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<https://orcid.org/0000-0002-4387-7115>**Kedi ve Köpeklerde Multimodal Akut Ağrı Yönetimi:
Bir Kapsam Derlemesi****Multimodal Acute Pain Management in Cats and Dogs:
A Scoping Review**Mehmet Cem KOLBAŞI¹, Yalçın Alper ÖZTURAN¹, İbrahim AKIN¹¹Aydın Adnan Menderes Üniversitesi, Cerrahi Anabilim Dalı, Aydın, Türkiye**ÖZ**

Multimodal analjezi (MMA), etkili ağrı yönetimi için umut verici ve bilimsel olarak kanıtlanmış bir yöntemdir. Çoklu ağrı yollarını hedeflemek için farklı ağrı kesici tekniklerini birleştiren MMA, tek yöntem içeren tedavilere kıyasla üstün etkinlik göstermiştir. Ancak daha iyi analizler ve karşılaştırmalar yapılabilmesi için bu alandaki çalışmaların standartlaştırılmasına ihtiyaç vardır. Veteriner hekimliğinde MMA ile ilgili literatürün kapsamlı bir şekilde incelenmesi, hayvanlar için ağrı yönetimini geliştirmek açısından hayati öneme sahiptir. Mevcut kapsam derlemesi, köpeklerde ve kedilerde multimodal analjezi ile ilgili mevcut literatürü sistematik olarak incelemeyi, incelemeler, vaka raporları ve klinik araştırmalardaki boşlukları belirlemeye odaklanmayı amaçlamaktadır. Önerilerde bulunarak, literatürlerdeki boşlukları belirleyerek ve analjezi ile ilgili vaka raporlarının gelişmesine yardımcı olarak gelecekteki MMA literatürünü geliştirmeyi amaçlıyoruz. Böylece veteriner hekimlikte multimodal analjezik stratejilerini geliştirmeyi amaçlayan gelecekteki çalışmalara ışık tutuyor. Sistematik incelemeler ve Meta-Analizler için Tercih Edilen Raporlama Ögeleri (PRISMA) Kapsam Belirleme İncelemeleri için Uzantı kılavuzunun ardından, PubMed kullanılarak bir literatür taraması yapıldı. Multimodal analjezi, ağrı yönetimi, kediler ve köpeklerle ilgili arama terimleri Boolean operatörleri kullanılarak birleştirildi. Çalışmaya dahil etme kriterleri, inceleme makalelerini, vaka raporlarını, vaka serilerini ve klinik deneyleri kapsayan, kedi ve köpeklerde akut multimodal analjezi çalışmalarına odaklandı. Dahil edilen çalışmaların temel özelliklerini ve bulgularını analiz etmek için veri çıkarma ve sentez yapıldı. Literatür taraması sonucunda 63 makale elde edildi. 19 derleme, 10 vaka sunumu ve seri ve 8 orijinal makale olmak üzere 37 makale çalışmaya dahil edildi. Sentez, çeşitli çalışma tasarımları, ilaç kullanımı ve kombinasyonları ile veteriner hekimlikte multimodal analjezinin kullanımına ilişkin giderek büyüyen bir literatür ortaya çıkardı. Bu kapsamlı inceleme, kedi ve köpeklerde akut ağrı tedavisinde multimodal analjezinin giderek daha fazla benimsendiğini vurgulamaktadır. Etkinliğine ilişkin kanıt tabanı genişlerken, özellikle standartlaştırılmış çalışma tasarımları ve raporlama kılavuzlarıyla ilgili boşlukları ve belirsizlikleri gidermek için daha fazla sistematik araştırmaya ihtiyaç vardır. Multimodal analjezi, tek ağrı giderici yöntemleri geride bırakarak etkili olduğunu kanıtlıyor.

