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POSTOPERATIVE ANALGESIC MANAGEMENT OF GERIATRIC DOGS THAT UNDERWENT SOFT TISSUE SURGERY

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Abstract
This study was performed in order to evaluate the postoperative analgesic management of geriatric dogs during the first 12 hours after the soft tissue surgery. The study was conducted on sixty dogs, aged between 8-16 years, that were presented at the Faculty of Veterinary Medicine of Bucharest for soft tissue surgery procedures, between August - November 2017. Patients were divided in four groups (15 dogs /group) assigned to a different analgesic management that we intended to evaluate (Group 1- Tramadol, Group 2- Lidocaine in constant rate infusion, Group 3- Acetaminophen, Group 4- Ketamine+Lidocaine). Premedication was made with Midazolam 0.2 mg/kg and Butorphanol 0.2 mg/kg, injected intramuscularly (IM). Induction was obtained with Propofol 4-6 mg/kg intravenously. All patients were intubated, and maintenance was performed with Isoflurane. All patients were evaluated after the procedures using the Glasgow Composite Pain Scale (GCPS). During the evaluation period, the best results were recorded in groups 2 and 3 which were given Lidocaine and Lidocaine+Ketamine in a constant rate infusion with a pain scale of 2/24, compared with lower results in groups 1 and 4 with a GCPS of 5/24, where additional analgesic medication was needed.

Key words: *analgesia, geriatric patient, Glasgow Composite Pain Scale.*

INTRODUCTION

Nowadays pain is described as a complex, multi-dimensional experience involving sensory and affective components. (Lumb & Jones, 5th Edition), being described by the International Association for the Study of Pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage (A Arntz, L Claassens, 2004).

At its simplest, pain can be classified as acute or chronic and according to the postoperative situation, it can be the most intense in the first 24 hours after surgery, declining gradually over time (Mathews K, et al., 2014). Acute pain, for exemple, can take different forms, depending on its severity, from mild to agonizing. Furthermore pain can also be divided into somatic pain, which arises in the skin (superficial) or in more profound tissues, like muscles, bones or joints (deep pain) and visceral pain (Robertson, 2002; Joshi and Gebhart, 2000). Regarding the causes of pain, it has been shown that pain can be produced particularly by tissue or nerve damage, inflammatory processes, viral infections or demyelination being characterised by pain hypersensitivity (Vinuela-Fernandez et al. 2007). It`s important to notice that patients, during and in the postoperative period suffer different changes and unpleasant events like pain, reduced organ function and prolonged hospitalisation (Kehlet H, Holte K. 2001). Therefore, the administration of an adequate postoperative analgesia is mandatory. Once noxious stimuli are formed, the peripheral nociceptors are activated, increasing the neuronal excitability, with a sensitization in the peripheral and central areas (Woolf C, Chong M., 1993). For a better understading, it`s important to know that the noxious stimulus is mediated by a nociceptive sensory system. Nociceptors represent the free endings of primary sensory neurons. The primary afferent nerve fibers that carry information from these free nerve endings to their central location consist of two main types: unmyelinated C fibers and myelinated A delta fibers. Activation of specific receptors and ion channels (present in most tissues and organs) in peripheral unmyelinated nerve endings by chemical, mechanical, or thermal stimuli causes the initiation of action potentials that propagate the

stimulus along the axons of primary afferent nerve fibers to synaptic sites in the dorsal horn of the spinal cord. This triggers the release of neurotransmitters, including glutamate and substance P, which activate neurons located in the spinal cord. (Perl ER., 2007).

