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Review

How Can Better Anaesthetic Combinations Be Performed? A Review of Current Knowledge

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Abstract

In the ever-developing world, the recent years have brought about a wide range of novelties and significant developments in the fields of veterinary anaesthesia and analgesia. In the not-too-distant past, it was believed that the pain threshold of animals was high and that pain was not felt by animals during surgery, when they were anaesthetised. It was considered that the only analgesic drugs that could be used during operation were non-steroidal anti-inflammatory drugs. Today, these suppositions are all accepted as fallacies across the world, and it is well-known that the administration of analgesic drugs should be started in the preoperative period. This article describes pain in animals, how pain perceived by the operated animal can be recognised, and if not treated, to which complications pain may lead. Furthermore, in the last part of the manuscript, complications associated with the use of atropine and α2-agonist combinations, and the adverse effects of anaesthesia-induced hypotension are also explained. This review is intended to provide an insight into recently developed novel practices and to elucidate some main issues, which may be confusing for the veterinary practitioner.

Keywords: *Anaesthesia, Analgesia, Pain, Cat, Dog*

Nasıl Daha İyi Anestezi Kombinasyonları Yapılabilir? Güncel Bilgilerin İncelenmesi

Özet

Gelişen dünya ile beraber son zamanlarda veteriner anestezi ve analjezi alanında da pek çok değişiklikler, yenilikler ve ilerlemeler kaydedilmiştir. Eskiden hayvanların ağrı eşiklerinin yüksek olduğuna ve operasyon sırasında anestezi altında iken ağrının hissedilmediğine inanılırdı. Operasyon sırasında tek kullanılabilecek analjezik ilacın nonsteroidal antiinflamatuvar olabileceği düşünülüyordu. Bu inanışların yanlış olduğu artık tüm dünyada kabul edilmektedir, analjezik ilaçların uygulanmasına preoperatif dönemde başlanması gerekliliği bilinmektedir. Bu makalede, hayvanlardaki ağrı, operasyon sırasında gelişen ağrının nasıl anlaşılabileceği ve tedavi edilmediği takdirde gelişebilecek komplikasyonlar anlatılmıştır. Ayrıca, makalenin sonunda atropin ile α2-agonist kombinasyonlarının komplikasyonları ve anestezi sırasında oluşan hipotansiyonun yan etkileri üzerinde de durulmaya çalışılmıştır. Bu derleme ile veteriner hekimlerin kafalarında karışıklık yaratan bazı konulara ışık tutulması, son yıllarda gelişen yeni uygulamalara ve ilaç kombinasyonlarına yer verilmesi amaçlanmıştır.

Anahtar sözcükler: *Anestezi, Analjezi, Ağrı, Kedi, Köpek*

INTRODUCTION

Anaesthesia means "loss of sensation in the entire body or any part of the body". Most people think that humans or animals do not feel pain during anaesthesia. However, today it is known that without the use of analgesics both humans and animals feel pain during anaesthesia. Most popular general anaesthetics do not have analgesic properties. They provide unconsciousness, but cannot inhibit the nociceptive pathways. No matter how high a dose they are administered at, these agents do not provide analgesia. The animal can feel pain during surgery, however, cannot react because of a surgical plane of anaesthesia. The aim of this review is to present the recognition of pain in animals, basis for analgesic use during anaesthesia, the appropriate time and analgesic combinations for administration, adverse effects of pain, some analgesic medications, methods to overcome possible complications during anaesthesia and the contraindication of using α2-agonists with anticholinergics.

PAIN IN ANIMALS

The International Association for the Study of Pain defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or

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described in terms of such damage [1]. Although great importance is attached to pain management and analgesic therapy today [2], unfortunately, research on analgesic therapy in veterinary medicine does not go back too far in history. The main reason for veterinary research having started late is fallacies. In the not-too-distant past, it was believed that animals did not suffer from pain as much as humans and it was considered that the pain threshold of animals was higher. Today, it is well known that these arguments are false, and it is well established that all procedures that cause pain in humans also cause pain in animals and require analgesic therapy. In the past, the majority of veterinary practitioners believed that pain was protective in that it limited the movement of the animal, and thereby, reduced the risk of tissue lesions. Furthermore, it was thought that, as analgesia masks disease symptoms, analgesic therapy would misdirect treatment. However, today, it is accepted that pain provides very little benefit, and in fact, causes great damage to the body [3-5].