ABSTRACT

Multimodal analgesia (MMA) is a promising and scientifically proven method for effective pain management. By combining different pain-relief techniques to target multiple pain pathways, MMA has demonstrated superior efficacy compared to unimodal treatments. However, there's a crucial need to standardize studies in this field for better analysis and comparison. Thoroughly mapping the literature on MMA in veterinary medicine is vital for advancing our understanding and improving pain management for animals. The present scoping review aims to systematically examine the current literature on multimodal analgesia in dogs and cats, focusing on identifying gaps in reviews, case reports, and clinical trials. We aim to improve future MMA literature by giving suggestions, identifying gaps, and helping standardize case reports regarding analgesia. Thereby informing future studies aimed at improving multimodal analgesic strategies in veterinary medicine. Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Extension for Scoping Reviews guidelines, a literature search was conducted using PubMed. Search terms related to multimodal analgesia, pain management, cats, and dogs were combined using Boolean operators. Inclusion criteria focused on acute multimodal analgesia studies in cats and dogs, encompassing review articles, case reports, case series and clinical trials. Data extraction and synthesis were performed to analyze key characteristics and findings of the included studies. The literature search yielded 63 articles, 19 reviews, 10 case reports and series, and 8 original article in total of 37 articles were met the inclusion criteria. The synthesis revealed a growing body of literature of the use of multimodal analgesia in veterinary medicine, with various study designs, use and combinations of drugs. This scoping review highlights the increasing adoption of multimodal analgesia in acute pain management for cats and dogs. While the evidence base for its effectiveness is expanding, further systematic investigations are needed to address gaps and uncertainties, particularly regarding standardized study designs and reporting guidelines. Multimodal analgesia proves effective, surpassing single pain-relieving methods.

INTRADUCTION

The International Association for the Study of Pain defined pain as "An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage".¹ Recently, this definition has been reviewed to include an important definition that the inability to communicate does not imply the absence of pain experience or the lack of need for analgesic treatment.² In veterinary medicine, the responsibility of recognizing and assessing pain falls upon veterinary professionals due to animals' inability to verbalize their pain as we humans do.³ This responsibility represents the necessity for veterinary professionals to possess the capability to recognize, assess, and manage pain in animals.⁴

Nociception, the body's ability to sense noxious stimuli, involves complex processes including transduction, transmission, modulation, and perception.⁵ Nociceptors are sensory nerve fibers functioning as free nerve endings found in the dorsal root and trigeminal ganglia.⁶ Transduction refers to the conversion of noxious stimuli into electrical activity in peripheral nociceptors. Transmission involves the propagation of nerve impulses throughout the nervous system. Modulation occurs through endogenous descending systems that alter nociceptive transmission. Perception, on the other hand, is the final process arising from transduction, transmission, and modulation of thalamocortical, reticular, and limbic function, resulting in the conscious subjective and emotional experience of pain.⁷

Pain and nociception are two separate concepts.⁸ Pain emerges from the conscious interpretation of nociception, forming a complex network in the brain.⁹ The absence of consciousness during general anesthesia results in the lack of pain perception despite nociception, as deeper brain centers linked to the autonomic nervous system, emotion, and memory play a role in the multifaceted experience of pain.^{5,10} Inadequate analgesia during surgery can lead to heightened central sensitization, resulting in intense pain upon consciousness. Additionally, insufficient analgesia under general anesthesia may lead to cardiac complications such as tachycardia, and cardiac arrhythmias, as well as respiratory complications like hypoventilation and hypoxemia.¹¹⁻¹³

When animals experience pain, changes occur in physiological parameters due to nociception. These changes include heart rate, respiration rate, rectal temperature, arterial blood pressure, and pupil dilation. Initially, the body responds to a painful stimulus with an increased response in a range of physiological parameters. However, as the cardiovascular system stabilizes, maintaining these

dynamic factors can be challenging, potentially weakening pain assessment.¹⁴ Additionally, these physiological parameters can be influenced by various factors such as fear and stress.¹⁵ In this context, that biochemical assessments alone may not provide a complete evaluation of pain.¹⁶

Recognition of acute pain requires regular assessment of the animal's pain signs. These signs are best identified through observation of the patient and interaction with them, coupled with information about the animal's medical/surgical condition and history.⁶ Guidelines in veterinary medicine strongly recommend the use of pain scoring tools for assessing pain.³ It's important to remember that the validity and reliability levels of these tools vary, and acute and chronic pain scales, or scales for dogs and cats, cannot be used interchangeably. Embracing pain scales encourages more effective pain management by reducing subjectivity and observer bias, enhancing overall quality of life for patients.^{3,6}