Postoperative analgesia is required all the time, no matter what type of surgery was conducted, allowing a better recovery of the animal and a quicker return to its physiological normality. However, patients hospitalized after an orthopedic surgery may require different classes of drugs compared to the ones that underwent a soft tissue surgery. Analgesia protocols can include classes of drugs like: nonsteroidal anti-inflammatory drugs, local anesthetics, dissociative agents, acetaminophen. Opioids are another class of drugs, offering good sedation and mild to very good analgesia. Tramadol, a drug recommended in both human and veterinary medicine, is considered an opioid-like drug, being a weak μ-receptor which can promote analgesia by 3 different ways: 1. Its active metabolite, O-desmethyltramadol, which has analgesic properties, but comparing with humans, animals are not able to produce this metabolite in the same amount, therefore the analgesia seems to be weak ; 2. creating a binding with its enantiomer to μ-opioid receptors or due to inhibition of the reuptake of norepinephrine and serotonine (Giorgi et al., 2009; DeRossi et al., 2013). This drug can be used for the treatment of moderate to severe pain, acute or cronic at a bolus dose of 1-2 mg/kg. Depending of the severity of pain, the dose can reach 8 mg/kg. (Costea R., 2017).

Lidocaine is a local anesthetic agent which belongs to amide group (Feary et al. 2005) used for regional anesthesia or systemic analgesia (Costea R., 2017). Its benefits in veterinary medicine is widespread, acting like an antiarrythmic drug, especially in the treatment of ventricular tachycardia. Lidocaine has also an anti-inflammatory, anti-endotoxic effect, being a prokinetic agent (Bettschart-Wolfensberger & Larenza 2007; Enderle et al. 2008; Dzikiti 2013). Systemically administration offers analgesia for different types of pain (Ness, T. J., 2000; Smith, L. J. et al., 2002). This drug has a short life, about 60-90 minutes, compared with other local anesthetics, therefore is recommended its use as a constant rate infusion (CRI- 0.5-2 mg/kg/h), after the administration of a loading dose of 1-2 mg/kg i.v. Has been shown that using this administration technique the anesthetist can achieve an effective plasma concentration for systemic analgesia (Bettschart-Wolfensberger & Larenza 2007; Ringer et al. 2007). Smith et al. (2014), suggested that an intraoperative CRI of lidocaine provided postoperative analgesia similar to morphine CRI after ophthalmologic surgery in dogs, when given a loading dose (1 mg/kg) followed by a CRI (25 μg/kg/ minute).

Ketamine is a dissociative drug, commonly used in both human and veterinary anaesthesia (Noemi R. et al., 2017), being a non-competitive antagonist of the N-methyl D-aspartate (NMDA) receptors that may prevent central sensitization and cumulative depolarization from occurring (Pozzi et al. 2006). Besides its anesthetic effect, lower sub-anesthetic doses have been administrated as an adjunctive analgesic agent in dogs (Slingsby & Waterman-Pearson 2000; Wagner et al. 2002; Sarrau et al. 2007). Most of the authors recommended first the administration of a loading dose of 0.15–0.7 mg/kg^{-1}) followed by a CRI (2–10 μg/kg^{-1}/minute^{-1}) (Wagner et al. 2002; Sarrau et al. 2007; Costea R., 2017). Due to the side effects, also, other authors consider that ketamine might be used as part of a multimodal analgesic approach but not as a sole method of providing pain relief in dogs after surgery (Wagner et al. 2002; Sarrau et al. 2007).

Acetaminophen is considered a safe analgesic and antipyretic drug at therapeutic doses for dogs, however an overdose can induce hepatotoxicity, being the one of the major causes of acute hepatic failure (Chun LJ. Et al, 2009).

MATERIALS AND METHODS

Our study was conducted in the Clinic of the Faculty of Veterinary Medicine Bucharest, from August 2017 to November 2017, on sixty geriatric patients. Breeds enrolled included various mixed and pure breed dogs with age between 8-16 years old and body weight between 5-45 kg. The patients were anesthetized for various soft tissue surgical

procedures: splenectomy, mammectomy, ovariohysterectomy. Physical examination, complete blood exams were also taken into account. Following paraclinical examination, four (4) groups were formed depending on the analgesic drugs that we intended to use. Each patient was considered an adequate candidate for anesthesia and American Society of Anesthesiologist (ASA) scores were recorded for each animal. Dogs with an ASA score of II or III were included in the study.

