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Efectividad de la apitoxina como tratamiento complementario para el manejo del dolor en perros con enfermedades musculoesqueléticas

Effectiveness of apitoxin as a complementary treatment for pain management in dogs with musculoskeletal diseases

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Palabras claves:
Dolor, picadura, Glasgow, analgesia, apiterapia

Resumen

El objetivo de este estudio fue evaluar el efecto analgésico y antiinflamatorio de la apitoxina, obtenida a través de picaduras de abejas (Apis mellifera), como tratamiento coadyuvante en enfermedades musculoesqueléticas en perros domésticos (Canis lupus familiaris), con el objetivo de mejorar la movilidad de los animales. La investigación se llevó a cabo entre agosto y diciembre en la Clínica Veterinaria "Entre Garras y Bigotes" en la ciudad de Quito. Se recopilaron datos de 15 perros de diversas razas, edades y sexos, todos con problemas de movilidad y dolor, evaluados mediante la escala de dolor de Glasgow. Los pacientes seleccionados fueron divididos en tres grupos: T1, al cual se le administró carprofeno 4.4 mg/kg cada 24 horas durante 5 días, junto con tres inoculaciones directas de apitoxina en el área afectada cada 48 horas por tres ocasiones; T2, que recibió exclusivamente tres picaduras de apitoxina en la zona afectada, cada 48 horas por 3 ocasiones; y T3, al cual se le administró exclusivamente carprofeno 4.4 mg/kg cada 24 horas durante 5 días. El análisis estadístico reveló que el grupo T1 experimentó cambios positivos en la evolución funcional. Sin embargo, al comparar los tratamientos y momentos de evaluación (p=0,598), se determinó que, independientemente del tratamiento aplicado, se observa una disminución en los signos de dolor.

Keywords:
Pain, sting, Glasgow, Analgesia, apitherapy.

Abstract

The objective of this study was to evaluate the analgesic and anti-inflammatory effect of apitoxin, obtained from bee stings (Apis mellifera), as a coadjuvant treatment in musculoskeletal diseases in domestic dogs (Canis lupus familiaris), with the aim of improving the mobility of the animals. The research was carried out between August and December at the Veterinary Clinic "Entre Garras y Bigotes" in the city of Quito. Data were collected from 15 dogs of various breeds, ages and sexes, all with mobility problems and pain, evaluated using the Glasgow Pain Scale. The selected patients were divided into three groups: T1, which was administered carprofen 4.4 mg/kg every 24 hours for 5 days, together with three direct inoculations of apitoxin in the affected area every 48 hours for three occasions; T2, which received exclusively three stings of apitoxin in the affected area, every 48 hours for 3 occasions; and T3, which was administered exclusively carprofen 4.4 mg/kg every 24 hours for 5 days. Statistical analysis revealed that the T1 group experienced positive changes in functional evolution. However, when comparing the treatments and evaluation times (p=0.598), it was determined that, regardless of the treatment applied, a decrease in the signs of pain was observed.

Introduction

Musculoskeletal diseases are common conditions in dogs, which can include osteoarthritis, hip dysplasia, ligament injuries, among others. These conditions often cause chronic pain and limitations in the animals' mobility, which significantly affects their quality of life.(Cuoto & W, 2020)

Pain management in dogs with musculoskeletal conditions is a fundamental aspect of their care. While there are various therapeutic options available, such as analgesics and physiotherapy treatments, some owners and veterinarians have shown interest in complementary or alternative approaches.(Meana, Higues, & Hernández, 2018).