There's a growing emphasis on proactive pain management strategies aimed at prevention and rapid detection of pain.¹⁷ Multimodal analgesia has emerged as a promising approach, integrating various medications and techniques to target different pain mechanisms simultaneously.³ This approach offers the potential for more effective pain control with lower medication doses and minimized side effects.¹⁷⁻¹⁹

Multimodal pain management (MMA) involves the concurrent use of two or more various pharmacological and non-pharmacological analgesic techniques.²⁰ Simultaneously applying medications and methods that affect different areas of the nociceptive mechanism provides the best approach to pain management.^{19,17} It includes the application of pain-relieving techniques before, during, and after surgery.⁶ Additionally, it considers all factors at operative moments that may contribute to peripheral and central sensitization and includes all kinds of medications and analgesic techniques for pain relief.¹²

This scoping review aims to systematically map the existing literature to assess the extent, range, and nature on multimodal analgesia studies in dogs and cats with a view to help standardize future study to systematically compare and analyze.

MATERIALS and METHOD

Protocol

The protocol of this scoping review was adopted according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Extension for Scoping Reviews²¹ and published on Figshare accessible at:

https://figshare.com/articles/preprint/Protocol_for_

Multimodal_Acute_Pain_Management_in_Cats_and_Dogs_A_Scoping_Review/25656408

Search Strategy

A literature search was conducted to locate relevant publications concerning the utilization of multimodal pain management in cats and dogs within the domain of veterinary medicine. The search was executed using the PubMed database, accessible at <https://pubmed.ncbi.nlm.nih.gov> (last accessed on March 28, 2024). PubMed index was used as a quality indicator. For articles not directly available via PubMed, additional resources were accessed through the Aydin Adnan Menderes University Library website, Research Gate, and Google Scholar. The research strategy was conducted using a combination of keywords linked through Boolean operators. The PubMed database search strategy used in the present review can be found in supplementary data 1. With this PubMed database search, including MeSH terms, an exact search strategy was utilized and can be replicated for further exploration.

Inclusion Criteria

The present scoping review addressed the following key elements of the research question according to the Population-Intervention-Comparison-Outcome (PICO) question approach as follows:

P: The population of interest is defined as dogs (*Canis familiaris*) and domestic cats (*Felis catus*).

I: Intervention is defined as multimodal analgesia.

C: Comparison includes findings in review articles, case reports, original research, and clinical trials.

O: Outcome involves assessing the utilization of multimodal analgesia approaches.

Exclusion Criteria

Chronic pain cases excluded from the review due to our focus on acute pain management. By narrowing our scope to acute contexts, we aimed to emphasize the importance of literature specifically addressing multimodal treatment strategies, drug combinations, and methods relevant to this acute timeframe. Yet, due to the limited number of articles resulting from our search strategy, we decided not to exclude certain references that discuss both chronic pain and the utilization of acute pain management strategies, which may have implications regarding the aim of this study.

Selection Process

All searched literature was uploaded to Zotero® citation management system (Version 6.0.26/26 April 2023, Virginia, USA), then exported to Rayyan online AI application²² for screening. Title/abstract screening and subsequent full-text screening were conducted by MCK and YA. IA resolved any disparities and

reviewed the final product. The PubMed database search strategy yielded 63 articles. Utilizing the Rayyan online AI application²² articles were screened based on their titles, abstracts, and keywords. If the given information is relevant to our criteria they are selected for full-text screening. Following this initial screening, 37 articles remained for further evaluation through the full screening process.

Data charting process

Microsoft Excel (Microsoft, Redmond, WA, USA) was used as a data extraction tool. In this scoping review, we charted various parameters to analyze the landscape of multimodal analgesia in acute pain of dogs and cats. The guideline of the Systematic Reviews and Meta-Analyses (PRISMA) Extension for Scoping Reviews²¹ was adopted. Review articles charting process encompassed seven core categories: author information, publication year, country of origin, study population details, article type, research aim, and key findings. Reviews article type categorized with review typology created by Grant and Booth²³. In case reports, our charting process encompassed seven primary categories: author information, publication year, country of origin, study population details, article type, research aim, and key findings. Additionally, we incorporated novel categories tailored to the objectives of our study, including pain assessment methods, the used MMA elements, and the outcome of analgesia. For clinical trials included in this scoping review charting process encompassed seven core categories: author information, publication year, country of origin, study population, article type, research aim, and key findings. Additionally, we incorporated specialized categories relevant to our study objectives, such as pain assessment methods, sample size, used MMA elements, and outcomes.