Why Should Analgesics Be Used?

Apart from the ethical perspective and moral compass, treatment of pain has major physiological and biological implications. Pain increases the secretion of catabolic hormones (cortisol, glucagon, and catecholamines) and decreases the secretion of anabolic hormones (insulin, testosterone). Furthermore, pain increases gluconeogenesis, glycogenolysis, proteolysis, and lipolysis, and causes protein loss and the weakening of muscles. Due to reduced collagen synthesis, pain is also associated with delayed wound healing. Stress induces the secretion of the adrenocorticotropic hormone (ACTH), which in return, leads to the secretion of cortisol. As a result of immunosuppression, both immunoglobulin synthesis and the resistance of the individual to diseases, decrease [6,7]. Catecholamines make the heart sensitive to arrhythmia and cause hypertension. The cardiac output and load, heart rate, and the oxygen consumption of the myocardium, all increase. This increase in cardiac parameters is dangerous if the cardiac reserves are low. Increased cardiac load requires a higher level of oxygen, and if the coronary arteries do not pump the required amount of blood to the heart, myocardial infarction occurs [4,8-10].

Renal failure may develop as a result of the vasoconstriction of the renal arteries. Hyperglycaemia occurs. While the respiratory rate increases, the tidal volume and cough reflex decrease, which eventually lead to pulmonary atelectasis. Small airways closed, intrapulmonary shunts and hypoxia are observed. These complications are particularly important in operations performed in the thoracic cavity and in the proximity of the diaphragm. Elevated carbon dioxide levels lead to respiratory acidosis. Acidosis causes arrhythmia and may even result in cardiac arrest [7,11,12].

When in pain, animals avoid movement, and long-term immobility increases the risk of embolism [5]. Pain often results in a prolonged hospital stay, immune suppression and secondary illness, inappetence, and cachexia. This is especially important in cats, in which hepatic lipidosis may occur as a result of inadequate caloric intake [5]. In particular, neuroendocrine responses to posttraumatic and postoperative pain may cause shock and death [4,10].

As there is a link between acute pain and chronic pain, it can be suggested to control acute pain in order to prevent the development of chronic pain [5,9].

Physiological pain is protective. It plays an adaptive role in the body's normal defence mechanism like touching a potentially damaging fire and initiating reflex avoidance strategies. Physiological pain alone is not important in clinical settings. On the other hand, if pain becomes permanent and is associated with severe tissue inflammation and nerve injury, then this type of pain is referred to as "pathological or clinical" pain. The clinical objective should be to minimize pathological pain while maintaining physiological pain [3,4]. It is useful to characterize clinical pain according to its duration, such as acute (recently occurring) and chronic (long-lasting) pain. Acute clinical pain arises from soft tissue trauma or inflammation, with the most common example being postoperative surgical pain. Actually, acute pain plays an adaptive role by facilitating tissue repair. If not promptly treated, acute pain turns into chronic pain. Chronic pain is maladaptive and offers no useful biological function or survival advantage. Cases of very severe acute pain or the development of chronic pain result in the manifestation of a hypersensitivity phenomenon referred to as "hyperalgesia". Hyperalgesia refers to an overly increased sensitivity to painful stimuli, and can be defined as the stimulation of both inactive nociceptive fibers, and high threshold nociceptive fibers, in healthy individuals [10,13]. The most advanced forms of hyperalgesia are allodynia, which refers to pain produced by a stimulus that is not normally noxious, and phantom pain, which is described as perceptions experienced by an individual in relation to a limb or an organ that is not physically part of the body [4]. The pain experienced by a soldier, who receives long-term treatment before an amputation, and even after an amputation he feels as if his arm was not amputated is a good example of phantom pain. Furthermore, the crying of a dog with an osteosarcoma in one of its limbs, when patted on its head, is due to the perception of being touched as pain,as a result of hyperalgesia.