Apitherapy

Apitherapy involves the use of bee venom or bee products for therapeutic and preventative purposes and is considered a form of complementary and alternative medicine with curative goals. Its origins date back over 6,000 years to ancient Egyptian medicine, and both the Greeks and Romans used bee products for medicinal purposes, as mentioned by Hippocrates, Aristotle and Galen. A more contemporary study of apitherapy, focusing specifically on bee venom, was pioneered by Australian physician Philip Terc in 1888. However, the more recent popularity of apitherapy is due to Charles Mraz, a beekeeper from Vermont, USA. In the 20th century, Philip Terc is recognized as the father of apitherapy, and Dr. Bodog F. Beck, who already used the term apitherapy to refer to this natural treatment.(Meana, Higues, & Hernández, 2018)

Bee venom or apitoxin

Etymologically the word comes from Latin*Apis*which means bee, and from the Greek*toxic*which means poison which comes from worker bees of various species that use it as a means of defense against predators.(Meana, Higues, & Hernández, 2018)

Bees store venom in a sac, a clear, aromatic liquid that is emptied into the stinger. It is produced in glands located at the back of the last abdominal segment. The venom is produced as a defense strategy and they cannot renew their supply once it is used.

Apitoxin is a product used in medicine for its anti-arthritic effect, in the preparation of anti-allergy drugs and as an anticoagulant.(Muñoz, Arnes, & Noro, 2013)

Apitoxin is a biomolecule associated with analgesic and anti-inflammatory principles, similar to what would be a NSAID, being widely used in inflammatory, rheumatic processes and neurological disorders, where the response to this toxin by organisms has been ancestrally used, by alternative medicine, while today this biomolecule is being used in research concerning human and animal medicine, with diverse results, and with a wide concern about the possible adverse and toxic effects of the product (Pascoal, et al., 2018),The apitoxin in the bee is stored in three receptacles, two of acidic content and the other of alkaline content, included inside its abdomen. The average production of*apitoxin*per bee 0.3 to 04 micrograms, but it is important to consider that if Apitoxin has scientific validation it would not be the first product related to a toxin or poison of animal origin, on the market, that benefits medicine. At present, an antimicrobial effect of Apitoxin together with Melittin against Staphylococcus spp. has been verified. However, its mechanism of action is not clearly described for this bacteria (Pereira, et al., 2020), but information has already been collected on its effect on the biofilm formation of Salmonella enterica (Arteaga, et al., 2019).

Regarding the effects of Apitoxin, its musculoskeletal action and its relationship with the circulatory system are known, which promotes greater irrigation in the affected area ((Arteaga, and others)

Biological effect of apitoxin

The therapeutic properties of apitoxin are mainly attributed to its hemodiluent and neurotropic capacity.

- It has radioprotective properties, which may help protect against injury caused by radiation used in cancer treatment.(Guimarães & Evangelista, 2014)
- It stimulates the immune system, promoting the formation of defensive cells and substances such as lymphocytes, macrophages, immunoglobulins and cortisol.(Guimarães & Evangelista, 2014)
- It reduces the protein content in blood plasma by altering the permeability of blood vessels, which is reflected in a decrease in heart rate and blood pressure, as well as changes in repolarization and atrioventricular conductivity.(Guimarães & Evangelista, 2014)
- It has antiarrhythmic properties, eliminating arrhythmias caused by electrical excitation and strophanthin inoculation.(Guimarães & Evangelista, 2014)
- It improves the conduction of nerve impulses and reduces demyelination, positively influencing the nervous system.(Urtubey, 2012)

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- It improves the functional activity of the pituitary-adrenal system, stimulating the production of endogenous corticosteroids and promoting better functioning of the liver and brain.(Guimarães & Evangelista, 2014)
- It inhibits the formation of edema, relieves pain and contains a polypeptide with anti-inflammatory activity.(Urtubey, 2012)
- It has a neurotropic action that improves the metabolism of the central and peripheral nervous system, counteracting the depression of the adrenal glands induced by steroid hormones.(Guimarães & Evangelista, 2014)
- It acts as a bacteriostatic and local anesthetic, increases the elimination of toxins and reduces bacterial growth.(Guimarães & Evangelista, 2014)
- Effective in the treatment of heart conditions by increasing blood fibrinolytic activity.(Urtubey, 2012)
- It exerts a beneficial immunological action in rheumatic diseases.(Guimarães & Evangelista, 2014)

