Effect of pre-emptive intra-articular analgesia on recovery, postoperative pain and Serum Amyloid A in horses undergoing arthroscopy

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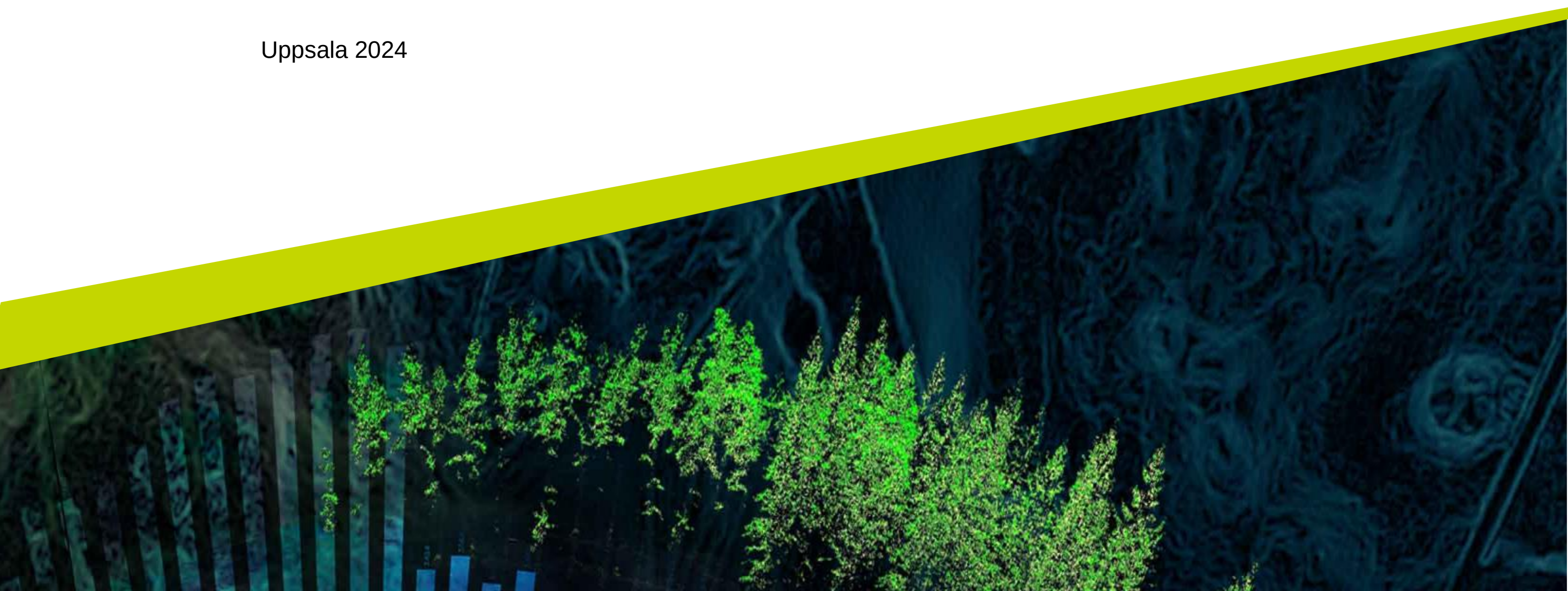

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Intra-artikulär analgesi och dess effekt på anestesi, uppvak, postoperativ smärta och Serum Amyloid A hos hästar som genomgår artroskopi

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Abstract

One of the most common reasons for orthopaedic pain in horses is osteochondrosis and osteochondrosis dissecans, which is a result of disturbance in the growth of the endochondral bone. A part of the treatment and diagnosis is arthroscopy, a type of surgery which is commonly performed at most large animal hospitals. In human studies arthroscopy has been classified as a painful surgery. However, today there is no standardised protocol for analgesia during this procedure, and it is the surgeon's discretion if intra-articular analgesia is to be administered or not in connection with the surgery. There are different opinions considering this matter; some surgeons says that arthroscopy is not a painful procedure, and that intra-articular analgesia can cause damage to the cartilage, while other claims that a multimodal analgesia and pain control results in a faster and better recovery and healing of the tissue, as well as improving animal welfare.

The purpose with this study was to examine if pre-emptive analgesia, in the form of an intra-articular administration of mepivacaine, decreases the intra- and postoperative pain in horses undergoing arthroscopic surgery in the fetlock, hock, and stifle. A total of 15 horses were included in the study, three of them received treatment and 12 horses received an injection with saline (controls). Evaluation of pain was done using a composite pain scale which incorporates both physiological and behavioural aspects. There were no significant differences in anaesthesia, recovery, postoperative pain score or SAA between the groups. The reasons for this may be due to the small number of horses included in each group and variability within group due to other biological factors. Therefore, the results were inconclusive and further investigation is needed.

Keywords: Arthroscopy, pain, OC, OCD, intra-articular analgesia, anaesthesia, recovery, pain score, SAA

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Abbreviations

CPS	Composite Pain Scale
EPS	Equine Pain Scale
EQUUS-FAP	Equine Utrecht University Scale of Facial Assessment of Pain
HGS	Horse Grimace Scale
IASP	International Association of the Study of Pain
NSAID	Nonsteroidal anti-inflammatory drugs
OC	Osteochondrosis
OCD	Osteochondrosis dissecans
SAA	Serum Amyloid A
SLU	Swedish University of Agricultural Sciences
UDS	University Animal Hospital

1. Introduction

Today many of the treatments and surgeries are performed during a balanced anaesthesia and with multimodal analgesia, which makes it easier to reduce pain caused by painful events during surgery. This is important for maintaining the welfare of the horse. The majority of horses arriving at large animal hospitals experience a degree of pain, as a result of an injury or an acute or chronic illness. The source of the pain can be activation of different nociceptors, and the pain can be associated with traumatic events or other disease mechanisms. Pain experience is a result of an emotional and sensory perception, and that, according to IASPs definition, is influenced by physiological, biological and social factors (IASP Announces Revised Definition of Pain [IASP 2020]). When assessing pain in horses, methods mainly focus on the emotional part since this is the part, which results in a change of behaviour. Examples of this are interactive behaviour, appetite, posture, or presence of pain face, all which lately have taken a bigger role in pain recognition in horses. Controlling pain related to surgery or other treatments does not only ensure good animal welfare, but also ensures faster and better recovery and healing of the tissue (Goldberg & Shaffran 2014; Gleerup & Lindegaard 2016). In the editorial "Pain therapy in horses" by Muir (2005), the author mentions that all pain therapy must be adapted to the specific individual, as well as the analgesia selected must be suitable for the severity and type of pain that is supposed to be treated. The author also mentions the importance of pre-emptive analgesia in decreasing the risk of developing central sensitisation, which in some cases can result in chronic pain.

One common elective surgery in horses is the arthroscopic removal of joint fragments in relation to OC. Osteochondrosis is a result of disturbance in the growth of the endochondral bone, and it is a common reason for orthopaedic pain in horses (James et al. 2016; Naccache et al. 2018; Bourebaba et al. 2019). One manifestation of OC is OCD, which causes inflammation, and may consequently result in pain and lameness. If joint fragments are not removed, they may cause lameness, which in athletic horses can result in the end of their career causing an economic loss for the owners (Agreste et al. 2021). Arthroscopy performed to remove joint fragments causes intra- and peri-articular trauma, which varies in intensity. In some instances, the surgeon only inspects the joint without intervention, whilst in others, arthroscopic removal of a bone fragment or other invasive interventions take place. Today there is no standardised analgesic protocol during this procedure, and it is the surgeon's discretion if intra-articular analgesia is administered or not. There are different opinions considering this matter; some surgeons says that arthroscopy is not a painful procedure, and that intra-articular analgesia can cause damage to the cartilage (Adler et al. 2021), while others claim that a multimodal analgesia and pain control results in a faster and better recovery and healing of the tissue, as well as improving animal welfare (Goldberg & Shaffran 2014). In human studies, arthroscopy has been classified as a painful surgery (Pavlin et al. 2004). Since the cartilage in the joint has a lack of neural innervation, it is not the interaction with the cartilage that causes the pain during an arthroscopy, but it is the interaction with the synovial membrane, which the surgeon must pass through when entering the joint (Park et al. 2011).

An earlier study on the subject has been performed, that evaluated the effect of intra-articular administration of mepivacaine on different anaesthetic variables like arterial blood pressure, heart rate and total isoflurane concentration intraoperative (Gaesser et al. 2020). Since the study was performed on horses under general anaesthesia, the parameters measured during the surgery were proxies for pain and could therefore be a result of reflexes. The result of the study was that the horses which received mepivacaine had fewer detectable reactions to surgical simulation, but there was no difference in recovery or blood pressure. This study focused on arthroscopy of the carpal joint. Therefore, the purpose of this thesis was to examine if pre-emptive analgesia, in the form of an intra-articular administration of mepivacaine, decreases the intra- and postoperative pain in horses undergoing arthroscopic surgery in fetlock, hock, and stifle. The study used a recovery rating scale, a behaviour-based pain assessment tool, and measurement of SAA concentration in blood to assess the degree of trauma induced by the surgery.