RESULTS

A search of the PubMed database (n=1) yielded a total of 63 (n=63) articles. After the search strategy articles (n=63) were screened based on our criteria mentioned above in material and methods. Following this initial screening, 37 (n=37) articles remained for further evaluation through the full screening process. Figure 1 represents the screening procedure conducted by MCK. Unfortunately, due to a shortage of qualified researchers available during the scoping review, duplicate screening could not be conducted. As a result of this screening process to produce a 100% alignment which is a limitation of our review. After screening is done, Data is extracted from full texts of included studies.

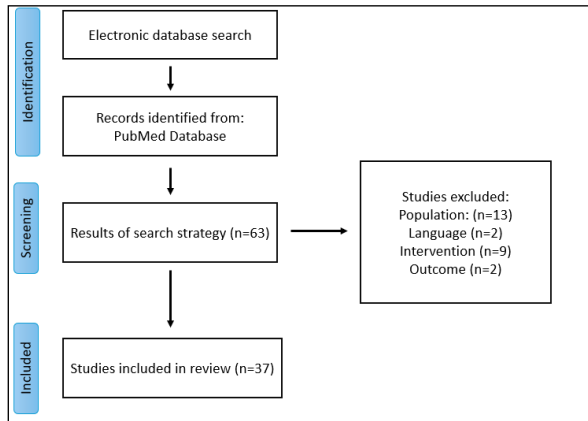


Figure 1. Adapted Prisma 2020 Flow Diagram^{24,25}

Reviews

Detailed information about included review articles were given in Tables 1 and 2. The studies, predominantly from the USA (n=10), also originated from Canada (n=3), Mexico (n=2), Italy (n=1), the UK (n=1), France (n=1), and Argentina (n=1). Various modalities were explored for pain management in dogs and cats. The most common was multimodal therapy (n=9), followed by local anesthetics (n=4), opioids (n=2), NSAIDs (n=1), magnesium (n=1), cannabinoids (n=1), and acupuncture (n=1). Study populations varied, including both dogs and cats (n=12), solely dogs (n=4), and solely cats (n=3). The majority of studies were literature reviews (n=17), with one meta-analysis (n=1) and one providing quality evidence (n=1). Only one study (n=1) reported funding.

All 19 review studies (n=19) included single doses and single application suggestions to analgesic methods but 12 of them provided detailed descriptions to apply them simultaneously.^{13,26-36} All of them give detailed adverse effects for single modalities and only 9²⁸⁻³⁶ of them give adverse effects regarding simultaneous uses of modalities. 17 of them approve of multimodal analgesia advantages and benefits, and none disapprove but 2^{34,36} of the reviews say there is no statistically significant difference between groups. These 2 articles are systemic reviews and the remaining 17 of them are traditional literature reviews.

Case Reports

Detailed information about case reports were provided in Table 3. A total of 10 studies were analyzed. The majority of the case reports and case series were conducted in the USA (n=4), followed by the UK (n=3), Chile, Switzerland, Greece, South Africa, and Brazil (n=1 each). Dogs were the most studied population (n=6), followed by cats (n=4). The types of articles included case reports (n=6) and case series (n=4). Various pain assessment methods were

employed across the studies, including short form of the Glasgow composite pain scale³⁷ (n=2), UNESP-Botucatu pain scale³⁸ (n=1), parasympathetic tone activity (n=1), and Modified 4avet pain scale³⁹ (n=1). Notably, some studies (n=5) did not report the specific pain assessment method used.

Table 1. An Overview of Included Review Articles.

Authors	Year	Country	Population	Citation Count*
Debuigne et al.	2024	France	Dog&Cat	4
Miranda-Cortés et al.	2023	Mexico	Dog&Cat	10
Cicirelli et al.	2022	Italy	Dog	9
Donati et al.	2021	Argentina	Dog	21
Domínguez-Oliva et al.	2021	Mexico	Dog&Cat	27
Grubb & Lobprise	2020	USA	Dog&Cat	125
Layne & de Miguel Garcia	2019	USA	Dog&Cat	9
Frank & Roynard	2018	USA	Dog	40
Berry	2015	Canada	Dog&Cat	72
de Vries & Putter	2015	UK	Cat	23
Corti	2014	USA	Dog&Cat	59
Fry et al.	2014	USA	Dog&Cat	79
Chohan	2010	USA	Dog&Cat	13
Lemke & Creighton	2010	Canada	Dog&Cat	243
Hansen	2008	USA	Dog&Cat	37
Robertson	2008	USA	Cat	170
Davis et al.	2008	USA	Cat	48
Lascelles et al.	2005	USA	Dog	173
Lemke & Dawson	2000	Canada	Dog&Cat	243

*Citation counts gathered from Google Scholar.