Chemical Composition

Apitoxin is the only hive product that is not dietary, but is considered pharmacological, since it has been ancestrally associated with multiple benefits due to its broad and complex composition, among which are: formic acid, hydrochloric acid, orthophosphoric acid, choline, tryptophan, among other molecules that allow an analgesic and anti-inflammatory action, as long as it acts synergistically and in the long term.Other proteins and peptides include melittin, apamin, mast cell granulation peptide, secapin, procamine and a protease inhibitor; it also contains amino acids. Among its active amines it contains histamine, dopamine and noradrenaline. Its ashes are rich in magnesium phosphate. It also contains glucose and fructose, phospholipids and volatile oils.(Muñoz, Arnes, & Noro, 2013)

Features and properties

Aqueous liquid, containing approximately 88% water, transparent, slightly yellow, with a bitter and acidic taste, with a density greater than that of water and a strong aromatic odor. Its density is 1.1313. Its pH is acidic and it is soluble in water.(Urtubey, 2012)

One such approach is the use of apitoxin, a bee venom that has been used in traditional medicine for centuries. Apitoxin contains a variety of bioactive compounds, such as melittin, phospholipase A2, and peptides, which are believed to possess analgesic and anti-inflammatory properties.(Padilla, Hernandez, & Reyes, 2001)

Several studies have investigated the effectiveness of apitoxin as an adjunctive treatment for pain management in different conditions, both in humans and animals. However, as of the cut-off date of my knowledge in September 2021, there is a paucity of specific research on its efficacy in dogs with musculoskeletal diseases.(Meana, Higues, & Hernández, 2018).

Function of apitoxin

Apitoxin acts as a local anesthetic and has anti-rheumatic properties by stimulating the adrenal glands, which are responsible for the production of cortisone. It also promotes the activation of the immune system by encouraging the formation of multinuclear cells, monocytes, macrophages, T and B lymphocytes. As a result, bee stings contribute to developing immunity against both the venom itself and certain infectious diseases. It also works as an astringent that treats skin problems, to combat skin infections such as allergies and dermatoses.(Muñoz, Arnes, & Noro, 2013)

Effects of apitoxin on the skin

Apitoxin acts as an astringent agent that addresses skin problems, being an excellent product to combat fungi, chilblains and skin infections such as allergies and dermatosis. In addition, its use can improve other skin abnormalities, such as the reduction of scars, the disappearance of eczema or skin ulcers. On the other hand, its natural analgesic and anti-inflammatory power helps to relieve discomfort derived from circulation problems such as phlebitis, hypertension, arrhythmias, blood clots, among others.(Urtubey, 2012)

Anti-inflammatory action*:*The Peptide 401 fraction of bee venom exerts a potent anti-inflammatory action by inhibiting the action of Cyclooxygenase and the biosynthesis of Prostaglandins that generate inflammation.(Meana, Higues, & Hernández, 2018)

Analgesic Action: The analgesic action of apitoxin is potent, the Adolapin fraction (polypeptide) inhibits the action of the cyclooxygenase enzyme and, therefore, the synthesis of Prostaglandins which, as is known, derives from the synthesis of Bradykinin, producer of pain associated with inflammation and stimulates the release of endorphins, powerful endogenous analgesics.(Meana, Higues, & Hernández, 2018).

Antibiotic and Bacteriostatic Action: Apitoxin has the capacity to inhibit the growth of bacteria such as Staphylococcus aureus, Streptococcus pyogenes, Diplococcus, among others, and fungi such as Candida albicans, functioning as a bacteriostatic agent. Its antifungal effect is evident in inoculated and cultured nutrient media, while its antibacterial action is mainly attributed to the Melittin fraction.(Meana, Higues, & Hernández, 2018)

Clinical manifestations of apitoxin inoculation

Bee stings depend on the anatomical location where the sting occurred, the number of stings, and the characteristics and allergic history of the individual involved. The venom produces an anaphylactic reaction, which may present with urticaria at the sting site, bronchoconstriction, laryngeal edema, and hypotension, and poisoning when there are a large number of stings.(Arteaga, and others)