For each group, premedication was made with butorphanol 0.2 mg/kg and midazolam 0.2 mg/kg administered intramuscularly (IM). Anesthesia was induced with Propofol (4-6 mg/kg IV). Spontaneous or intermittent positive-pressure ventilation (IPPV) were maintained by the use of a volume-cycled ventilator delivering 12-15 breaths/minute to achieve a target end-tidal CO_2 of 35-45 mm/Hg. Oxygen flow was initially delivered at 2 L/min with the vaporizer set to achieve an end-tidal concentration C% of 2.0% isoflurane within 10 minutes of induction. After the target concentration was achieved, oxygen flow was decreased to (500+10/kg) L/min, and isoflurane was constantly maintained at 1.5 vol. % in all cases.

Crystalloid solutions were administered at a rate of 3-5 ml/kg/h IV throughout anesthesia. ECG, heart rate, $etCo_2$, SpO_2 and esophageal temperature were monitored. Temperature was maintained between 37ºC-38 ºC by using a warm electrical blanket.

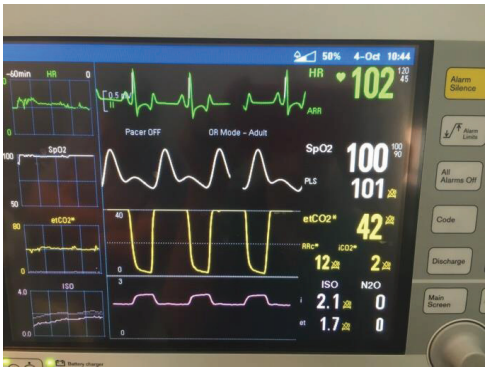

Fig. 1. Patient monitoring

At the end of the surgery the isoflurane was switched off and the residual anesthetic was flushed from the breathing circuit. Patients were extubated when they began to breathe spontaneously. The patients were taken into the ICU department where they received, according to the group classification: tramadol 2 mg/kg IV every 12 hours, patients from Group 1, Group 2 a CRI with Lidocaine (1 mg/kg IV ``loading dose`` then 0.025 mg/kg/min), acetaminophen 10 mg/kg every 12 hours was given to Group 3 and for the 4th group, a mixed Lidocaine and Ketamine in a CRI was administered (Lidocaine 1 mg/kg ``loading dose then 0.025 mg/kg/min + Ketamine 0.2-2 mg/kg/h).

All patients were evaluated using the Glasgow Composite Pain Scale (GCPS). Behavior categories used to assess pain included vocalization, attention to wound area, mobility, response to touch, demeanor and posture/activity. A categorical score was assigned within each behavior category based on the severity of the behavior or the response observed (Table 1). Potential cumulative pain scores ranged from 0 (least painful) to 23 (most painful). To ensure interpretative consistency, a single person was trained in evaluating the dogs for pain. The person was blinded to treatment. The person first observed the dog`s behavior from a distance so as not to disturb the dog, then the assessor increased his interaction with the dog, including manipulation of the surgical site and removing the dog from the cage to allow the dog to move around.

Table 1. Glasgow Composite Pain Scale (GCPS)

Behavior Category	Score	Definition
Vocalization	0	Quiet
	1	Whimpering or crying
	2	Groaning
	3	Screaming
Attention	0	Ignoring
	1	Looking
	2	Rubbing
	3	Chewing
Mobility	0	Normal
	1	Lame
	2	Slow or reluctant
	3	Stiff
	4	Refuses to move
Response to touch	0	Do nothing
	1	Looks around
	2	Flinch
	3	Growl or guard area
	4	Snap
	5	Cry

Demeanor	0	Happy and content and bouncy
	1	Quiet
	2	Indifferent or nonresponsive to surroundings
	3	Nervous, anxious or fearful
	4	Depressed or nonresponsive to stimulation
Posture/ activity	0	Comfortable
	1	Unsettled

Based on the dogs' response, each of the six behavior categories were scored. Records of the GCPS for each patient were assessed at 15 min., 30 min., 45 min., 1, 2, 6 and 12 hours after the analgesic drug was given. The results for the four groups were compared and analyzed according to the protocol`s effect at 12 hours after the first administration.