Clinical Trials

Detailed pieces of information about clinical trials are provided in Tables 4 and 5. A total of eight (n=8) studies were included in the analysis, originating from the USA (n=3), Brazil (n=3), Canada (n=1), and Italy (n=1). The study populations primarily focused on dogs (n=7), with one study focusing on cats (n=1). The number of samples varied across studies, ranging from 16 to 92.

Various methods for assessing pain were used in each study, including CMPS: The Glasgow composite measure pain scale, MNT: Mechanical nociceptive threshold, DIVAS: Dynamic interactive visual analogue scale, UMPS: University of Melbourne pain scale, CPS: Composite pain score, VAS: Visual analogue scale and CSOM: Client-specific outcome measures.

DISCUSSION

Despite there being no published reviews encountered on the subject before 2000, there was an observed increase after then (Table 1), indicating a growing interest in multimodal analgesia for acute pain. Most of the published papers comprehensively reviewed both dogs and cats, alongside papers focusing solely on dogs or cats. As different species may require specific multimodal approaches in pain management, species focused papers may be

necessary to gain a clearer understanding of multimodal pain management.

The present research aimed to provide a synthesis of evidence and recommendations derived from various studies shaping pain management practices in veterinary medicine. The compilation articles resulting from this study were designed to demonstrate that relying on multiple modalities (e.g., local anesthetics, opioids, NSAIDs, etc.) rather than a

single pain-relieving method is more effective (Table 2). This approach could be considered beneficial in managing pain more comprehensively by addressing it through various mechanisms. While Debuigne et al. (2024) indicated weak evidence for the perioperative use of magnesium,³⁶ Miranda-Cortés et al. (2023) suggested cannabinoids as a potentially effective alternative for pain management in dogs and cats.³⁵

Table 2. Objectives and Claimed Conclusions of Included Review Articles on Multimodal Analgesia.

Authors	Objective	Claimed Conclusion
Debuigne et al., 2024	Analgesic efficacy of magnesium	Weak evidence for its perioperative use alongside systemic multimodal analgesia
Miranda-Cortés et al.,2023	The potential role of cannabinoids in pain management	Effective multimodal analgesic alternative for dogs and cats.
Cicirelli et al.,2022	Local anesthetic techniques for canine ovarioectomy	Multimodal analgesia techniques are effective in managing postoperative pain
Donati et al.,2021	Efficacy of tramadol for postoperative analgesia in dogs	Tramadol administration may offer minimal to no difference in rescue analgesia requirement compared to multimodal therapy
Domínguez-Oliva et al.,2021	Comparative analysis of the tramadol and tapentadol in dogs and cats	Tramadol should be administered as a multimodal analgesia protocol in both species, particularly dogs
Grubb & Lobprise,2020	Local anesthetics' regional administration techniques	Thorax, thoracic limbs and brachial plexus blocks can be used as part of a multimodal protocol
Layne & de Miguel Garcia,2019	Regional anesthesia techniques of canine ear	Nerve blocks for regional anesthesia are an important aspect of a multimodal anesthetic approach
Frank & Roynard,2018	Integrative treatment approaches in veterinary rehabilitation	There's increasing interest in multimodal analgesia for post-neurologic injury
Berry,2015	Analgesia in the perioperative period	Multimodal analgesic plans should be created for individual patients and modified according to pain assessments
de Vries & Putter,2015	Anesthesia in cat dentistry	A multimodal analgesic protocol should be applied, including local anesthetic techniques when indicated
Corti,2014	Non-pharmaceutical approaches to pain management	Multimodal approach offers reduced side effects, dose, and frequency in medications
Fry et al.,2014	Acupuncture in postoperative pain management	Acupuncture should be strongly considered as a part of multimodal pain management plans
Chohan,2010	Aesthetic management strategies for orthopedic patients	An aggressive and multimodal approach toward management of acute orthopedic pain
Lemke & Creighton,2010	Perioperative pain management	In the perioperative setting, a multimodal analgesic protocol can be simplified to balanced anesthetic and pain management protocol
Robertson,2008	Pain management for cats and dogs	Multimodal approach would be beneficial in acute pain
Hansen,2008	Acute pain management in veterinary intensive care	Local anesthetic infusions of multimodal agents may be considered as a standard care in acute pain
Davis et al.,2007	Perioperative pain management in feline fibrosarcoma	Multimodal approach is indicated to achieve adequate post operative pain control
Lascalles et al.,2005	Safe and effective use of NSAIDs	NSAIDs are more effective preemptively in multimodal analgesia for acute perioperative pain
Lemke & Dawson,2000	Local anesthetics use for pain management in cats and dogs	The importance and effectiveness of local and regional anesthetic techniques in managing pain in small animals, particularly dogs and cats