2. Literature review

2.1 Pain

Pain experience is complex, as it is the result of both an emotional and sensory perception. IASPs definition of pain in humans is:

> "An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage.
>
> Six key notes and etymology:
> - Pain is always a personal experience that is influenced to varying degrees by biological, psychological, and social factors.
> - Pain and nociception are different phenomena. Pain cannot be inferred solely from activity in sensory neurons.
> - Through their life experiences, individuals learn the concept of pain.
> - A person's report of an experience as pain should be respected.
> - Although pain usually serves an adaptive role, it may have adverse effects on function and social and psychological well-being.
> - Verbal description is only one of several behaviors to express pain; inability to communicate does not negate the possibility that a human or a nonhuman animal experiences pain." (IASP 2020)

Many of these cues also makes sense for animals. However, it is noted that verbalizing is not necessary to be able to experience pain. The sensory perception of pain is the cause of activation of nociceptors (Muir 2010). Nociceptors are high-threshold receptors, and the ones most associated with trauma and surgery are the nociceptors related to peripheral and central sensitisation (Muir 2005; Bussières et al. 2008). Peripheral sensitisation is developed when peripheral nociceptors are activated by a change in the local environment, for example by a change in temperature, pH, or electrolytes. Central sensitisation is developed when peripheral nociceptors are activated by an injury, for example during a surgery. Central and peripheral sensitisation are similar when looking at the molecular mechanisms since both result in an increase in inflammatory mediators and upregulation in complex enzyme systems.

The pain pathway can be divided into transduction, transmission, modulation and perception (Goldberg & Shaffran 2014). Transduction is the activation of the nociceptors, which initiates the nociceptive process, the encoding and processing of a noxious stimulus. The stimulus that the nociceptors receive is translated into electrical signals which travels along afferent nerve fibres. During the transmission phase the electrical signals are picked up by nerve endings and are thereafter transmitted to the central nervous system (CNS). In the modulation phase, the transmissions impulses can be either inhibited or amplified. This is done via ascending pathways in the dorsal horn, which is an area that consists of interneurons which transmits information to the somatosensory cortex in the cerebrum. Here, the perception and awareness of pain take place.

Nociceptive pain is essential for our survival by its activation of withdrawal reflexes and behavioural as well as autonomic nerve system responses, which helps in preventing tissue damage (Muir 2005). Pain is also strongly associated with stress since the awareness and experience of pain results in a higher circulating concentration of adrenaline and glucocorticoids (Goldberg & Shaffran 2014). When assessing pain in non-human animals there are different aspects that should be taken into consideration, like for example physiological response, functioning of the body and behaviour (McLennan et al. 2019). An increase in heart rate and body temperature is not always an indicator of pain but can merely be a result of stress. Stress can in some cases induce typical facial expressions related to pain (Lundblad et al. 2021), but it can also induce some degree of analgesia (Butler & Finn 2009). However, as mentioned earlier in this section, pain is not always necessarily a negative thing, since it is also a survival instinct (Muir 2005; Goldberg & Shaffran 2014). It is important to bear in mind that pain is a protective mechanism, which during evolution has helped the species survival (Gleerup & Lindegaard 2016).

Furthermore, pain can be either acute or chronic (McLennan et al. 2019). The acute pain does not extend beyond the healing process, and the inflammation and damage that causes the pain responds to drugs used as part of pain therapy. Chronic pain is more complex and induces changes in the central nervous system. It extends beyond the healing process in comparison with acute pain. Postoperative pain is classified as acute pain, with pain driven by nociception in relation to the tissue trauma and inflammation.

2.1.1 Measurement of pain

Pain has a large emotional component, which is expressed by the horses' behaviour. There are also physiological markers, for example serum cortisol, that have a correlation to pain (Robertson et al. 1990; Gleerup & Lindegaard 2016), however, these physiological markers measure nociception, which is not necessarily the same thing as the horse's perception of pain. As mentioned in IASPs definition of pain – nociception and pain should not be mistaken for the same thing. Factors influencing the display of pain related signs in horses include the presence of stress (Lundblad et al. 2021).

Cortisol concentrations are associated with pain, but cortisol levels are also influenced by several other factors, for example anaesthesia and drug treatment, which can make it hard to evaluate when looking at pain in relation to a specific surgery. An older study examining the concentrations of serum cortisol in horses undergoing arthroscopic surgery has been performed by Robertson et al (1990). The authors reached the conclusion that there was a significant peak in cortisol concentration towards the end of surgery, however the concentration went back to normal only a few hours postoperatively.

2.1.2 Pain related behaviour

Horses express pain in different ways. As mentioned above, pain is mainly an emotional experience, which can make it hard to evaluate since horses are not capable of verbal communication. Even though specific pain behaviours are well described, horses are also individuals. Early exposure to pain can lower the threshold of the nociceptors, resulting in an increase in pain related behaviour in the adult horse (McLennan et al. 2019). However, display can also be influenced by several other factors, for example human interference, stress, or anaesthetics. Even the sex of the horse can influence the expression of pain, where male horses tend to express less pain related behaviour compared to females. Despite all these factors, it has been showed that behavioural expressions are more valid in assessing pain than any biochemical or physiological marker (Ashley et al. 2005).

In a study examining facial looks in horses during pain, the equine pain face was described as a display of facial actions involving withdrawn or tense stare, dilated nostrils and tension in the lips, chin, and facial muscles (Gleerup et al. 2015). By observing the simultaneous occurrence of these expressions, one can assess if a horse experiences pain or not. Other behavioural expressions which are indicators of pain are kicking at the abdomen (visceral pain), pawing with the front legs, turning the head to look at the painful area, head movement and reaction to palpation (Bussières et al. 2008). What type of pain related behaviour a horse expresses also depends on the source of the pain, for example if it is somatic, including orthopaedic pain, or visceral (Goldberg & Shaffran 2014). All these expression types can be used for the construction of behaviourally based pain assessment tools.

2.1.3 Pain assessment

Systematic assessment of pain is useful when working with horses because it is a form of validation if the horse experiences pain or not during a course of disease. In addition, using a scale for assessment makes it faster and more reliable for clinicians to valuate different patients. According to Gleerup & Lindegaard (2016), the greater challenge is to recognize and evaluate the pain – and thereby a great responsibility is on the observer. Measurements used for evaluating pain should be valid and reliable (Bussières et al. 2008; McLennan et al. 2019).

To be able to notice a difference in behaviour it is important to create a baseline. By studying the horse before a surgery or a noxious stimulus it is possible to compare the results and therefore notice a behavioural change. By adjusting the drug treatment to the surgery and expected trauma, the horses should experience less pain and therefore fewer behavioural changes should be noted. Since mammals have the same neurobiological setup, surgeries which are classified as painful in human will most likely result in pain in other mammals as well (Poulter et al. 2018).

There are several different scales that can be used to evaluate pain in horses. In an earlier study performed at SLU, the authors Ask et al. (2020) compared four different pain scales (HGS, EQUUS-FAP, EPS and CPS) and their correlation with induced orthopaedic pain and movement asymmetry in horses. The authors reached the conclusion that posture, behaviour and facial expression were the pain scale items mostly related to orthopaedic pain and movement asymmetry in horses. Posture was strongest associated with orthopaedic pain, which is a part of the CPS- and EPS-scale (Ask et al. 2020). HGS and EQUUS-FAP mostly assess presence of the equine pain face.

Composite pain scale

CPS-scale has been validated for orthopaedic pain (Bussières et al. 2008). The scale is composed by a number of multifactorial numerical rating and include both behavioural and physiological parameters. All individual categories are rated between 0-3, where 0 is normality (no signs of pain) and 3 is when all the modalities consistent with pain is acquired. Finally, all scores summed and the total score of the rating is 39. The pain assessment is performed over a period of 5 minutes.

When evaluating orthopaedic pain in horses, physiological parameters do not influence the total pain score as much as behavioural parameters (Bussières et al. 2008). The CPS-scale has in earlier studies shown the be an effective tool when it comes to assessing pain in horses on a daily basis (Van Loon et al. 2010). When looking more closely at this pain scale, it can be useful not only for validating orthopaedic pain (Bussières et al. 2008), but there are also several parameters that can be applied to visceral pain (Van Loon et al. 2010). In a study performed by Van Loon et al. (2010), the authors reached the conclusion that the CPS-scale is suitable for scoring postoperative pain since general anaesthesia does not have any significant influence on the total pain score.

Equine pain scale

The EPS scale is a composite scale containing behavioural items, including the "pain face", and it has been recommended for general pain (Ask et al. 2020). The scale contains of nine different behavioural categories, which are ranked 0-4 where 0 is no evidence of pain whereas 4 is when most pain related behaviour can be seen. No physiological parameters are included in the scale. The highest pain score is a total of 36. The pain assessment is done over a period of 2 minutes.

