases reached 53.4%. This difference generates a low association between experiments (X 2 = 0.118) so the general correlation between emesis time and the dose of Tranexamic Acid was studied, which also resulted low (ρ = 0.044), being at the same time a low value for Experiment 1 (ρ = 0.118) and moderately high for Experiment 2 (ρ = 0.552). These values were determined by the Spearman Correlation Coefficient (rho) and suggest that the doses are the predominant factor in achieving emesis.

Relationship between dose and occurrence of vomiting

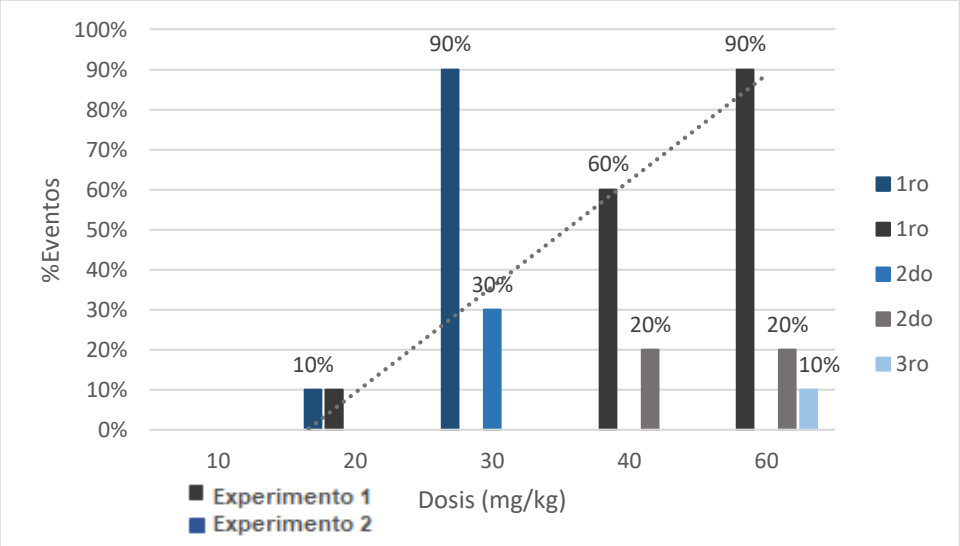

Figure 1. Cases of emesis in relation to the dose used

The dose used is associated with the number of cases of vomiting present (p=0.0001), where at 10 mg/kg there is no response, while at 20 mg/kg the dose presents 10% (2/20) of the possible cases (One from Experiment 1 and one from Experiment 2), compared to 90% (9/10) of 30 mg/kg in Experiment 1; 60% (6/10) of 40 mg/kg and 90% (9/10) of 60 mg/kg in Experiment 2.

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Dose relationship and animal response time

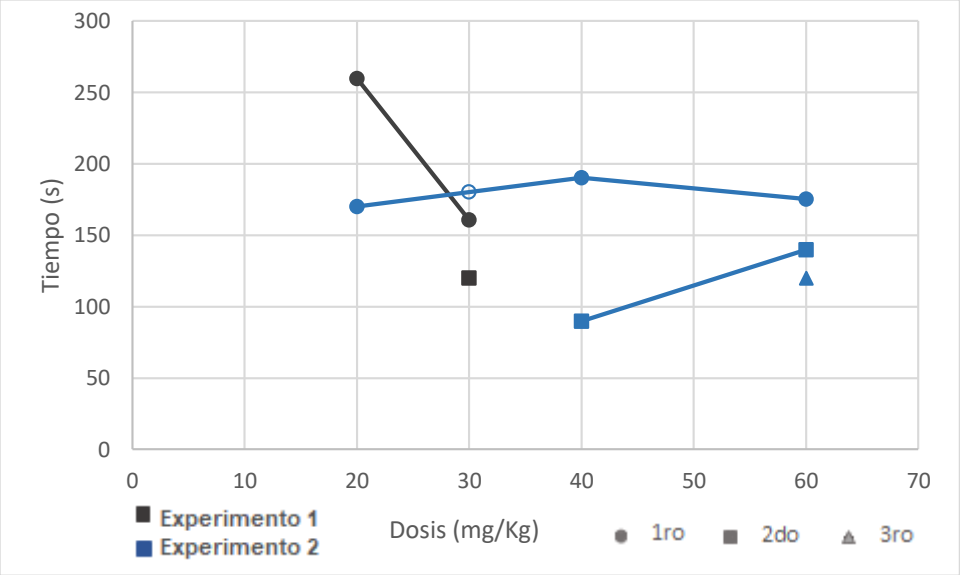

Figure 2. Relationship between emesis time and tranexamic acid dose

Figure 2 shows the mean times in which each dose of Tranexamic Acid achieved the vomiting effect in relation to each Experiment (p = 0.265). In this case in Experiment 1 of gray tones, the dose of 10 mg / kg did not produce any case of emesis, the dose of 20 mg / kg administered later achieved 1 case of emesis and finally the dose of 30 mg / kg achieved 9 cases of emesis with an average of 161 seconds (+ 38.53), there being 3 cases of repetition at 132 seconds (+ 20.78). In Experiment 2 with blue tones, the first dose of 20 mg/kg produced a direct case of emesis at 170 seconds, while the next visit with a dose of 40 mg/kg produced 6 cases of emesis with an average of 190.50 seconds (+42.49), of which 2 repeated at 140 seconds (+70.71). Finally, with a dose of 60 mg/kg, 9 cases of emesis were obtained at 175.44 seconds (+31.21), the case being repeated in 2 animals at 90 seconds in both cases and one of them vomited again at 100 seconds. Based on these results, with higher doses of 30 mg/kg, emesis is obtained in the animals and from 40 mg/kg onwards, repeated vomiting is achieved. The repetition of the cases is observed with different geometric figures in the markers.