Methodology

Hypothetico-deductive method

Taking into account the information collected, it was found that apitoxin has several benefits, one of them acting as an anti-inflammatory and analgesic. Using the hypothetical-deductive method it was deduced that the application of apitoxin in dogs with musculoskeletal diseases would have a favorable effect, but the hypothesis that it would not give the expected result was not ruled out.(Arteaga, and others)

Experimental method

For the present investigation, three groups were formed. Group 1 received treatment with apitoxin every 48 hours, together with carprofen. Group 2 was treated only with carprofen, administered at a dose of 4.4 mg/kg every 24 hours for 3 days. Group 3 was treated exclusively with apitoxin, with an application frequency of every 48 hours for 3 sessions. Data were collected from each patient and pain was assessed using the Glasgow pain scale. This methodological approach allowed us to both precisely control the treatments to which each animal was subjected and to obtain the necessary information to carry out an adequate follow-up.(Muñoz, Arnes, & Noro, 2013)

Techniques

Observation technique

The methodology used in this research included observation techniques in all phases of the process, from the meticulous selection of animals to the inoculation of apitoxin, the collection of samples, the evaluation of pain, and laboratory tests. This comprehensive approach made it possible to obtain in an exhaustive manner the data necessary for the development and analysis of the research in question.

Experimental design

Treatment assignment was carried out considering the level of pain evidenced by each animal participating in the study. Group 1 included dogs that had previously been treated and showed less severe effects on their musculoskeletal problem. Treatment 2 included dogs with high pain, since the apitoxin inoculation was carried out every 48 hours. Treatment 3 was reserved for those canines with moderate-high pain, also with the frequency of apitoxin inoculation every 48 hours. In this way, the three treatments were standardized, ensuring a coherent and consistent comparison between them.

Treatments

Three treatments were carried out, each involving groups of five animals. This experimental design allowed for a representative sample to be obtained, providing the necessary basis for a reliable and significant statistical analysis.

T 1(Experimental): This consisted of inoculating the affected area with apitoxin, carried out every 48 hours for a total of three occasions. This procedure was complemented with the administration of carprofen, at a dose of 4.4 mg per kilogram, for a continuous period of five days. This combination of interventions was implemented with the aim of comprehensively and long-term evaluating the effects of apitoxin in conjunction with carprofen in the experimental treatment.

T2.(Experimental)

Apitoxin inoculation was implemented in the affected area, following a precise cadence of 48 hours, and this process was systematically repeated on a set of three occasions. This temporal and iterative strategy was designed with the purpose of examining in detail the response of the affected area to the application of apitoxin, thus allowing a more complete evaluation of the possible effects over multiple instances.

T3.(Experimental)

This protocol involved the administration of carprofen at a specific dose of 4.4 mg per kilogram of body weight, continuing this regimen for a sustained period of five days. The choice of this duration was based on the need to examine the effects of carprofen over a significant period of time, thus allowing a thorough evaluation of its impact in the experimental setting.

Essay management

- A thorough history taking, complemented by a thorough and systematic physical examination, was carried out on each participating animal. This comprehensive approach not only made it possible to collect a detailed clinical history of each individual, but also provided the essential information for making an effective clinical diagnosis. The combination of these two assessment phases ensured a complete and accurate assessment of the health of each animal, thus facilitating an appropriate and personalized clinical approach.
- Physiological constants were taken, including temperature, respiratory rate, heart rate, weight and capillary refill time in each animal. A thorough physical examination was then carried out, addressing both general and specific aspects. In this analysis, symmetry defects were observed in detail, evaluating the gait, posture and attitude of each individual. Special attention was paid to identifying

possible external indicators of compromised health, such as the presence of wounds, alopecia or exudates. This comprehensive approach to physical examination allowed for a complete and detailed assessment of the condition of each animal.