The concept of the "equine pain face" was created by Gleerup et al. (2015) by applying a nociceptive stimulus (capsaicin or ischemia) to the horses participating in the trial. Thereafter the horses' heads were video recorded, both with and without an observer present. The authors reached the conclusion that a certain pattern of facial expressions (the "Pain Face": ears rotated, triangular eye contour, squared muzzle, dilated nostril, and strained chewing muscles) were present in all horses receiving a pain induction, but they were not present simultaneously all at the same time. Another conclusion was that the horses did not suppress all facial expressions when the observer were present, however they were not expressed as obviously since the horses interacted with the observer.

The EPS was developed with components from several different reviewed papers, for example CPS and the Pain face (Gleerup & Lindegaard 2016). Its clinical validation is ongoing, and its relevance is that it is much faster to score than the CPS.

2.2 Osteochondrosis and osteochondritis dissecans

Osteochondrosis is a common reason for orthopaedic pain in horses. It can in theory occur in all joints, however it is more likely to develop in the fetlock, hock, and stifle (Naccache et al. 2018). The condition is a result of disturbance in the growth of the endochondral bone, resulting in a failure in vascularization and calcification resulting in a failure of the cartilage to develop into bone (James et al. 2016; Ortved 2017; Bourebaba et al. 2019). Lesions usually develop between the weightbearing and non-weightbearing surface, and in some cases, especially in younger horses, the lesions are found bilaterally (Ortved 2017). Clinical signs are not always present, and in some horses the condition is often discovered during routine radiography. However, if not treated it can lead to further damage and inflammation in the joint, and clinical signs such as lameness, can therefore manifest later in the development of the disease (Adler et al. 2021).

The condition is often seen in young growing animals and in athletic horses. It is a multifactorial disease which can be a result of nutritional or endocrinological factors, deformities in the joint, genetics, trauma, or too little or too excessive exercise (Van Weeren 2006; James et al. 2016; Naccache et al. 2018; Bourebaba et al. 2019). OCD is a type of manifestation of OC, resulting in a focal bone- or cartilage flap which can either be partially attached to the bone or floating around loose in the joint. This causes an inflammation, that in many cases results in pain, lameness, and effusion in the joint. If the flap is not removed it increases the risk of the horse developing osteoarthritis. The clinical signs can vary from mild to severe (Ortved 2017).

2.2.1 Diagnosis

The condition can be diagnosed using radiography. However there are some cases where the bone/cartilage flap cannot be visualized on the X-rays depending on the joint and its location (James et al. 2016). Therefore, arthroscopy is a good diagnostic tool for finding lesions located on the articular surface, and may be used as a part of the treatment.

2.3 Arthroscopy

Arthroscopy is a standard procedure which is performed at most large animal hospitals, and it is consider a golden standard method for different type of intra-articular pathologies, both for diagnosis and treatment (Singer 2022). The surgery is conducted by entering the joint with a camera through a portal (McIlwraith et al. 2005). Depending on the joint and lesion, one or more portals may be necessary. By entering the joint cavity and inserting a camera, the surgeon will have a greater overview of the joint, and can thereby carry out different interventions such as debridement of cartilage or removal of bone fragments. Debridement is performed until only healthy tissue remains (Bourebaba et al. 2019). This will inevitably induce a degree of tissue trauma.

In human studies, arthroscopy has been classified as a painful surgery, where over half the patients showed a reduced activity after the incision (Pavlin et al. 2004). When looking at the joint and its structures, the cartilage in the joint has a lack of neural innervation. This means that it is not the interaction with the cartilage that causes the pain during an arthroscopy (Park et al. 2011). Instead, it is the interaction with the synovial membrane, which the surgeon must pass through when entering the joint.

2.3.1 Anaesthesia

When undergoing an arthroscopy, the horses are generally put in dorsal recumbency under general anaesthesia (McIlwraith et al. 2005). Horses undergoing general anaesthesia have a higher mortality rate compare to other animal species, were most anaesthetic related deaths are not cardio- or respiratory related (Senior 2013). Non-cardiorespiratory deaths can for example be fracturing a bone in the recovery or horses developing postanaesthetic myopathy. Therefore, a stable and well-balanced anaesthesia is a keystone when it comes to anaesthesia in horses (Gaesser et al. 2020). One way to achieve this, as well as decreasing the amount of inhalation gas needed, is the use of multimodal analgesia.

Recovery

After surgery the horses are transferred to recovery, a room built to give the horses an optimal environment when attempting to stand after general anaesthesia. When using inhalation gas during general anaesthesia, it is important that the horse lie still when arriving at recovery. The horse should lie either on the side or in a sternal position, for about 15-20 minutes to allow the horse to exhale the gas used during the anaesthesia (Hubbell 2005). When the horse lies in sternal position it allows the horse to regain a more normal breathing pattern and ventilation, as well as improving the heart rate and arterial blood pressure (Steffey et al. 1990; Hubbell 2005). One method commonly used to increase the time that the horse is lying down, preferably in sternal recumbency, before trying to stand is to give a small dose sedation intravenously. A common sedative used for this situation is xylazine, which is an alfa-2-agonist which has a shorter duration, approximately 30 minutes (Papich 2021). This sedative is also analgesic.

Different factors that influence the recovery time include the physical condition of the horse, the duration of the surgery and the amount and type of anaesthesia gas used. The type of incision that has been made, as well as the amount of trauma caused by it, also affects the recovery time.

There are different classification methods that can be used to determine the quality of the recovery. One commonly used method is a subjective scale of 0-5, where 5 is the best quality of the recovery with no ataxia and the horse stood up at the first attempt while 0 means that it was a tough and violent recovery where the horse was struggling to stand for a longer period of time (Young & Taylor 1993).

2.4 Analgesia

Reducing pain related to surgery or other treatment is necessary to ensure animal welfare (Gleerup & Lindegaard 2016; McLennan et al. 2019). Surgery today is well optimized, and reducing pain caused by invasive surgery has been made easier by using a balanced anaesthesia and multimodal analgesia, thereby making it easier to maintain good welfare for the horse. Arthroscopy is a surgery which sometimes is performed on young horses without any clinical signs. This is often done since abnormalities connected to OC/OCD have been found on radiographs. These horses usually makes a good candidate for arthroscopic removal of joint fragments (Bazay 2022), since performing the surgery before clinical signs manifest decreases the risk of the horses developing progressive joint destruction, osteoarthritis (Caron 2003). As mentioned earlier, this can result in the end of an athletic career, and an economic loss for the owner (Adler et al. 2021).

Multimodal analgesia refers to blocking the nociceptive pathway in different places which results in greater pain control (Goldberg & Shaffran 2014). Controlling pain is also an important aspect for the recovery and postoperative rehabilitation. Multimodal analgesia and pain control results in an improved recovery and faster healing of the tissue (Goldberg & Shaffran 2014).

2.4.1 Local anaesthetics

Local anaesthetics can be useful when wanting to achieve a pre-emptive analgesia in a well-defined site. The effect of the most local anaesthetics is a result of an expansion of the cell membrane generating a closure of sodium channels located in the membrane (Day & Skarda 1991). When the sodium channels are closed the depolarization is inhibited which results in a blockade of the nerve conduction. Pre-emptive analgesia refers to the administration of a drug, for example local anaesthetics, before the surgical incision and tissue injury have activated the nociceptors (Rosero & Joshi 2014). Administration of pre-emptive analgesic therapy decreases the risk of developing central sensitization, as well as suppressing stress-related consequences of acute pain, which is still active despite the anaesthesia (Muir 2005; Goldberg & Shaffran 2014).

An earlier study evaluating the effect of a pre-emptive intra-articular administration of local anaesthetic has shown it to be an effective pain management tool after arthroscopic surgery (Goodwin et al. 2005). Unfortunately, a high dose of local anaesthetic is toxic for the chondrocytes in the joint. A comparison of lidocaine, bupivacaine and mepivacaine showed that mepivacaine is the local anaesthetic which is least cytotoxic (Park et al. 2011). Bupivacaine, which is the most toxic of the substances mentioned above, can cause the cell to undergo apoptosis or in some cases become necrotic. The risk of this happening is especially high if there already is an injury to the cartilage. However, the cytotoxic effect is both dose and time dependent (Adler et al. 2021).

Mepivacaine has a fast onset of action (5-10 minutes), and a duration of 2-3 hours (Day & Skarda 1991; Goldberg & Shaffran 2014). The onset of action for bupivacaine is intermediate (15-20 minutes). However, the duration is longer, approximately 3-6 hours. These substances may be a better option when requiring a more long-lasting analgesia, for example an analgesia that last from intraoperative to the postoperative period (Matthews & Carroll 2007). However, in many cases it is not recommended to use because of their toxic effect on the equine articular chondrocytes (Sanchez & Robertson 2014).