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Relationship between dose, time and frequency of vomiting

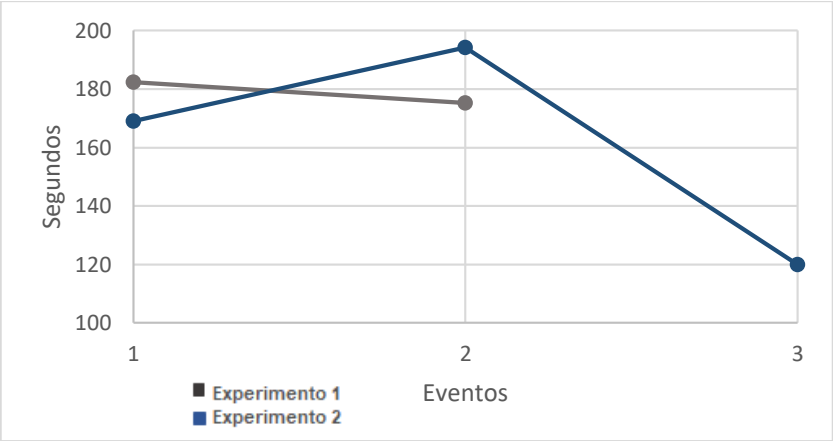

Figure 3. Relationship between the number of cases of emesis and the dose of tranexamic acid

Figure 3 shows the times taken by an animal to respond and the number of times the animal vomits. In this case there is no clear difference in the number of events over time (p=0.381), and neither is the type of experiment affecting the response time (p=0.381), since there is only one animal that vomited three times, this is considered as an isolated event. The response time with respect to the first and second vomiting event ranges from 6.33 to 11.89 seconds. The response time for the first vomiting in Experiment 1 is 169 seconds (+50.73), for the second it rises to 175.33 seconds (+50.85), while in Experiment 2 the response time for the first vomiting in Experiment 1 is 182.42 seconds (+32.77), for the second it rises to 194.33 seconds (+28.91).

Discussion

Both experiments determined that tranexamic acid-induced emesis in cats is dose-dependent, with most vomiting occurring at higher doses. The efficacy of induced emesis did not exceed 230 seconds in either experiment or at higher doses. The frequency of vomiting after administration of tranexamic acid, either in a single dose or in escalating doses, did not result in more than 3 episodes per individual.

Although this study assesses the efficacy of tranexamic acid in healthy cats, the size of the experiment is small and controlled. Studies with more diverse populations and other stomach contents are suggested to determine its efficacy (11). The lack of studies on the pharmacokinetics of tranexamic acid in cats makes its use uncertain, and further research is required to understand its mechanism of action related to feline vomiting (12).

The safety of tranexamic acid should be evaluated in larger and more diverse study groups, considering effects other than emesis or hyperfibrinolysis (13). Compared with drugs such as apomorphine and 3% hydrogen peroxide, which have emetic effects in dogs

but are not effective in cats, tranexamic acid may be an effective and minimally invasive option. The need for further studies in larger and more diverse groups, as well as safety assessments due to its antifibrinolytic effect, is underlined.

Conclusions

- The results obtained after administration of tranexamic acid in cats revealed a clear dose dependence for inducing the emetic effect. It was observed that a dose of 30 mg/kg was necessary to induce vomiting in all cats, whereas lower single doses failed to induce vomiting consistently.
- It is important to note that in all cases, the frequency of vomiting did not exceed three episodes per cat. Furthermore, it was observed that emesis ended within a maximum time of 250 seconds, suggesting a rapid and effective response to tranexamic acid.
- The findings of this study have important clinical implications for the management of cases of poisoning or foreign body ingestion in cats. The dose-dependent nature of tranexamic acid in inducing vomiting highlights its potential utility in veterinary emergency situations. However, the need for further research in more diverse populations and under more representative clinical conditions is recognized to assess the safety and efficacy of tranexamic acid in practical settings.
- Furthermore, further studies addressing the specific pharmacokinetics of tranexamic acid in cats are suggested, providing a more complete understanding of its safety profile and clinical application. These future investigations are critical to support and contextualize the results of this initial study, as well as to ensure informed and safe clinical decision-making in veterinary practice.

Conflict of interest

I, Mario David Vaca Granda, have no conflict of interest with the article presented.

Authors' contribution statement

This article is intended to contribute to the therapeutics and management of feline medicine.

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