ADDITION OF ANALGESIA IN ANAESTHESIA PROTOCOLS: IS IT NECESSARY OR NOT?

Loss of consciousness does not mean that the pain pathways are inactivated. Most general anaesthetics, including isoflurane, sevoflurane, propofol, and thiopental,

do not have analgesic properties. They provide unconsciousness, but cannot inhibit the nociceptive pathways. No matter how high a dose they are administered at, these agents do not provide analgesia. The patient can feel pain during surgery, however, cannot react because of a surgical plane of anaesthesia. It is still beneficial to inhibit pain pathways by using some analgesic drugs. Nowadays, preemptive and multimodal analgesia have become popular techniques used for this purpose. When general anaesthesia is used for surgery, the administration of drugs with analgesic properties should be included in the anaesthesia protocol [14-17]. Intraoperative use of multimodal analgesic therapy also reduces total anaesthetic requirements and autonomic responses to painful surgical stimulation [10,18-20].

The perception of intraoperative pain by an anaesthetized animal can be understood from an increase in the heart rate and blood pressure. While the anaesthesia continues and the monitored parameters remain stable, a sudden increase observed in the cardiac rhythm and blood pressure (approximately 30%) with the onset of the painful phase of the surgical operation (movement of the fracture ends during osteosynthesis, the distention of the peritoneum during laparotomy or surgical intervention performed near nerves etc.) shows the inadequacy of the analgesia procedure that has been followed as part of the anaesthesia protocol [11,15,21]. A medical malpractice performed in such cases is to administer a higher anaesthetic dose to the operated animal during increased heart rate caused by the perception of pain. In fact, the veterinary surgeon should only reduce the sympathetic stimulus, by deepening the anaesthesia, and should also decrease tachycardia. It should be noted that, if not administered with any analgesic, an anaesthetized animal shall perceive pain, even if unconscious. The adverse effects of pain on the body start during the surgical operation. An animal with postoperative pain is most likely to recover from anaesthesia poorly. In such cases, the animal may even damage the operation site while awakening. While the anaesthetic agents used before the 1980s provided a slow and slumbery recovery from anaesthesia, today, preparations (i.e. propofol, thiopental, isoflurane, sevoflurane), which enable the animal to recover from anaesthesia within only a few minutes after the end of the surgical operation, are available. If adequate analgesia is not achieved, then recovery from the anaesthesia established with these novel agents occurs fast, but also painfully.

In order to minimize intraoperative and postoperative pain, analgesics need to be administered at the appropriate time intervals and at the appropriate doses. In this context, recently, the clinically evolving concept "preemptive analgesia" has gained importance. Preemptive analgesia involves the administration of analgesics before the exposure of the animal to the painful stimulus, and in a sense, implies the elimination of pain even before it occurs. Thereby, pain management can be achieved without the development of hyperalgesia. The most appropriate stage to administer analgesics to an animal scheduled for surgical operation is the preoperative period [8,15,22,23].

Both the mechanism of action and the time course of the effects of all analgesics, which are routinely used in clinical practice today, are well known. The prior administration of the analgesic preferred for the surgical operation to be performed, and the repetition of the dose at the half-life of the analgesic, followed by an appropriate use of the agent in the postoperative period, will ensure that the patient recovers with little or no pain. It should be borne in mind that no analgesic can set pain to zero. Therefore, the goal of the administration of analgesics should be to eliminate pain or, at the very least, make the animal comfortable [14,15].

ANALGESICS THAT CAN BE USED DURING OPERATION

As each animal presents with varying levels of injury or illness, and experiences different levels of pain, individual drug selection and dosage are essential rather than the application of a standard protocol for all patients. Several groups of analgesic drugs are available for use in cats and dogs, which include opioids, α2-agonists, ketamine, NSAIDs (nonsteroidal antiinflamatory drugs) and local anaesthetics [9,10,24,25] that have been explained in below.