- A thorough focused physical examination was performed, prioritizing the meticulous inspection and palpation of the various anatomical regions of each patient in order to detect responses to pain, identify areas of firmness or increased temperature. Likewise, percussion and auscultation of the chest were performed in order to comprehensively evaluate the cardiovascular and pulmonary health of each individual.
- After verifying the presence of pain and musculoskeletal disorders, 15 participating patients were selected, 10 of whom underwent treatment with apitoxin while 5 patients formed the control group. This decision is based on the medical evidence supporting the use of apitoxin, whose bioactive components have been shown to have analgesic and anti-inflammatory properties.
- Five patients were administered Treatment 1, which involved direct inoculation of apitoxin every 48 hours into the affected area, repeating this application on three occasions. This therapeutic protocol was complemented by the simultaneous administration of carprofen, prescribed at a dose of 4.4 mg per kilogram of body weight, over a continuous period of five days. The combination of apitoxin inoculation and pharmacological treatment with carprofen was strategically implemented with the aim of enhancing the therapeutic effects, thus covering both the analgesic and anti-inflammatory aspects. This comprehensive approach aims to provide an effective and balanced response to the musculoskeletal conditions present in these canine individuals.
- A group of five dogs were given treatment 2, which involved direct inoculation of apitoxin by sting, with a frequency of application every 48 hours, focusing specifically on the affected area. This therapeutic protocol is characterized by the punctual and repetitive application of apitoxin at the mentioned interval, thus providing a precise therapeutic strategy to address the musculoskeletal conditions observed in these canines.
- The remaining five dogs were designated as a control group and were exclusively subjected to a treatment regimen based on the administration of carprofen. This drug was administered at a specific dose of 4.4 mg per kilogram of body weight, maintaining this pharmacological protocol for a continuous period of five days. The choice of this approach was based on the need to establish a comparison group that received only the anti-inflammatory treatment unrelated to apitoxin.

Inoculation of apitoxin

The bees used in this research belong to the Apis mellifera species and were collected in Solanda, located in the city of Quito, province of Pichincha, Ecuador. These bees feed mainly on the natural flora present in the city's streams and parks.

During the experimental procedure, the bee was grabbed by the wings with a pair of forceps, shaking it slightly before placing it on the affected area. Once positioned, the bee proceeded to sting the animal. Three seconds after the sting, the bee was removed and the stinger was immediately removed. A period of 15 minutes was waited to verify the absence of any allergic reaction.

In anticipation of possible anaphylactic reactions, preventive materials such as an oxygen source, fluid therapy and medications such as corticosteroids and antihistamines were available. These additional measures guaranteed the safety and well-being of the animals involved in the study, providing a controlled environment prepared to deal with any eventuality during the experimental procedure.

Analysis and discussion of the results

In order to evaluate the analgesic effect of apitoxin as an adjuvant in the treatment of musculoskeletal diseases in domestic canines, bee stings were implemented as an intervention. Pain assessment was carried out using the Glasgow Pain Assessment Scale, applying bee stings periodically every 48 hours. Through this scale, aspects such as mobility and the presence of signs of pain were evaluated, both before and after the application of apitoxin. This comprehensive methodological approach allowed for a detailed and comparative evaluation of the analgesic efficacy of apitoxin in the context of musculoskeletal conditions in canines.

Results

For this study, a total of 15 patients were selected, evenly distributed in three treatments under a completely randomized design. Of these, 5 presented degenerative diseases, 4 fractures and 6 dislocations, thus covering a diversity of musculoskeletal conditions, which were distributed in 3 groups of 5 members each. The experimental model included T 1, including 5 patients with a weight of 8.0 (+2.2) kg and 11 (+6.9) years of age to whom 4.4 mg / kg of Carprofen was administered together with 3 inoculations of apitoxin; T 2, with 5 dogs with a weight of 7.2 (+2.1) kg and 6.9 (+7.2) years of age, in which 3 inoculations of apitoxin were performed every 48 hours; and T 3 as a control treatment, with weights of 7.2 (+1.9) kg and 13 (+4.9) years of age, in which 4.4 mg/kg of Carprofen was applied.

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In the statistical analysis, no statistically significant differences were found when comparing the effects of the treatments with respect to the variable age (p=0.813) or weight (p=0.513). These results indicate a homogeneous and equitable distribution of the baseline conditions between the treatment groups, strengthening the validity of the experimental design.