2.5 Serum Amyloid A

Serum amyloid A is a fast acting and sensitive acute phase protein produced in the liver (Sanchez-Teran et al. 2016). If inflammation occurs, the concentration of systemic SAA increases rapidly (Jacobsen & Andersen 2007; Jacobsen 2007). In studies conducted to evaluate SAA as an acute phase protein in horses, SAA reached the highest concentration around 48 hours after the inflammation started (Nunokawa et al. 1993; Hultén et al. 2002). SAA has a short half-life which makes it a useful tool to evaluate the effect of a treatment as well as resolution of the development of a disease. The concentrations of SAA in serum increases following the intensity of trauma, for example one caused by an invasive surgery (Jacobsen et al. 2009). In the study performed by Jacobsen et al. (2009), the authors mentioned that invasive surgeries cause an increase in SAA, and that the increase depends on the trauma caused by the incision. The study also discusses the probability of a correlation between the experience of the surgeon and the increase in several of the inflammatory markers. Another study, examining the systemic concentrations of SAA after arthroscopic lavage and arthrocentesis, could see an increase of SAA after surgery (Sanchez-Teran et al. 2016). However, the size of the increase varied depending on the horse.

In earlier studies the authors reached the conclusion that general anaesthesia alone does not seem to influence SAA as much as other parameters, for example cortisol (Jacobsen et al. 2009; Sanchez-Teran et al. 2016). Thereby, SAA may be a suitable parameter to analyse the intensity of the trauma occurred during surgery without a significant influence on the concentrations from other factors, such as anaesthesia.

3. Material and method

3.1 Material

Material used for collection of data during this study were anaesthesia protocols, CPS-scale (table 1), pain scoring from video surveillance in the stables and a tablet used for registration of the horse's status and for insertion of data during the pain scoring session. For the SAA-test blood was collected in serum test tubes, and the blood was taken from the permanent cannula.

The horses which were included in the study were horses remitted to UDS for arthroscopic surgery. Both one- and multilimbed arthroscopies were included in the study. The horses had to meet the following criteria: arthroscopy in the hock, fetlock, or stifle; that they had not received NSAID at least two days prior to arrival and that the horse was >1 year in age. For every horse participating in the study the collection of data was performed for a total of three days.

In this study the CPS-scale was used for pain scoring. The decision was based upon that the CPS-scale is validated for orthopaedic pain as well as it could easily be used when evaluating behavioural expressions on recordings. Since the EPS-scale is more focused on general pain, and it assesses the presence of a pain face which was hard to evaluate in detail on videos, this scale was not used during this study.

Table 1. Multifactorial numerical rating CPS (Bussières et al. 2008).

Data		Score
Behaviour		
Kicking at abdomen	Quietly standing, no kicking	0
	Occasional kicking at abdomen (1-2 times/5 min)	1
	Frequent kicking at abdomen (3-4 times/5 min)	2
	Excessive kicking at abdomen (>5 times/5 min), intermittent attempts to lie down and roll	3
Pawing on the floor (pointing, hanging limbs)	Quietly standing, no pawing	0
	Occasional pawing (1-2 times/5 min)	1
	Frequent pawing (3-4 times/5 min)	2
	Excessive pawing (>5 times/ 5 min)	3
Head movement	No evidence of discomfort, head straight ahead for the most part	0
	Intermittent head movements laterally or vertically, occasional looking at flanks (1-2 times/5 min), lip curling (1-2 times/ 5 min)	1
	Intermittent and rapid head movements laterally or vertically, frequent looking at flank (3-4 times/5 min), lip curling (3-4 times/5 min)	2
	Continuous head movements, excessively looking at flank (>5 times/5 min), lip curling (>5 times/5 min)	3

Appearance	Bright and alert, occasional head movements, no reluctance to move	0
	Bright, lowered head and ears, no reluctance to move	1
	Restlessness, pricked up ears, abnormal facial expressions, dilated pupils	2
	Excited, continuous body movements, abnormal facial expression	3
Posture (weight distribution, comfort)	Stands quietly, normal walk	0
	Occasional weight shift, slight muscle tremors	1
	Non-weight bearing, abnormal weight distribution	2
	Analgesic posture (attempts to urinate), prostration, muscle tremors)	3
Appetite	Eats hay readily	0
	Hesitates to eat hay	1
	Shows little interest in hay, eats very little or takes hay in mouth but does not chew or swallow	2
	Neither shows interest in nor eats hay	3
Sweating	No obvious signs of sweat	0
	Damp to the touch	1
	Wet to the touch, beads of sweat are apparent over the horse’s body	2
	Excessive sweating, beads of water running off the animal	3
Response to treatment		
Interactive behaviour	Pays attention to people	0
	Exaggerated response to auditory stimulus	1
	Excessive-to-aggressive response to auditory stimulus	2
	Stupor, prostration, no response to auditory stimulus	3
Response to palpation of painful area	No reaction to palpation	0
	Mild reaction to palpation	1
	Resistance to palpation	2
	Violent reaction to palpation	3
Physiologic data		
Respiratory rate	Normal compared to initial value (increase <10%)	0
	11-30% increase	1
	31-50% increase	2
	>50% increase	3
Heart rate	Normal compared to initial value (increase <10%)	0
	11-30% increase	1
	31-50% increase	2
	>50% increase	3
Rectal temperature	Normal compared to initial value (variation < 0,5°C)	0
	Variation less 1°C	1
	Variation less 1,5°C	2
	Variation less 2°C	3
Digestive sounds	Normal motility	0
	Decreased motility	1
	No motility	2
	Hypermotility	3
Total		…/39

3.2 Method

The study was conducted as a study blinded to treatment. Horses participating in the study randomly received a number at arrival to the clinic. Number 1-20 for fetlocks, 21-40 for hocks and 41-50 for stifle. The numbers were decided beforehand if it was a treatment or control. Scheme of the timeline and procedures for each horse is presented in figure 1.

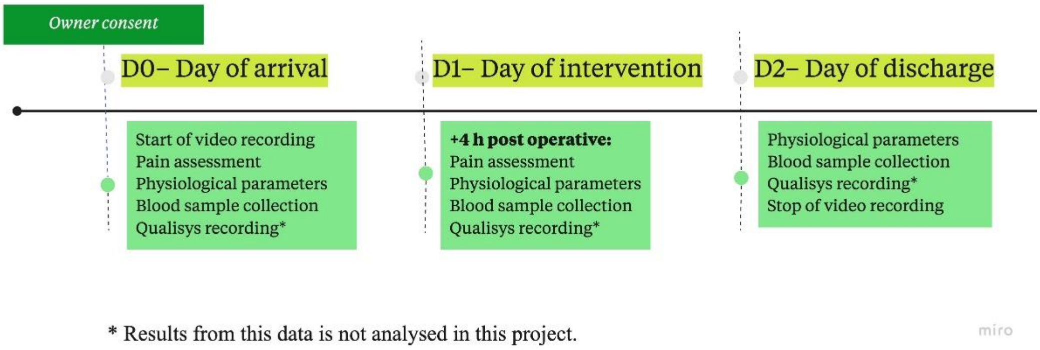

Figure 1. Scheme of the timeline and procedures with the horses participating in the study. Pain assessment +8 hours postoperative is not included in the figure. Illustration made by Sofia Forsman.

Day 0 – arrival at clinic

The horses arrived at the clinic the day before the scheduled surgery. At the arrival of the horse an insertion of a permanent cannula was performed, and blood samples for SAA analyses were collected. Physiological parameters (heart rate, respiratory rate, digestive sounds, rectal temperature, reaction to palpation) were collected.

Day 1 - surgery

Preoperative the horses were prepared for surgery according to UDS standard routine. Therefore, all the horses participating in the study received one dose of NSAID and morphine in the premedication according to a standard protocol (table 2). An injection of either saline or mepivacaine 20 mg/ml was administered into the joint/joints according to the blinding procedure. The doses were set beforehand: fetlock 200 mg, tarsus 400 mg and 400 mg in each compartment of the joint in the knee. After the injection the surgeon was not allowed to make any incision until at least 10 minutes had passed. During the operation no CRI or other analgesia was allowed to be used. The recovery after the surgery were recorded. Four hours postoperative physiological parameters and blood samples were collected.

Table 2. Anaesthesia protocol used for the horses in the study.

My data		Concentration (mg/ml)	Dose (mg/kg)
Premedication			
Acepromazin	Plegicil	10	0.01-0.03
Flunixin	Finadyne	50	1.1
Induction			
Romifidin	Sedivet	10	0.1
Morfin	Morfin meda	10	0.1
Midazolam	Midazolam	5	0.03-0.05
Ketaminol	Ketamin	100	2.2-2.5
Maintenance			
Isoflurane			As needed
Dobutamin			As needed
Recovery			
Romifidin	Sedivet	10	0.1-0.3
Xylazin			As needed
Fenylnefrin			As needed

Day 2 – 16-24 hours after surgery

The morning after the surgery blood samples were collected and status was taken before the first postoperative NSAID was administrated. Another blood sample were collected two hours after the administration of NSAID.

Pain scoring

The horses were recorded in their boxes during their entire stay at the clinic. Pain scoring was performed digitally by looking at 5-minute videos cut from the recordings of the horses stay at the clinic at the time intervals: day 0 (baseline), and +4, +8 and +24 hours postoperative. The videoclips were selected by a third part, that was not involved in the assessment of pain. The pain assessment was performed by two coders (S.K and S.F) on separate locations to not influence each other.