Opioids

Opioids are the most commonly preferred drugs for intraoperative and early postoperative analgesia. Their analgesic effect is strong as they block several pain pathways [10,26]. The most commonly used opioid drugs in Turkey are morphine, butorphanol and fentanyl. Some of the adverse effects associated with the use of these drugs are bradycardia, respiratory depression, hypotension, agitation and emesis. Although opioids are generally feared to have serious side effects, in contrast to human beings, cats and dogs seem to be remarkably resistant to these side effects, and serious side effects are surprisingly rare when these agents are used with care [8,11,27]. For example, opioid induced-bradycardia is generally not life-threatening and usually does not require treatment. Often it can be ameliorated with fluid therapy. If the patient is hypovolemic, hypovolemia should be treated before opioid-induced bradycardia, because no benefit has been shown to be achieved with anticholinergics in the hypovolemic patient [9]. As opioid induced-bradycardia is vagally mediated, when necessary, treatment can be accomplished with anticholinergic drugs (atropine or glycopyrrolate) [28]. Although clinically significant respiratory depression from opioids is uncommon, it can occur when opioids are combined with other drugs that have respiratory depressant effects. Bradycardia and hypotension are mostly observed when

opioids are administered intravenously [11,13,19]. The greatest advantage of opioids is the ability to titrate their dose to effect; and if an overdose or side effects occur, naloxone, which is an opioid antagonist, can also be titrated to remove these adverse effects as the analgesic effect continues [5,28].

The cheapest opioid in our country, and in the world, is morphine. It is a very effective analgesic in dogs and cats, and its dose should be calculated precisely when used in cats. If the clinician is not familiar with the use of opioids, and fears about side effects, a safeway of use is to administer effective low doses of opioids to healthy and young animals for the desired effect (e.g. sedation, relaxation, termination of pain, and maintenance of tranquilization during manipulation) [11]. If the desired effects do not occur within 3 minutes after intravenous administration then the dose is repeated until the desired effect is achieved. Once the analgesic and relaxing effects of the opioid is observed, the veterinary clinician may easily prefer to widen the scope of use of opioids. Occasionally, agitation and anxiety can be recorded and many of these patients vocalize continuously while treated with morphine. If a dog develops this type of response, the clinician has 5 options: (1) administering higher doses of morphine as higher doses cause sedation, (2) administering α2-adrenergic agonists both for sedation and additive analgesic effect, (3) combining the first and second options, (4) reversing the effect with the intravenous administration of butorphanol (as butorphanol is a mixed agonist-antagonist opioid, its analgesic effect continues while anxiety disappears as a side effect) and (5) administering naloxone for the reversal of the effect of morphine. As naloxone is an opioid antagonist, dose calculation (0.001-0.02 mg/kg, IM, IV) should be made carefully, because high doses of naloxone antagonize both the analgesic and its side effects [11,29]. Matthews [30] recommended using the naloxone dilution technique to reverse the side effects of opioids while their analgesic effects continue. When this technique is used for larger animals, 0.25 ml of naloxone (0.4 mg/ml) diluted in 10 ml of saline is used for titration. Once the side effects are reversed and a state of rest is achieved, the administration is terminated.

The first choice for animals, which are referred to the clinics for trauma or acute pain (e.g. peritonitis, pancreatitis) and cannot be treated due to this pain, should be opioids. These patients may also present with premature ventricular contractions (PVCs) or tachyarrhythmia as a result of trauma and/or pain. Attempts to control pain with the administration of sedatives or anaesthetics may cause further cardiovascular deterioration. The administration of opioids to these patients for analgesia can also be advantageous by enhancing the vagal tone [9,11].

Cats have a low tolerance to high doses of morphine and they more often show disorientation and agitation, and overdose often produces delirium. Hansen [11] recorded that marked mydriasis occurs after the administration of an adequate analgesic dose, and suggested that further administration of opioids after the onset of mydriasis is much more likely to produce agitation. Because of the common side effects of morphine in cats, butorphanol might be the first choice for cats with mild to moderate pain.