Table 1.

Inter-variable correlations of the Glasgow Scale x Weight and Age

	Locomotion	Position	State	TOTAL	Age	Weight
Locomotion	**X**					
Pressure	0.399*	**X**				
State	0.311*	0.729**	**X**			
TOTAL	0.857**	0.739**	0.696**	**X**		
Age	0.501*	0.566*	0.583*	0.685**	**X**	
Weight	0.170	0.328	0.107	0.244	-0.082	**X**

** p values<0.05*
***p values<0.01*

A correlation analysis was established (p<0.05) to define the relationships between the variables of the Scale (Locomotion, Pressure and General Condition) and those involved in the experiment (age and weight) in Table 1. The Total Pain Value of the Glasgow Scale has a high and moderately high correlation (*p<0.01*)with its components of locomotion or motor response, posture or visual response and general condition of the patient. The moderately high correlation stands out (*p<0.01*)between the total pain value and the age of the patient. All the variables that make up the Glasgow scale are highly correlated (*p<0.01*)The only one with moderate values (p<0.05) was the one between locomotion and the general condition of the patient.Similarly, age also has a moderately high relationship with pain.(p<0.05).From this premise, a Kruskall and Wallis analysis (p<0.05) can be established, of the effect of the use of apitoxin in the three treatments, from the total value on the Glasgow scale.

Table 2.

Contingency Table of Pain Assessment between Treatments using the Kruskall-Wallis test (p≤0.05)

Treatment	**Moment**	**N**	**Locomotion***(Mean (SD)/Median)*	**Pressure***(Mean (SD)/Median)*	**State***(Mean (SD)/Median)*	**Total***(Mean (SD)/Median)*	**p-value**
T1 (Carprofe	Before	5	2.20 (+/-0.83) /2	4.00 (+/-2.24) /3	1.40 (+/-0.54) /1	7.60 (+/-3.05) /6	0.941

n 4.4 mg/kg + Apitoxin)							
T2 (Apitoxin)		5	2.40 (+/-0.54) /2	3.60 (+/-1.52) /3	1.40(+/-0.54) /1	7.40 (+/-2.19) /6	
T3 (Carprofen 4.4 mg/kg)		5	3.00 (+/-1.73) /2	4.20 (+/-1.64) /3	1.60(+/-0.89) /1	8.80 (+/-4.09) /6	
T1 (Carprofen 4.4 mg/kg + Apitoxin)		5	1.00 (+/-1.41) /0	3.20 (+/-0.45) /3	1.40 (+/-0.54) /1	5.60 (+/-1.82) /5	
T2 (Apitoxin)	After	5	0.40 (+/-0.89) /0	3.00(+/-1.22) /3	1.40 (+/-0.54) /1	4.80 (+/-2.28) /4	0.749
T3 (Carprofen 4.4 mg/kg)		5	0.80 (+/-1.10) /0	3.00(+/-0.00) /3	1.40 (+/-0.54) /1	5.20 (+/-1.64) /4	
Before Analgesic Rescue	T1, T2, T3	15	2.53 (+/-1.13) /2	3.93 (+/-1.71) /3	1.47 (+/-0.64) /1	7.93 (+/-3.03) /6	*0.006
After Analgesic Rescue		15	0.73 (+/-1.10) /0	3.07 (+/-0.70) /3	1.40 (+/-0.51) /1	5.20 (+/-1.82) /4	