Anaesthesia

The anaesthesia was evaluated from the anaesthesia protocol which was recorded automatically by the anaesthesia monitor (Tafonius) during the surgery. From the protocol, the length of the surgery was noted, as well as the highest and lowest value for the systolic and diastolic blood pressure and heart rate, and a mean value was calculated for each one of them. The quality of the recovery was assessed by two different observers according to the scale (grades 0-5) created by Taylor and Young (1993).

Rescue analgesia

If the horses participating in the study became very painful during their stay at the clinic, rescue analgesia could be administrated to ensure animal welfare. This was decided by the veterinarian on duty. The horses were excluded from the study if analgesia was administrated beyond the protocol both intra- or postoperative.

3.2.1 Statistical methods

Analysis was done on an individual level since the groups (treatment and control) were unbalanced.

Cohens kappa

Cohens kappa was done in R (version 3.4.1). This method was used to perform agreement analyses between the two coders total pain score from the pain scoring, as well as it was used to calculate an interrater agreement in each coder.

Linear regression

Linear regression was done in R (version 3.4.1). This method was used to analyse the relationship/correlation between total pain score and SAA 24 hours post-operative.

4. Results

A total of 15 horses were included in the study (table 3). When the collection of data ended the horses received a new ID number (1-15) to make it easier to present the data for each horse. Three of the horses received treatment (horses´ number 2, 3 and 15). Two of the horses had arthroscopy performed in the fetlock, and one of them in the stifle. None of the horses admitted to the clinic for arthroscopy in the hock/hocks received treatment. The other 12 horses included in the study were controls and received an injection with saline, both horses undergoing arthroscopy in fetlock, hock and stifle were included in this group. The breed of the majority of the horses were standardbred trotter, and most of the horses were between 1-2 years in age. 8 of the horses underwent arthroscopy in one joint, while 7 of the horses had bilateral procedures.

Table 3. Table presenting the horses included in the study. Displaying their age, breed, diagnosis and in which joint/joints the incision was made.

Horse	**Age (year)**	**Breed**	**Diagnosis**	**Uni-/bilateral**	**Joint(s)**
1	1.5	Standardbred trotter	OC	Unilateral	Fetlock
2	6	Swedish warmblood	Fissure, loose bone fragment, no OC	Unilateral	Fetlock
3	2.5	Swedish warmblood	OCD	Bilateral	Fetlock
4	11	Swedish riding pony	Alterations in joint	Unilateral	Fetlock
5	1.5	Standardbred trotter	OC	Unilateral	Fetlock
6	1.5	Standardbred trotter	Loose fragment in joint, no OC	Bilateral	Fetlock
7	7.5	Crossbreed pony	Arthritis	Bilateral	Fetlock
8	1	Standardbred trotter	OC	Unilateral	Hock
9	1	Standardbred trotter	OCD	Unilateral	Hock
10	1	Standardbred trotter	OCD	Bilateral	Hock
11	1	Standardbred trotter	OCD	Bilateral	Hock
12	1	Standardbred trotter	OCD	Bilateral	Hock
13	14	Icelandic horse	Arthritis	Unilateral	Stifle
14	17	Arabian	Alterations in joints	Bilateral	Stifle
15	6	Swedish Warmblood	Bone cyst	Bilateral	Stifle

4.1 Pain score

4.1.1 Agreement analysis

In some horses there were a noticeable difference in the pain score from the pain assessment performed by the two coders, and it was therefore decided to do an agreement analysis according to Cohens kappa (figure 2). The analysis showed that there was a high intra-rater agreement (98%) in each coder, which means that each coder is consistent in their assessment. In six out of nine categories (overall agreement, head movements, number of flank looks, number of kicking, number of pawing and sweating) there are a moderate to near perfect agreement (50-89% agreement). However, there were a few behavioural parameters that had a lower agreement (4.2-34%) when looking at the estimate value, and those behaviours were total number of lip curling (which together with number of flank looks decided the pain score on the head movement category), posture and appearance. These categories may therefore be the reason for the diversity in the results from the pain assessment.

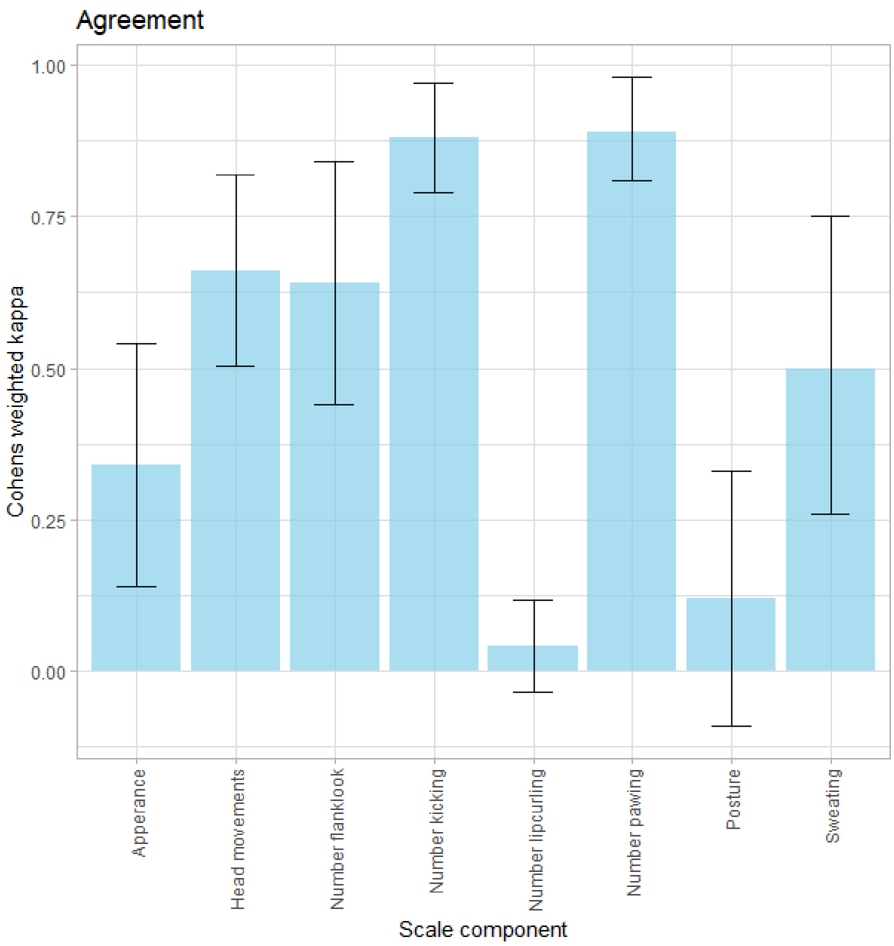

Figure 2. Image presenting the results from the agreement analysis according to Cohens kappa.

4.1.2 Pain scoring

The physiological parameters were collected but excluded from the study since they were not collected at the same time as the pain assessment was done. This resulted in a maximum total pain score of 24. Since all the assessment of pain was done by studying the horse for 5 minutes by looking at videoclips, the appetite and interactive behaviour was not always possible to assess depending on if the horse had hay in the box or not as well as if there were someone to interact with in the stable, resulting in that these two parameters only could be evaluated in some of the horses. Since there were a diversity in the two coders total pain score a mean value was calculated by summarizing the total pain score from the two coders and then dividing into two. Each coder assessed the horses on videoclips without any influence from each other.

Comparing the total pain score (presented in figure 3) for the horses which received treatment (horse number 2, 3 and 15) and the horses in the control group there are no significant difference between them. Horse number 2 had the lowest pain score in the baseline assessment, and the pain score then increased postoperative (4 and 8 hours postoperative) but started to decrease 24 hours postoperative, however it did not go back to the baseline value. The same pattern in the pain score can be seen in horse number 5 and 11, which did not receive any treatment. Horse number 3 had the highest pain score in the baseline assessment, and the pain score decreased postoperatively reaching its lowest value 24 hours postoperative. Horse number 15 had the same total pain score in the baseline assessment as in the one 4 hours postoperative (which makes the baseline marker hidden under the red post 4 hours marker in figure 3). The horse only hade a slight increase in pain score post-operative.

When looking at the total pain score in the control group, there is a large variation between the different horses. Horse number 1 had the highest pain score 24 hours postoperative, in comparison to horse number 6, 12 and 13 which had their lowest total pain score during the pain assessment done at the same time. Most of the horses obtained the highest pain score 4 or 8 hours postoperative.