Adjuvant Analgesics

Adjuvant analgesic drugs are not first-choice analgesics and are generally used in combination with other known traditional analgesics as a part of the multimodal analgesic approach. Multimodal analgesia refers to the blockade of different pain pathways by the combined use of various analgesics and techniques. Thereby, an effective analgesia is achieved at low doses and with little side effects through the synergistic effects of different pharmaceuticals [25]. The pharmaceuticals most commonly used for multimodal analgesia are ketamine, α2-agonists, lidocaine, and tricyclic antidepressants like gabapentin.

Ketamine has been used as an anaesthetic agent for more than 30 years in veterinary medicine. Ketamine belongs to the group of dissociative anaesthetics and its high doses are combined with other agents for general anaesthesia. In the 1980s, it was discovered that ketamine was an antagonist of the N-methyl D-aspartate (NMDA) receptors in the spinal cord. Since this discovery, ketamine has been used as an adjunctive analgesic in humans. In clinical practice, it is suggested that low doses of ketamine be used for analgesia. When administered at low doses, ketamine can enhance analgesia and eliminate the hypersensitivity phenomenon [31]. Thereby, it also aids in the management of acute postoperative pain, acute posttraumatic pain, neuropathic pain, preoperative analgesia, and chronic pain [13,14,30,32,33]. Slingsby and Waterman-Pearson [34] reported that the preoperative and postoperative administration of 2.5 mg/kg of ketamine by intramuscular route to animals anaesthetized for ovariohysterectomy reduced the total pain score, and decreased both the need for rescue analgesia and the risk of postoperative wound hyperalgesia, in comparison to the control animals. In another study [35], it was shown that, when administered to cats as an analgesic agent at different doses, ketamine reduced the minimum alveolar concentration (MAC) of isoflurane by 45-75%. Muir et al.[36] reported that the administration of a ketamine infusion of 0.6 mg/kg/h to dogs reduced the MAC of isoflurane by 25%. Furthermore, Wagner et al.[37] indicated that, the preoperative and postoperative administration of ketamine to dogs, which underwent forelimb amputation, reduced the pain score. These researchers also observed that the operated animals, which were administered with ketamine, were more active during the first 3 days after operation, in comparison to the animals, which were not administered with ketamine. In many other similar studies, ketamine has been suggested to be administered as a constant rate infusion (CRI) and to be included in balanced anaesthesia protocols. Like α2-adrenergic agonists, ketamine

can also be combined with opioids to reduce the total opioid dose for the management of pain [21,29,32].

α2-*adrenergic agonists* (xylazine, medetomidine) are preferred for preemptive analgesia, yet their analgesic effects are not as strong as those of opioids. Therefore, they are considered to be inadequate for producing the intraoperative analgesia required for very painful surgical operations (osteosynthesis, cervical disk operations, spinal cord operations, amputations, neurosurgery, total ear canal operations, etc.). The combined administration of α2-adrenergic agonists with opioids may result in additive or synergistic drug interactions, and thereby, reduce the dose of the analgesic drug used [10,14,25,32,38,39]. The combination of medetomidine and ketamine is mostly preferred for castration and ovariohysterectomy in cats and dogs in many countries. However, it is important to recognize that although adequate analgesia is achieved with the use of α2-adrenergic agonists and ketamine, the duration of this analgesia is limited to, and often less than that of the sedative effect [24,32,40].

Lidocaine, in addition to its local anaesthetic effects, has been shown to alleviate hyperalgesia and to reduce opioid requirements during and after surgery when administered as a constant rate infusion [9,32]. While the mechanism underlying the nervous transmission block caused by the peripheral administration of lidocaine has been completely resolved, the analgesic mechanism of the intravenous administration of lidocaine is yet not solved. Several researches conducted in humans have shown that, following major abdominal operations, lidocaine increases gastrointestinal functions, reduces postoperative pain and the need for the use of opioids, and also shortens the hospitalization and rehabilitation periods [32,41,42]. A single dose of 2 mg/kg lidocaine should result in a short period of analgesia and MAC reduction. For this reason, it may be added to anaesthesia induction protocols [9]. While it has been shown that the administration of lidocaine, as a CRI of 0.05 mg/kg/min, reduces the MAC of isoflurane by 19-29% in dogs anaesthetized with isoflurane [36,43], it has also been reported that the use of lidocaine infusions up to 0.12 mg/kg/min are safe in dogs anaesthetized with isoflurane [44]. Pypendrop and Ikliw [45] have reported that cats are sensitive to lidocaine toxicity, and have suggested this agent not to be used in cats as it causes cardiovascular depression during anaesthesia.