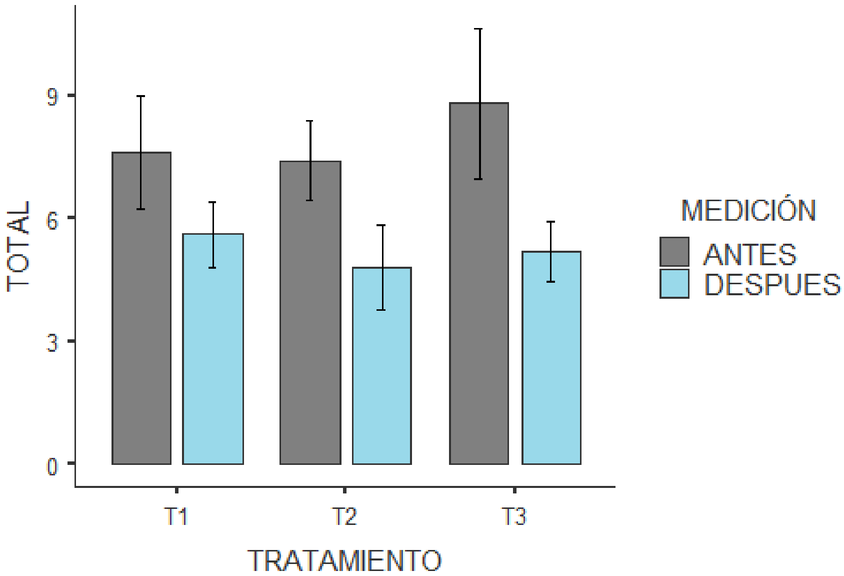
* p values<0.05

The three treatments (T1, T2 and T3) showed a similar assessment on the Glasgow Pain Scale both in the first (p=0.941) and in the last evaluation (p=0.749). The evaluation of pain after anesthetic rescue varied significantly (p=0.006) compared to the initial values, which are presented in detail in Table 2. Regarding the variation of each component of the scale, the canine's locomotion capacity stands out as the key factor for the modification of the final result (p=0.001), with no significant variations observed between treatments (p=0.628).

In relation to the other components, the assessment experiences minor variations both between treatments and at different times (p>0.05), slightly improving posture over time and slightly favouring the use of apitoxin in this characteristic compared to the first measure (p<0.05), according to the Post-Hoc statistical tests of the treatment-by-time interactions.

Figure 1.

Total Glasgow Scale Rating Between Treatments



The analysis of the interaction between Treatments and Evaluation Moments (p=0.598) revealed that, regardless of the treatment applied, the signs of pain decrease after the trauma. This dynamic is clearly illustrated in Figure 1, where it can be seen that no treatment modality presents higher or lower ratings compared to the others. Finally, in relation to the Type of Event (degenerative, fractures or dislocations), no significant effect was observed (p=0.229) on the final assessment of the treatments.

Discussion

Behavior in the face of illness or pain is characterized as an adaptive response driven by cytokinins related to infection and inflammation (Piotti, et al., 2024). This study revealed that age emerges as a crucial factor in the manifestation of pain signs on the Glasgow scale, evidencing a significant and high correlation (0.685) between these variables.

The appropriate use of analgesia in preoperative procedures plays a crucial role in the recovery of patients undergoing trauma surgeries. In this study, interventions performed before applying treatments in animals during surgical procedures were investigated, and their impact on pain response was assessed using the Glasgow scale (Villacrés and Castillo, 2023). The efficacy of NSAIDs, such as ketoprofen, in analgesia has been supported by their positive effects on patient recovery (Ravuri, et al., 2022). Furthermore, individual factors such as sex can influence the accurate assessment of a pain scale during patient recovery (Cruz-Campos and Maldonado-Cornejo, 2023), regardless of the scale used.

Therefore, it is important to note that an animal's previous experience with various levels of pain, whether pathological or physiological, can affect its response. Therefore, this study considered the type of trauma or level of pain to which the animal was exposed, classifying them as degenerative, fractures or dislocations to distinguish between chronic and acute. However, it was observed that this factor was not decisive in the final results of this research.

The use of NSAIDs, such as ketoprofen or carprofen, both intraoperatively and postoperatively, has been widely recognized for its effectiveness in the management of pain associated with traumatic surgeries (Bautista, 2017). The administration of carprofen prior to the intervention, according to previous studies (Bergmann and Kramer, 2007), has been shown to induce an improved postoperative analgesic response, thanks to its ability to inhibit cyclooxygenases. However, the need to perform analgesic rescue after the intervention suggests a lack of consideration in relation to the level of preexisting pain in the patient.