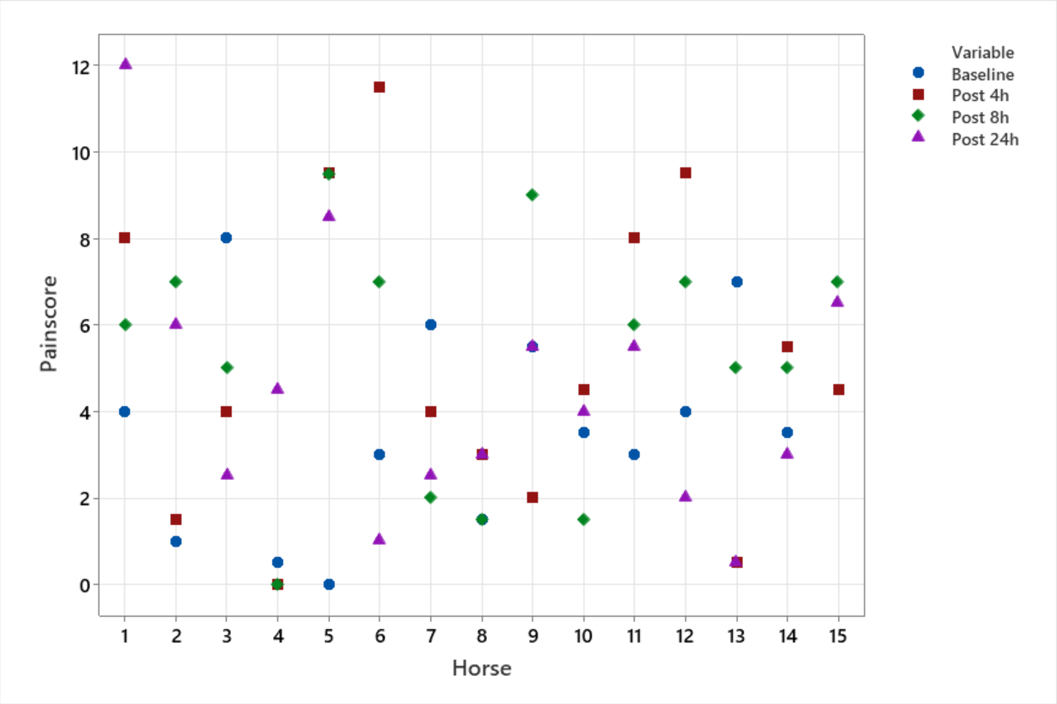

Figure 3. Image displaying the total pain score at four different times (baseline, 4 hours-, 8 hours- and 24 hours postoperative), according to the CPS-scale. The values presented are mean values from the two coders.

4.2 Anaesthesia

4.2.1 Blood pressure

The maximum and minimum values of the systolic and diastolic blood pressure were taken from the anaesthesia protocols which was recorded automatically by Tafonius during the surgery. The mean value was thereafter calculated for each horse. The blood pressure is relatively similar when comparing the two groups (figure 4), except from the mean value were there are a slight difference, were the horse's receiving treatment have a lower mean value.

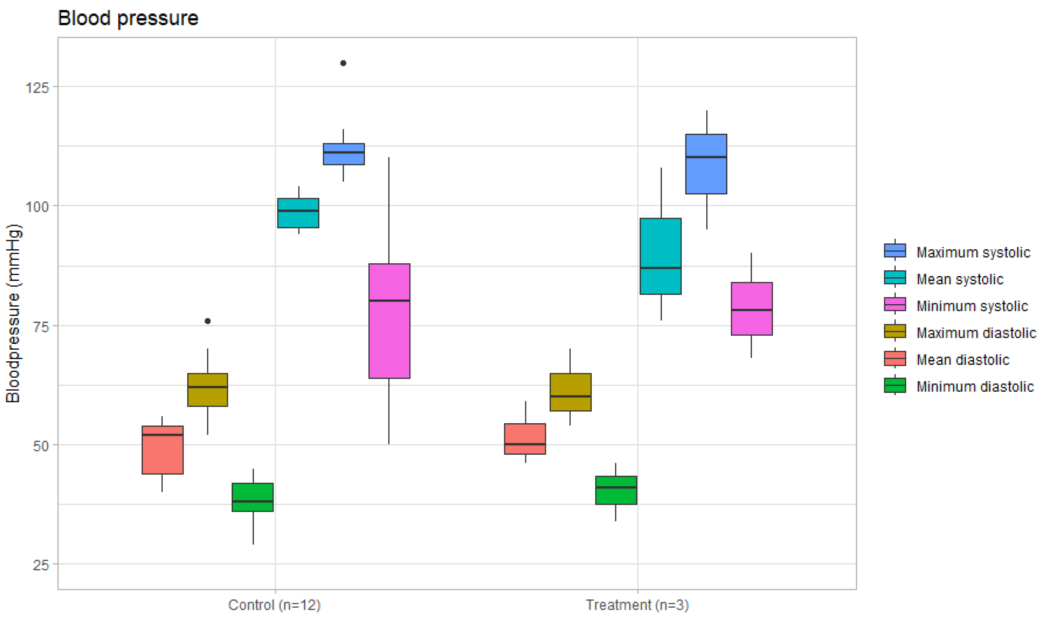

*Figure 4. Boxplot displaying the maximum, minimum and mean value of the systolic and diastolic blood pressure measured in mmHg during arthroscopic surgery. The horses are divided into two groups: treatment and control. The line in the middle of the boxplot is the median for each group. The upper and lower hinges correspond to the first and third quartiles, and the whisker do not extend from the hinge further than 1.5 * inter-quartile range. The outlying points are plotted individually, and that is data which goes beyond the end of the whiskers. This gives roughly a 95% confidence interval for comparing medians (McGill et al. 1978).*

4.2.2 Heart rate

The maximum and minimum values were collected the same way as for the blood pressure. The mean value for each horse was calculated. There was no significant difference between the two groups except that the horses which received treatment had a lower minimum heart rate compared to those in the control group (figure 5).

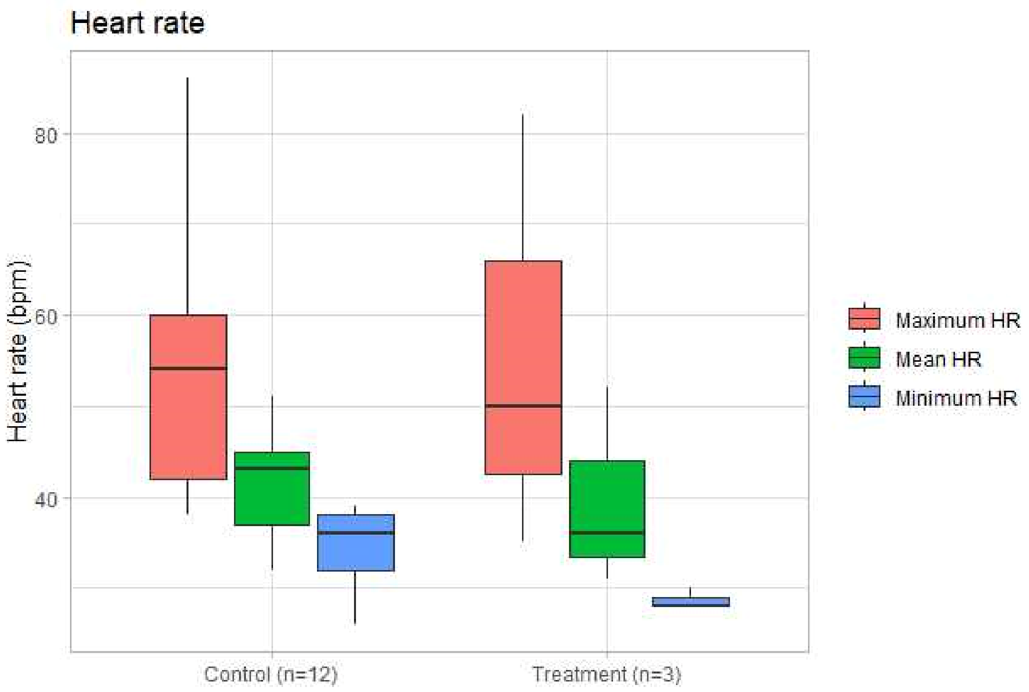

*Figure 5. Boxplot displaying the maximum, minimum and mean value of the horses during arthroscopic surgery. The horses are divided into two groups: treatment and control. The line in the middle of the boxplot is the median for each group. The upper and lower hinges correspond to the first and third quartiles, and the whisker do not extend from the hinge further than 1.5 * inter-quartile range. The outlying points are plotted individually, and that is data which goes beyond the end of the whiskers. This gives roughly a 95% confidence interval for comparing medians (McGill et al. 1978).*

4.2.3 Surgery time

The surgery time that the horses was collected from the anaesthesia protocol and from notes written by the person which attended the surgery. This was the total time that the horses were under general anaesthesia. The total operation time for one of the horses (number 4) were missing. There is a large variation in operation time (figure 6), both depending on if the horse had arthroscopy performed uni- or bilateral and depending on the condition of the joint as well as the measures taken during the surgery.