Some studies, particularly regarding opioids, suggest that individual pain-relieving agents may exhibit limited efficacy compared to multimodal analgesia (MMA).^{13,26-30} For instance, Donati et al. (2021) reported minimal differences when comparing tramadol to MMA protocols.³⁴ The significance of local anesthetics and nerve blocks in multimodal analgesia is emphasized,^{29,32,40,41} particularly highlighting the potential reduction in opioid and inhalant anesthetic dosages during surgical procedures.^{26,32} The importance of tailoring pain management strategies to the individual needs of each patient is underscored.^{28,13,30} Berry (2015)

emphasizes the importance of developing patient-specific multimodal analgesia plans and adjusting them based on pain assessments. Some studies also suggest that traditional non-pharmaceutical methods (e.g., acupuncture, physiotherapy) can be effectively integrated into multimodal analgesia protocols.^{31,42}

In the present study, 10 case reports involving various pain assessment methods and treatment modalities in veterinary surgical cases were examined (Table 3). Literature reveals evidence of using various pain management tools tailored to specific cases and their effectiveness. The effectiveness of multimodal analgesia in pain management is evident from the

examined case reports. For instance, Goich et al. (2019) and Asorey et al. (2020) reported successful alleviation of complex pain conditions such as allodynia and hyperalgesia with multimodal analgesia.^{43,44} Sack et al. (2022) introduced opioid use in addition to local anesthetics for surgical

management of fibrosing pleuritis secondary to idiopathic chylothorax in cats.⁴⁵ Citarella et al. (2023) demonstrated successful pain management in dogs undergoing enucleation surgery with opioid-free anesthesia (retrobulbar block and NSAID use).⁴⁶

Table 3. Detailed Summaries of Included Case Reports and Case Series based on Multimodal Analgesia.

Authors	Year	Country	Pain Assessment Methods	MMA Elements	Objective	Pain Related Finding
Citarella et al.	2023	Switzerland/UK/ Greece	CMPS	Retrobulbar Block and NSAID's	Opioid-free anesthesia in fourteen dogs undergoing enucleation	Effective at managing the anesthesia and perioperative analgesia
Perry et al.	2023	USA	PE	Opioids, cortizole and LA	Severe multiple systemic disorders with hypertrophic osteodystrophy in a dog	NA
Dawson et al.	2022	USA	PE	Opioids, LA, OPA	Severe burn treatment with maggot debridement, cellular fish skin grafts and autologous skin cell suspension	Pain management is crucial in severe burn injury
Sack et al.	2022	USA	NA	Opioids and OPA	Surgical management of fibrosing pleuritis secondary to idiopathic chylothorax in cat	NA
Asorey et al.	2020	UK	CMPS	Opioids, NSAID's, LAB	New loco-regional anesthesia in dogs	Successful pain management
Goich et al.	2019	Chili	UNESP and PRB	Opioids, NSAID's, LAB, OPA, electroacupuncture.	Multimodal analgesia for treatment of allodynia and hyperalgesia	Multimodal interventions were employed to alleviate pain and allodynia
Steagall & Monteiro-Steagall	2013	Brazil	PRB and PE	Opioids, LAB, OPA, NSAID's, ice packing	Perioperative multimodal analgesia in 3 cats	Successful treatment of acute pain in three cats using a multimodal approach
James et al.	2011	South Africa	NA	Opioids and NSAID's	Patent ductus arteriosus surgery	The post-operative pain was well controlled
Vettorato & Corletto	2011	UK	Modified 4avet	Opioids, NSAID's and gabapentin	Gabapentin as part of multi-modal analgesia in two cats suffering multiple injuries	Gabapentin as adjuvant for the treatment of hyperalgesia and allodynia in cats should be considered
Wells et al.	2009	USA	PE	Opioids and OPA	Management of a dog with severe rhabdomyolysis	NA