Constant rate infusions (CRI) have recently gained popularity in perioperative (pre-, intra-, and post) analgesia [17,46,47]. There are several advantages to this technique, as a steady level of analgesia is more likely to be achieved and the mountains and peaks associated with intermittent analgesic use are avoided. Morphine, lidocaine and ketamine can be added to the intravenous solution. 12 mg of morphine, 150 mg of lidocaine and 30 mg of ketamine in 500 ml of surgical fluid, dripped at the standard surgical fluid rate (10 ml/kg/h), provide analgesia and MAC reduction during surgery. Multimodal analgesia can be achieved with this cocktail solution. If prepared under sterile conditions, it can be stored for use for a long time. In addition, this cocktail can be administered for postoperative analgesia at a dose of 2 ml/kg/h [24]. The author frequently uses triple combinations in dogs and dual combinations (morphine and ketamine) in cats due to their sensitivity to lidocaine.

Nonsteroidal Anti-Inflammatory Drugs (NSAIDS)

Systemic inflammatory response sensitizes the peripheral nervous system and can turn a normal somatic stimulus into a painful stimulus (remember how you felt last time when you had a fever!). This is because of the systemic release of inflammatory mediators [11]. As well as having central analgesic effects, NSAIDs may also reduce the peripheral inflammatory response associated with surgery, and thus, may provide sufficient analgesia for mild to moderate pain [25,29].

Once acute severe pain is controlled with an opioid, NSAIDs may be administered. The NSAIDs most commonly used in cats and dogs are ketoprofen, meloxicam, tolfenamic acid, flunixin meglumine, and carprofen (carprofen is registered only for dogs and can be used only once in cats). NSAIDs should be avoided until the renal, hepatic, circulatory, and coagulation status of the patient is known [5,14,28,29].

COMBINATION OF ALPHA2-AGONISTS WITH ANTICHOLINERGICS FOR ANAESTHESIA: IS IT RIGHT OR NOT?

α2-agonists, including xylazine, medetomidine and dexmedetomidine, are the most widely used sedatives in veterinary medicine [3,21,48-51]. These drugs are also administered during general anaesthesia to improve analgesia and to decrease the dose of the anaesthetics used. The most commonly observed clinical side effects after the administration of α2-agonists are peripheral vasoconstriction and reflex bradycardia [32,51,52]. There is no doubt that if bradycardia becomes profound, it should be treated. The question is: "Should we use anticholinergics for the treatment of bradycardia to save life or not?" Formerly, atropine had been frequently used to prevent bradycardia induced by α2-agonists [53], and the data sheet (package insert) for Rompun (commercial xylazine preparation) states that premedication with atropine may be advantageous in dogs. However, data reported in previous studies is based on the assessment of only the heart rate. For the past 20 years, it is known that such a correction is not always advantageous [53,54]. The administration of anticholinergics before α2-agonists effectively prevents bradycardia. However, the administration of anticholinergics either prior to, at the same time with, or after high doses

of medetomidine has been shown to result in severe hypertension, tachycardia, tachyarrhythmia, atrioventricular blockade, and pulsus internans [1,53,55-59]. There are contradictory opinions with respect to the prevention and treatment of α2 agonist-induced bradycardia. Some authors have recommended reversal with α2-agonists as the safest remedy for α2 agonist-induced bradycardia [1,53,58].

The underlying mechanism of α2 agonist-induced bradycardia can be explained as follows: α2-agonists show biphasic effects on blood pressure. Their first effects are vasoconstriction, caused by the activation of the peripheral α2-receptors of blood vessels, and resulting hypertension. Systolic blood pressures of approximately 200-250 mmHg have been recorded in dogs [32,52,53,57,58,60]. The vasoconstriction observed in the periphery also occurs in the coronary arteries, which decreases the blood flow, and thus, the amount of oxygen transported, to the heart. Due to the subsequent deepening of anaesthesia and the decrease of the sympathetic tone, the hypotensive phase occurs, during which bradycardia develops [1]. The occurrence of bradycardia when the blood supply of the heart decreases, is in fact a compensatory response, as it reduces the activity of the heart muscle, and thereby, decreases the oxygen and energy requirements of the myocardium.