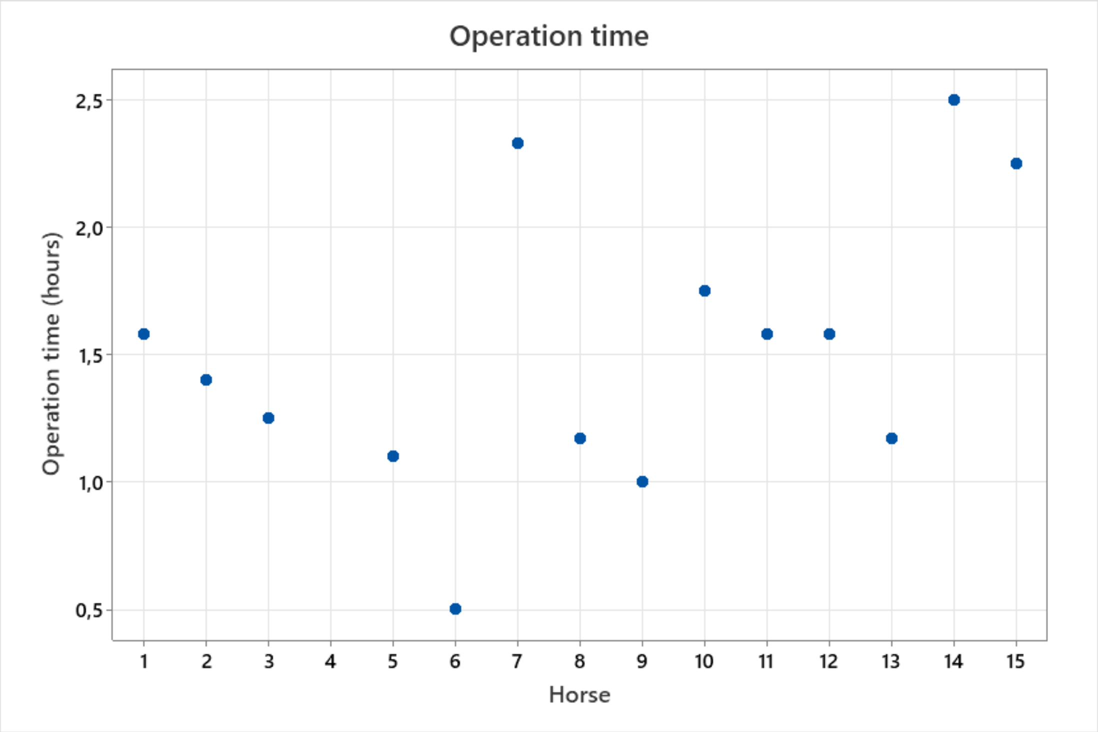

Figure 6. Plot displaying the operation time in hours for each of the horse.

4.2.4 Recovery

The quality of the recovery was scored according to the scale made by (Young & Taylor 1993). Most of the horses were scored by two coders, however some of the videos from the recovery did not work properly, and therefore the anestheiologist score in the horses journals was used. One of the horses (number 9) did not have a video of the recovery or a score in the journal, and will therefore not be included in this section. 9 out of 14 horses had a score of 5 (excellent recovery), whereas only two horses had a recovery score of 4, two horses had a score of 3 and only one horse had a score of 1 (poor recovery). Of the horses which received treatment, two horses had a score of 5 (horse number 2 and 3) while one had a score of 3 (horse number 15). The horses with a lower quality of the recovery were the horses which had some of the longer operation times.

4.3 SAA

The SAA samples were collected and saved in a freezer until the end of the period of collecting data. All samples were then sent and analysed in the same lab (Clinical Chemistry at UDS) during the same session. All the samples were complete except for horse number two, which is therefore not included in this section. Since it is a bad imprecision for values below 5, all the values <5 is not presented in exact concentration. The result of the SAA analysis is presented in table 4.

Table 4. Results of the SAA analysis. The concentration is in mg/L.

Horse	Baseline	+4 h postop	+ 16-24 h postop
Treatment			
3	<5.0	<5.0	9.5
15	<5.0	<5.0	482.1
Control			
1	<5.0	<5.0	<5.0
4	<5.0	<5.0	213.6
5	<5.0	<5.0	141.8
6	<5.0	<5.0	<5.0
7	<5.0	<5.0	53.8
8	<5.0	<5.0	<5.0
9	106.5	31.3	197.5
10	<5.0	<5.0	269.7
11	<5.0	<5.0	<5.0
12	<5.0	9.0	741.1
13	<5.0	<5.0	6.6
14	<5.0	<5.0	20.1

11 out of 14 horses had an increase in SAA 24 hours postoperative. The highest increase (concentration >100 mg/L) could be analysed in horse number 4, 5, 9, 10, 12 and 15. There was one of the horses (control) that had an increased SAA concentration preoperative, and this horse was also one of them that had a higher pain score during the baseline pain assessment. The SAA concentration decreased 4 hours postoperative, as well as the pain score (figure 3). However, the concentration increased again 24 hours postoperative, as well as the pain score, which can be an indicator of that the concentrations of SAA and the total pain score reflects the trauma in the joint. The horses which had the highest increase in the SAA concentrations were the horses which had a recovery quality 3 out 5.

Most of the horses which had the higher increases in SAA concentrations were the horses with the diagnosis OCD. Horse number 4 also had a high increase, and this horse had alterations in the joint, probably because of a trauma according to the surgeon. The horses with arthritis and OC generally had lower SAA concentrations 24 hours postoperative compared to those with OCD. There seem to be no correlation between age, joint or uni-/bilateral arthroscopies and the SAA-concentrations in the blood.

Since the increase in SAA concentrations is mostly at 24 hours postoperative, the concentrations were plotted against the total pain score at 24 hours postoperative (figure 7). There plot demonstrated that there was no correlation between the SAA concentration and the total pain score 24 hours postoperatively.

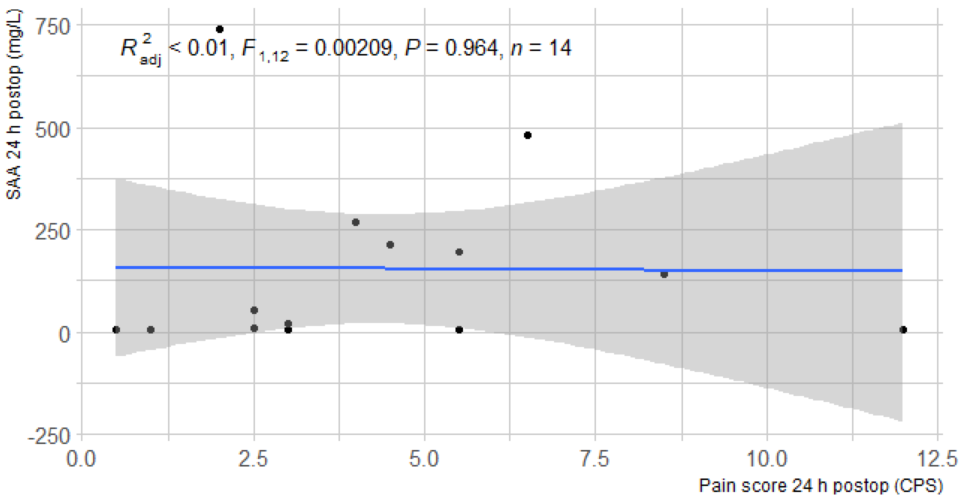

Figure 7. SAA concentrations at 24 hours postoperative plotted against pain score at 24 hours postoperative. Line drawn using linear regression. Grey area represents a 95% confidence interval.

5. Discussion

This study was conducted as a clinical study where the treatment of the horses were blinded. The horses received a number when arriving at the clinic and it was already decided beforehand if the number was supposed to receive mepivacaine (treatment) or saline (control). This resulted in an unbalanced dataset with 12 of the horses participating in the study receiving saline, and only three of the horses receiving mepivacaine. This makes significance testing irrelevant. This problem could have been avoided by keeping the blinding lots in smaller sections, like for example lots of six horses in each section, or by having one person deciding the number of the horse to make sure that the groups remained balanced. The low number of horses was unexpected based on a survey of earlier admittances at the UDS hospital.

In this study the CPS-scale was used for pain scoring. As mentioned during the materials section, the decision was based on the fact that the CPS-scale is validated for orthopaedic pain as well as it could easily be used when evaluating behavioural expressions on recordings. The EPS-scale was also an option, but since the scale is more focused on general pain, one concern was that the scale would not be sensitive enough to pick up small differences in orthopaedic pain. Therefore, this scale was not used during this study. Since earlier studies has shown that physiological parameters do not affect the total pain score as much as the behavioural ones (Bussières et al. 2008), the physiological parameters where collected but excluded from the study since they were not collected during the same time as the pain scoring was performed. Therefore, the horses could only receive a maximum of total pain score of 24. As mentioned in the result the horse’s appetite and interactive behaviour was not possible to assess in all horses, resulting in that some horses may have received a lower pain score than they should have if these parameters could have been assessed. However, this reflects a clinical situation where a pain score would have been taken during a non-standardized time, highlighting that the pain scores are not correlated to the amount of pain the horses. Instead, the scales indicate whether or not there is high probability of pain.

Also worth mentioning is that a great deal of these horses, especially the Standard-breds, had not shown any clinical signs prior to surgery indicating that the horses were in pain from their joint disease. Many of these horses were admitted because of radiographic findings on routinely performed radiographs searching for different manifestations of OC and OCD in predilection sites. This also makes it hard to evaluate their pain by using the pain scale, since these horses probably do not yet suffer from orthopaedic pain caused by the findings. However, this also creates a good baseline value, and an increase or decrease in pain score postoperatively can then be an indicator of the pain caused by the surgery, or if the incision and the treatment performed results in that the horses experience more or less pain than earlier. Another aspect to have in mind is that the horses which already experience pain before the surgery, and which already have clinical symptoms, are harder to evaluate, since they do not get as representative baseline value as the horses which are not in pain before the surgery.