UNESP: Botucatu multidimensional feline pain assessment scale, **PRB:** Pain-related behaviors, **PE:** Physical examinations, **CMPS:** The Glasgow composite measure pain scale, **NA:** Not available, **OPA:** Other pharmacologic agents, **LAB:** Locoregional anesthesia block.

Vettorato & Corletto (2011) suggested the use of adjuvants in multimodal analgesia (gabapentin) for treating hyperalgesia and allodynia in cats and dogs.⁴⁷ Overall, the examination of case reports indicates the utilization of various pain assessment methods (e.g., physical examination, Glasgow Composite Pain Scale) and treatment modalities (e.g., opioids, NSAIDs, local anesthetics, etc.). This underscores the wide array of

tools available to veterinary practitioners for managing various pain conditions. Further publications of case reports focusing on multimodal pain management are deemed necessary to advance pain management strategies in surgical practices. The present study summarizes the clinical trials related to multimodal analgesia conducted by researchers from different countries in Table 4.

Table 4. An Overview of Included Multimodal Analgesia Clinical Trials and Study Designs.

Authors	Article Type	Country	Population	Sample Size	Used MMA Elements	Pain Assessment Methods
Lambertini et al., 2018	Prospective, blinded RCT	Italy	Dog	45	Opioids, NSAID and LA	DIVAS, CMPS and MNT
Watanabe et al., 2018	Prospective, randomized, blinded, RCT	Canada	Dog	24	Opioids and NSAID	DIVAS and CMPS
Minto et al., 2013	Prospective, RCT	Brazil	Dog	20	Opioids and NSAID	UMPS
Camargo et al., 2011	Prospective, blinded RCT	Brazil	Dog	25	Opioids and NSAID	DIVAS
Kim et al., 2011	Prospective, blinded RCT	USA/Korea	Dog	16	Opioids and LA	CMPS
Fitzpatrick et al., 2010	Prospective RCT	USA	Dog	92	Opioids, NSAID and LA	CMPS
Brondani et al., 2009	Double-blind placebo-controlled RCT	Brazil	Cat	40	Opioids and NSAID	VAS, CPS and cortisol measurement
Lascelles et al., 2008	Prospective, blinded, placebo-controlled RCT	USA	Dog	31	NMDA antagonist and NSAID	CSOM

CMPS: The Glasgow composite measure pain scale, **MNT:** Mechanical nociceptive threshold, **DIVAS:** Dynamic interactive visual analogue scale, **UMPS:** University of Melbourne pain scale, **CPS:** Composite pain score, **VAS:** Visual analogue scale, **CSOM:** Client-specific outcome measures, **RCT:** Randomized controlled trial; **NSAID:** Nonsteroidal anti-inflammatory drug, **LA:** Local anesthetic, **NMDA:** N-Methyl-D-aspartate receptor antagonist.

Table 5. Objectives and Multimodal Analgesia Related Findings in Included Clinical Trials.