In the context of this study, the application of carprofen allowed establishing a conventional control against pain events, whether chronic or acute, in canines. However, it is crucial to highlight that this approach did not take into account the corrective interventions carried out on the animals, which could have influenced the observed results.

Implementation of adequate analgesia, complemented by effective pain assessment, becomes an essential component to ensure a successful outcome and prevent over-reliance on pharmacotherapy, as noted by Bradbrook and Clark (2018). In this study, these parameters were addressed, considering pain as a phenomenon that causes discomfort in pets. It was recognized that the pain response can be managed both pharmacologically and non-pharmacologically, regardless of the pain adaptation period experienced by the canine. Assuming this consideration is crucial to more comprehensively understanding the complexities surrounding pain management in canines and may offer valuable insights into the influence of external events on the response to analgesic therapy.

The prevalence of allergic reactions to apitoxin varies throughout the world, with reports ranging from 6% of the population (Piñero Gutiérrez, 2020) to more severe cases reaching 14% (Flores Ruiz, et al., 2015). This factor becomes one of the most controversial aspects in relation to the use of this product, since it shows notable prevalences in the human population. However, these figures have not prevented the development of apitherapy programs around the world, with the region being no exception.

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This argument, however, is countered by empirical evidence indicating that these figures are lower compared to other drugs, such as beta-lactams, which have allergic reaction rates of over 30% (Rodríguez and Benítez, 2020). In the case of dogs, it has been observed that apitoxin generally produces momentary variations in the hematological count and blood pressure (Muñoz, et al., 2013). However, it should be considered that, despite the extensive information available on control protocols with antihistamines in cases of allergic reactions in canine patients, as in humans, the dose of the toxin is directly adjusted to the weight of the animal.

Based on these data, in this study the response to apitoxin was monitored in all dogs tested, and it was found that none of them had a negative response. In addition, it was observed that weight did not affect the final results, suggesting that there was no evident risk in the animals tested.

Conclusions

- In this study, it was observed that the behavioural response, assessed by the Glasgow Scale, is intrinsically linked to the factors that led the animal to receive the treatment, being especially influenced by the level of pain previously experienced by the animal. After stabilizing the animal, the therapy was applied, and no signs of increased pain attributable to the bee stings were evident.
- Apitoxin in the body triggers a rapid response, although the need for its long-term use for more complete evaluation is underlined. Although this study formulated a hypothesis about short- and medium-term responses in trauma patients, no statistically significant differences were found in the evaluation between the treatments. It is notable that treatment with Apitoxin alone did not differ significantly from those supplemented with Carprofen. These findings highlight the need for additional research to further understand the effectiveness and differences between the therapeutic approaches used in this study.
- The use of apitherapy is emerging as a genuine alternative in natural medicine, supported by research (Cabrera, et al., 2017). Products from the hive are noted for their healing properties, intrinsically linked to human activities (Pulsan, 2015). The very origin of bees becomes a factor interconnected with the health of the population and members of the ecosystem, particularly in the canine context.
- The existing literature on this topic tends to be more linked to cultural factors (Outdot, 2023) and the clinical method (García, et al., 2007), giving rise to the use of apitherapy in focused studies and particular cases. This document stands out as one of the few records that merges cultural practices with medicinal and veterinary practices. In doing so, it contributes significantly to the comprehensive understanding of apitherapy, opening new perspectives that connect cultural traditions with medical and veterinary practices.

- The use of apitherapy is a real alternative in natural medicine (Cabrera, et al., 2017) where all hive products have curative values and are closely related to human activities (Pulsan, 2015) where the very origin of the bee is a factor that interacts with the health of the population and the members of the ecosystem, in this case the canine. The bibliography on the subject is more associated with cultural factors (Outdot, 2023) and the clinical method (García, et al., 2007), which lead to the use of apitherapy as focused and case studies, so this document constitutes one of the few records that associates cultural practices with medicinal and veterinary practices.

Conflict of interest

The authors declare that there is no conflict of interest in relation to the submitted article.

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