In a study performed by Van Loon et al. (2010), the authors examined if the CPS was reliable and could differentiate between horses with orthopaedic pain and control horses. They reached the conclusion that CPS was reliable for pain assessment after orthopaedic surgery, and that the scale could differentiate horses with orthopaedic pain from the horses which were free of pain. However, the study does not specify which type of incision was performed on the horses admitted for orthopaedic surgery, and if they suffered from orthopaedic pain caused by their condition. When having that in mind, this pain scale may not be enough alone to evaluate orthopaedic pain caused by the incision in horses which do not yet suffer from the condition that is treated. Even if the CPS-scale is validated for orthopaedic pain, and earlier studies have proven it to be able to differentiate horses with orthopaedic pain and pain free horses, there are several parameters in the scale where the observer is studying the horse in general. There is only one parameter, posture (weight distribution, comfort), included in the protocol that may be affected by a mild orthopaedic pain. However, since horses often shift the weight between the hind legs when standing/resting, this is most applicable if there were an obvious abnormality in the weight distribution, for example if the horse was resting a front leg or only resting one hind leg during a longer period, which is hard to evaluate when only studying the horse for a total of 5 minutes.

When looking at the results from the pain score there are several different aspects that need to be taken into consideration, for example: which time during the day the assessment was performed, the horse's acclimatization to the box, primary disease, how much trauma was caused by surgery, healing process, operation time and recovery. In an article written by Flannelly et al. (2018), the author discuss different threats to the validity of these types of studies. Some of the threats are hard to evade in clinical studies, while others can be eliminated by trying to use as controlled environment as possible. For example, the time that the assessment was performed was similar for all horses: evening during the arrival, the afternoon and evening (+ 4 and +8) postoperatively as well as the morning after the surgery before 8 o'clock. An example is horse number 3, which had the highest total pain score in the baseline assessment, and the pain score decreased postoperatively reaching its lowest value 24 hours postoperative. This could be a result of the treatment, as well as it can be a result of the fact that the horse starting to acclimatize to the box and to the new environment. An earlier study evaluating if the total pain score achieved using HGS was affected by different emotional conditions (both positive and negative), the authors did not see any difference between the horses exposed to different emotional conditions and the ones in the control group (Dalla Costa et al. 2017). However, this pain scale (HGS) is a facial-expression-based scale, which is different compared to the CPS used in this study which assesses the behaviour. Since stress itself can cause behavioural changes (Weger & Sandi 2018), it can be hard to differentiate stress and pain in some individuals when only looking at the horse's behaviour. Stress can also be analgesic by an activation of descending inhibitory pain pathways; this is called stress induced analgesia and can hide orthopaedic pain (Butler & Finn 2009).

Furthermore, as presented in the results there is a large variation in total pain score between the different horses in the control group. While horse number 1 had the highest pain score 24 hours postoperatively, horse number 6, 12 and 13 received the lowest total pain score during the pain assessment done at the same time. One thing to bear in mind when evaluating these horses is that the history of the horses in regard to their earlier experiences was unknown, which could greatly influence the measurements. Therefore, it is a possibility that an increased pain score both pre- and postoperative can be a result of stress, and not of pain, which makes it hard to be 100% sure that it is pain that has been assessed when using the CPS. The horses were also assessed only hours after the general anaesthesia, which could result in that the drugs used during the anaesthesia still influencing the horse, which can affect the horses experience of pain as well as behaviour. This is hard to differentiate, and therefore pain assessment was done at different times post-operatively to receive a more reliable result. However, since arthroscopy has been classified as a painful surgery in humans (Pavlin et al. 2004), and humans and horses have similar neurobiological system, the surgery should induce pain in horses as well, causing some sort of discomfort postoperatively. Unfortunately, there are no studies concerning the subject if horses experience pain after uncomplicated arthroscopies, like for example removal of a joint fragment in an otherwise healthy joint.

When looking at anaesthesia, there is no significant difference in systolic and diastolic blood pressure (maximum, minimum and mean value) when comparing the horses which received an intra-articular administration of mepivacaine and those which received saline. Based on this small number, there was no indication of effect. Horse number 13 had a higher systolic blood pressure than the other horses, both when it comes to the maximum and minimum value, as well as the mean value. However, the operation time for this specific horse was very short, which can be an indicator that the blood pressure did not get the same time to stabilize, as well as it can be a normal variation.

Another aspect in the anaesthesia worth mentioning is that the horses with a lower quality of the recovery were the same horses that had the longer anaesthesia times. Several studies concerning this subject has been performed, where an correlation between longer anaesthesia time and lower quality of recovery has been seen (Young & Taylor 1993; Vermedal et al. 2021). This may be because a longer time spent under general anaesthesia results in that the horse has inhaled more inhalation gas and has been in dorsal recumbency longer. It has been known for some time that dorsal recumbency cause atelectasis in certain regions in the lungs, causing an impaired arterial oxygenation (Nyman & Hedenstierna 1989). Impaired arterial oxygenation results in hypoxaemia, and in an earlier study experimentally-induced hypoxaemia resulted in reduced muscle oxygenation in anaesthetized horses (Portier et al. 2009). This may therefore affect the quality of the recovery, resulting in the horse finding it harder to stand up on the first try. However, since there only were 15 horses included in the study, the correlation between lower quality of the recovery and longer anaesthesia times, could also be a coincidence.

When looking at the SAA concentrations there was one horse in the control group with a high concentration preoperatively (>100 mg/L). This horse also had a high pain score during the baseline pain assessment. When the concentrations of SAA decreased postoperatively, so did the total pain score. However, the SAA concentration increased again 24 hours postoperatively, as well as the total pain score, which can be an indicator that the SAA and pain score reflects the trauma in the joint. The horses which had the highest increase in the SAA concentrations were the horses which had a recovery quality 3 out 5, Because of the low number of total horses included in the study, it is impossible to evaluate if this is a coincidence or if there is a correlation between the trauma caused by the surgery (which may result in a higher SAA) and a lower quality of the recovery.

In addition, most of the horses with the highest increase in SAA were the horses with the diagnosis OCD. This may be because the surgeon causes a greater trauma when removing the fragment and cleaning up the joint. In earlier studies evaluating SAA concentrations related to orthopaedic pain, there is a strong correlation between increased SAA and the trauma caused by surgery, both in serum and in synovial fluid (Jacobsen et al. 2006, 2009; Stievani et al. 2018). The SAA concentration in synovial fluid is correlated to the joint disease, and since there is a diffusion of SAA from the blood into the joint cavity, there is a strong correlation between plasma levels of SAA and the concentrations in synovial fluid (Seny et al. 2013). However, there are few studies examining the exact correlation between SAA, OCD and trauma caused by surgery as a part of the treatment.

5.1 Conclusion

To summarize this discussion, there were no noticeable difference in anaesthesia, recovery, postoperative pain score or SAA between the horses receiving an intra-articular administration with mepivacaine compared to those who received saline in connection with arthroscopic surgery. However, as mentioned earlier in the discussion it can be hard to assess mild orthopaedic pain with a pain scale, even if it is one validated for orthopaedic pain. Therefore, it is difficult to draw any conclusions concerning the postoperative pain score in this study. To evaluate this further a larger study should be performed, including more horses and especially a greater number of horses receiving treatment. Despite the lack of conclusive results, the methodologies we developed proved useful and achievable even in a clinical setting.

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Popular science summary

Pain results in an unpleasant feeling, which is a result of a sensory input and emotional experience. There are several different sources of pain, as well as different types of pain. How one individual experience pain depends on several factors, like for example earlier pain experiences. Pain related to the skeletal is often referred to as orthopaedic pain, and one of the most common reasons for this type of pain in horses is osteochondrosis (OC). Osteochondrosis is a disease which effect the development of the cartilage in the joint, which can if left untreated result in pain and lameness. A part of the treatment is therefore to go into the joint with a camera and remove damaged cartilage as well as loose pieces floating around in the joint. Studies in human reports this type of procedure as painful, which can be perceived by the patient both during and after the surgery. To receive a better healing of the tissue, as well as ensuring good animal welfare pain relief is of a great importance. One type of pain relief is local anaesthetics, which can be administrated directly into the joint before the first incision. The purpose with this study was to evaluate if this type of pain relief is effective during this type of procedure.

This was done by looking at how much pain the horses were in, both before and after the surgery, with the help of a behavioural scale measuring different types of pain-related behaviours in horses. The surgery is done under general anaesthesia, which means that the horses are asleep during the procedure. During this time different parameters such as blood pressure and total operation time is collected, and the recovery after the surgery was recorded and analysed. This allows the study to evaluate different parameters during the anaesthesia, which can be related to pain. Another aspect that was included in this study was the analysis of inflammatory markers in the blood to see if there was a change in degree of inflammation.

The study reported no obvious difference in pain, anaesthesia or inflammatory markers in the horses which received pain relief compared to those which received saline, but further investigation is required.

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