Authors	Objective	MMA Related Findings
Lambertini et al., 2018	Compare postoperative analgesia ropivacaine or bupivacaine in dogs undergoing ovariohysterectomy in the scope of multimodal analgesia	Ropivacaine and bupivacaine yielded similar postoperative pain relief, whereas morphine and carprofen combination failed to prevent rescue analgesia in almost half of the cases
Watanabe et al., 2018	analgesic efficacy of carprofen in combination with one of two commercial formulations of buprenorphine post ovariohysterectomy	Preoperative buprenorphine and carprofen combination effectively relieved postoperative pain in most dogs with no significant difference in rescue analgesia need
Minto et al., 2013	Evaluate two different mastectomy techniques in dogs	Multimodal analgesia is recommended for postoperative pain control in dogs undergoing mastectomy
Camargo et al., 2011	compare the post-operative analgesic effects of butorphanol or firocoxib in dogs post ovariohysterectomy	Firocoxib outperformed butorphanol for post-operative pain, suitable for multimodal but not standalone use
Kim et al., 2011	The efficacy of sprayed intraperitoneal bupivacaine in laparoscopic ovariohysterectomized dogs	Sprayed intraperitoneal bupivacaine effectively relieved postoperative pain and stress, indicating its potential in multimodal pain management
Fitzpatrick et al., 2010	Assessing the impact of bupivacaine infiltration at the incision site as part of a multimodal analgesia protocol (incisional block) on postoperative pain relief and incisional healing	Local bupivacaine infiltration as part of a multimodal analgesic protocol did not provide additional pain relief in dogs undergoing ovariohysterectomy
Brondani et al., 2009	Investigating the analgesic efficacy of tramadol and/or vedaprofen in cats undergoing ovariohysterectomy	Vedaprofen+tramadol pre and post operatively prevented hyperalgesia, reduces cortisol levels, pain scores, and rescue analgesia needs compared to unimodal use
Lascelles et al., 2008	Amantadine in a multimodal analgesic regimen for alleviation of refractory osteoarthritis pain in dogs	Amantadine may be a useful adjunct therapy for the clinical management of dogs with osteoarthritic pain in multimodal therapy

In total, there are 8 studies involving dogs and 1 study involving cats. The study with the largest sample size includes 92 dogs, while the smallest sample size consists of 16 dogs. Although the studies are predominantly conducted on dogs, one study examines the cat population, emphasizing the need for research on cats. Among the utilized multimodal analgesia elements are opioids, NSAIDs, local anesthetics, and NMDA antagonists. Pain assessment methods include DIVAS, CMPS, MNT, UMPS, VAS, CPS, cortisol measurement, and CSOM. These data

also demonstrate the inclusion of various evaluation methods in multimodal analgesia research. In addition to the multimodal analgesia elements commonly used in the current literature, further advanced studies tailored to specific animal species (especially cats) and surgical procedures should be designed and standardized with the integration of new drugs and techniques to achieve more efficient results in this field.

The examination of clinical studies highlights an important research area in the literature, comparing

the effectiveness of multimodal analgesia protocols and different pain management strategies (Table 5). The suggestion that amantadine could serve as an adjunct therapy in alleviating osteoarthritic pain (Lascelles et al., 2008) may be considered when investigating the clinical use of various components of multimodal analgesia protocols. Fitzpatrick et al. (2010) noted that local bupivacaine infiltration did not provide additional benefit in relieving postoperative pain in dogs undergoing ovariohysterectomy. This finding may prompt questioning of the role of local anesthetics in multimodal analgesia protocols. While Lambertini et al. (2018) indicated that ropivacaine and bupivacaine had similar effects on postoperative analgesia after ovariohysterectomy, the combination of morphine and carprofen failed to prevent rescue analgesia. In cats undergoing ovariohysterectomy, the combination of vedaprofen and tramadol was found to prevent hyperalgesia and reduce the need for rescue analgesia.⁴⁸ Kim et al. (2011) reported that intraperitoneal bupivacaine effectively reduced postoperative pain and stress in dogs undergoing laparoscopic ovariohysterectomy, indicating its potential in multimodal pain management.⁴⁹ These results can be considered when comparing the effectiveness of components of multimodal analgesia during the ovariohysterectomy process. Camargo et al. (2011) compared the effects of butorphanol and firocoxib on postoperative pain, concluding that firocoxib was more effective than butorphanol and suitable for multimodal analgesia.⁵⁰ Preoperative administration of buprenorphine and carprofen effectively alleviated postoperative pain in most dogs without a significant difference in the need for rescue analgesia.⁵¹ These studies may guide the design and implementation of multimodal analgesia protocols in veterinary medicine and provide direction for future research.

CONCLUSION

The present study aimed to provide a general overview of the options encountered by veterinary practitioners when applying multimodal analgesia and the scientific rationales underlying these options. As a result, it has been demonstrated that comprehensive knowledge is needed for effective pain management in cats and dogs undergoing surgical procedures involving multimodal analgesia.

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