Although anticholinergics alleviate the decrease in heart rate following the administration of α2-agonists, these drugs also increase the magnitude and duration of the hypertensive phase caused by α2-agonists. It has also been reported that, in dogs, hypertension is even greater when higher doses of α2-agonists are used [54]. The administration of anticholinergics, including atropine and glycopyrrolate, disrupts this compensation mechanism and causes an increase in heart rate and myocardial oxygen consumption. The administration of anticholinergics when the coronary arteries are constricted, in other words, when the myocardial blood supply is decreased, is a fatal mistake, as the oxygen and energy requirements of the myocardium increase if cardiac perfusion is not improved [1,59].

In clinical practice, α2-agonists are mostly used in combination with ketamine to establish anaesthesia, as ketamine has sympathomimetic effects. In other words, ketamine not only increases heart rate and cardiac output, but also arterial pressure and myocardial oxygen consumption. Therefore, hypotension and bradycardia induced by α2-agonists can be ameliorated, to some degree, by subsequent ketamine administration. The concurrent administration of anticholinergics with α2 agonist-ketamine combinations should also be avoided, because a prolonged high heart rate may occur. Xylazine-ketamine combinations are usually restricted to healthy animals and should not be used in patients with myocardial disease or reduced cardiopulmonary reserve [1].

HYPOTENSION DURING ANAESTHESIA

Hypotension is the most common perianaesthetic complication in veterinary patients. Normal systolic, diastolic, and mean arterial blood pressures in nonanaesthetized small animals are 100-160, 60-100, and 80-120 mm Hg, respectively. If systolic and mean blood pressures are measured below 80 and 60 mm Hg, respectively, this condition is referred to as hypotension. Hypotension, if not treated, can result in decreased perfusion to vital organs and death. Various anaesthetic agents such as α2-agonists, propofol, thiopental, isoflurane, sevoflurane, and opioids have hypotensive effects. Intravenous crystalloid fluid solutions at a dose of 10 ml/kg/h should be given to alleviate anaesthesia-induced hypotension. Treatment of acute blood loss due to haemorrhage includes crystalloid fluid replacement at a dose of three times the blood volume lost [61-63]. If intraoperative anaesthesia is deeper than required, side effects resulting from hypotension and hypertension increase.

When the animal is hypotensive, nonsteroidal anti-inflammatory drugs should not be used because they prevent the production of prostaglandins. Prostaglandins (PGs) have an important role in the auto-regulation of renal blood supply. As NSAIDs inhibit the production of PGs, their use in hypotensive, bleeding and dehydrated animals, may cause nephron damage and lead to complications as severe as acute renal failure. For this reason, if there is a risk of intraoperative hypotension (in view of the most anaesthetic drugs is hypotensive and some clinicians performing intraoperative fluid administration at an almost negligible level, which both imply that the majority of anaesthesia procedures are associated with the occurrence of hypotension), it is suggested that NSAIDs should not be used [5,14,28,29].

CONCLUSION and RECOMMENDATION

None of the drugs used to establish anaesthesia and analgesia are perfect, and further research is conducted with an aim to achieve the best intraoperative anaesthesia and analgesia with the least complications. Combination of drugs is essential for multimodal analgesia and balanced anesthesia. Without multimodal treatment, we cannot achieve a perfect anaesthesia. It should also be noted that, the addition of analgesic drugs to anaesthetic combinations not only lowers the amount of anaesthetics required, but also reduces the risk of complications that may result from the use of high doses of anaesthetics. Clinicians must be prepared to determine the best choice.

In conclusion, if we do not try novel drugs and persist with using conventional drugs, we can never do “better”.

Various analgesic and anaesthetic protocols are available for cats and dogs, and it is recommended that "tried and true" guidelines be used rather than "sticking to traditional or outdated dogma".

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