All dogs were observed for adverse reactions following pain medication therapy. Adverse reactions were characterized as minor if they were self-limiting and did not require additional therapy. Minor reactions included sedation, dysphoria, salivation and loss of appetite.

RESULTS AND DISCUSSION

Four treatment groups were created with a number of 15 patients in each group and a total of 60 dogs.

Breeds of dogs included mixed breed dogs (n=26), Labrador Retrievers (n=11), Golden Retrievers (n=6), German Shepherd Dog (n=4), Bichon (n=10), West Highland Terrier (n=3).

The analgesic protocols were well tolerated throughout the study period. Minor adverse effects occurred in 3/15 (20%) dogs from Group 3 which had a Lidocaine + Ketamine medication therapy, represented by salivation and vocalization versus 0 adverse effects reported in the other three groups. Overall 5/60 (8.33%) dogs required additional rescue analgesic therapy based on their pain scores. This included 3 dogs from Group 1 treated with tramadol, and 2 dogs from Group 4 treated with acetaminophen.

During the evaluation period, the best results were recorded in groups 2 and 3 which were given lidocaine and lidocaine+ketamine in a constant rate infusion with a pain scale of 2/24, compared with a poor result in groups 1 and 4 with a Glasgow pain score of 5/24, where additional analgesic medication was needed.

Table 2. Adverse effects and additional rescue doses of drugs

	Nr.	Adverse effects of the analgesic drugs	Additional rescue doses
Group 1 Tramadol	15	0	3
Group 2 Lidocaine	15	0	0
Group 3 Lidocaina+ Ketamina	15	3 salivation vocalization	0
Group 4 Acetaminophen	15	0	2

Analgesic drugs have been widely used for postoperative pain management in dogs (Wagner et al., 2002; Steagall et al., 2006; Lin et al., 2008; Uilenreef et al. 2008; Ortega & Cruz, 2011; Columbano et al., 2012). In this study, we compared the effects of acetaminophen, tramadol, lidocaine, lidocaine and ketamine administered postoperatively as analgesics for dogs that underwent soft tissue surgeries. We found a difference in clinical analgesic effects of acetaminophen and tramadol compared with Lidocaine and Lidocaine/Ketamine constant rate infusion.

A Glasgow Composite Measure Pain Scores through the study period were different between groups 1 and 4 compared to groups 2 and 3.

Tabel 3. Evaluation of GCPS at 12 hours after drug administration

	G 1	G 2	G 3	G 4
Vocalization	1	1	0	1
Attention to wound	0	0	0	0
Mobility	2	1	1	2
Response to touch	1	0	0	1
Demeanor	1	0	0	1
Posture	0	0	0	0

G1-Tramadol, G2- Lidocaine CRI, G3- Lidocaine+Ketamine CRI, G4- Acetaminophen

According to our study this may represent the low capacity of tramadol and acetaminophen to

produce acceptable levels of analgesia in the immediate postoperative period, when used in singular analgesic protocols.

CONCLUSIONS

This study represents a clinical investigation of acetaminophen, tramadol, lidocaine and lidocaine/ketamine analgesia in geriatric dogs.
Based on this study, the analgesic effect of tramadol and acetaminophen at the doses of 2 mg/kg iv respectively 10 mg/kg iv were not satisfactory compared with the analgesic effect given by the continuous infusions of Lidocaine at 0.025 mg/kg/min with a loading dose of 1 mg/kg iv. and Lidocaine (1 mg/kg loading dose then 0.025 mg/kg/min CRI) +Ketamine (0.2-2 mg/kg/h CRI).
Some adverse reactions were recorded after administration of Ketamine+Lidocaine, like vocalization and salivation, therefore we recommend the use of Ketamine with another analgesic drug that also has sedative effect.
A multimodal analgesia it is considered to be effective in reducing postoperative pain after soft tissue procedures.

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