Veterinary analgesia: State of the Art

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The major change in the state of the art of veterinary analgesia in recent years has been one of attitude rather than techniques or drugs. There is increasing realization in public awareness that animals may suffer pain and require analgesia. In the U.K this is becoming a driving force for veterinary surgeons to administer analgesics. In combination with this awareness of anaesthesia and analgesia has been used as a marketing ploy on the part of pharmaceutical companies. Another factor may be the increasing proportion of women in the veterinary as surveys in attitudes to post operative pain and analgesia have shown that women are more likely to administer analgesia than men.

There have been changes in analgesic practice in response to the above. These can be examined by looking at new drug introduction or altered uses of traditional drugs

Non-Steroidal Anti-inflammatory Drugs for Perioperative Pain Control

The first change was the development and introduction of carprofen into clinical use, in the 1990's. This was the first non-steroidal anti-inflammatory drug licenced for preoperative use in small animals. It was shown to be as effective as some of the opioids for post-operative pain relief, could be given by injection initially and then the analgesia continued into the post-operative period with oral medication. It has been associated with few of the side effects of the traditional NSAIDs. Although its mode of action is not completely clear, it has very marked anti-inflammatory properties without causing prostaglandin inhibition unlike the traditional NSAIDs. It has some preferential cyclo-oxygenase 2 (COX 2) inhibitory properties. Although it appears to have few side effects, some animals do seem to have gastrointestinal sensitivity to it and there are also reports of reversible liver dysfunction after its use. Subsequently meloxicam has been licenced for perioperative use. Again this has 'good' COX 1: COX 2 ratio and has been shown to be as effective if not more so than carprofen for perioperative pain.

To have maximum benefit, NSAIDs should be given prior to the initiation of the inflammatory process i.e prior to surgery, hence the advantage of having two drugs with pre-operative indications and supposedly reduced renal and gastrointestinal side-effects.

Although not licenced for perioperative use a new NSAID has been brought out - tepoxalin (Zubrin – Schering – Plough). This drug is a COX 1, lipoxygenase (LOX) dual inhibitor, thus having inhibitory actions on prostaglandin and leukotriene production. Its formulation employs the fast melt technology as outlined in the lecture on pre-emptive analgesia. Whilst its actions on inflammation may not be as dramatic as some other NSAIDs it may prove to be a more effective analgesic via central actions.

Local anaesthetics and Local Analgesic Techniques

Local analgesics and local techniques have been neglected in small animal veterinary practice, but have major advantages. They require minimal equipment, have a local action rather than a systemic action, can provide complete analgesia or sensory blockade and dramatically reduce the dose of general anaesthetic agents required. The disadvantage of these techniques is that application requires technical skill which like all skills must be learnt and is not particularly well taught in veterinary schools. A variety of local analgesic techniques may be employed depending on the surgical site ranging from local infiltration and specific nerve blocks to epidural or spinal analgesia and intravenous regional analgesia. The most commonly used agent is still lignocaine but bupivicaine and ropivicaine are gaining popularity.

Opioids

Methadone and pethidine are the only two full opioid agonists with animal licences in Europe, but many other opioids are used in veterinary practice. Fentanyl and shorter acting opioids (alfentanyl and remifentanil) are increasingly being used by continuous infusion intraoperatively with the infusion rate being varied with the intensity of surgical stimulation. These infusions are only safely used when facilities for IPPV are available and can be used. Fentanyl is also used to provide analgesia in conscious animals by its transdermal patch formulation. The hig lipid solubility of this drug which precludes its epidural use, makes it ideal for this means of administration. The slow sustained release gives a peak effect of 12 hours in cats and approximately 24 hours in dogs although it has a longer duration in cats (5 days) than dogs (3 days). Vaiaious size patches are available and one should choose a patch which will give between 2-4 mcg/kg/h release.

The novel opioid tramadol will be discusses later at this meeting. It is relatively new and in addition to its opioid actions also acts by enhancing serotoninergic and adrenergic pathways. It has fewer side effects that traditional opioids.

Of the partial agonists, butorphanol and buprenorphine have animal licences. Butorphanol is a kappa agonist and so has rather different actions to the traditional mu agents, probably providing more sedation and less analgesia by itself. However there may be a synergistic effect with alpha-2 agents to give profound sedation and perhaps analgesia. Buprenorphine is the classic partial mu agonist or agonist/antagonist. However there is evidence that the

off quoted bell shaped dose response curve may only apply at very high doses and at clinical doses may not have an effect, hence increasing doses within reason may increase effect. The disadvantage of this drug is that anecdotally it has marked dysphoric effects.

Alpha-2 Agonist Drugs

Initally these drugs were marketed as having marked analgesic effects. However over reliance on this property in combination with their marked cardiovascular effects lead to some disillusionment with the drugs, particularly at the high doses initially recommended. Following experimental studies showing the distribution of alpha-2 adrenoceptors in relation to opioid receptors and elucidation of their mechanisms of action, there has been increasing interest in the use of low doses (1-2 mcg/kg medetomidine)of the drugs in combination with opioids for sedation and analgesia and their use by continuous infusion post-operatively (0.2-0.5 mcg/kg/h medetomidine). Medetomidine is a racemic mixture and the dextrorotatory form has been produced for human use. There is also interest in this form for animal use as the potentially lower doses may have reduced side effects.

Ketamine

Whilst not a new drug, ketamine is enjoying increased interest as an analgesic rather than as a dissociative anaesthetic. This is partially due to the increasing knowledge regarding the role of NMDA receptors in hyperalgesia. Very low doses are being employed (0.1 mg/kg) to good effect in some situations e.g somatic rather than visceral pain.

Conclusions

Little has changed in analgesic drugs that are used; but how these drugs are administered and the attitude of the people prescribing them is changing. In the past cancer was regarded as one disease, now this is recognised not as a disease but as the pattern of behaviour of a wide variety of pathologies. Likewise in future, pain may be used as a blanket expression which covers a widely diverse set of diagnosed experiences, each of which may be amenable to different treatments. Improvements in the diagnosis of the specific mechanism of a particular nocioception will allow improved targeted therapy. At the moment there is still an art to making an animal comfortable after trauma which cannot be reproduced by recipe analgesia.