Is Pain a Contributing Factor?

Pain is Whatever the Patient Says It Is
The characteristics of pain may vary according to patient presentation. Working on the basis that 'pain is whatever the patient says it is' can lead us into some challenges with our dogs and cats when assessing chronic pain, and a pain trial can help here.

Pain trials are a valuable tool to use in managing your chronic pain cases. In this article we review how we use pain trials, what we should consider alongside this, and we make some recommendations.

An analgesic trial, or pain trial, involves the prescription of analgesic(s) where we are suspicious of pain. The response to this intervention is then monitored to determine if the clinical signs have resolved with analgesic treatment.

So Where Do We Start?
Common questions are which analgesics to choose and how to monitor the response to those? We will review some commonly used analgesic options and discuss some tools to use to monitor progress.

We Need Outcome Measures
Diagnosis of chronic pain is often not easy and can be greatly assisted by an analgesic trial. Key to this is monitoring the response to treatment. This can be done in a variety of ways. A really simple option which I find valuable is asking the client to define some pain behaviours – these are changes in the pet's behaviour that the owner associates with pain.

These are also known as Caregiver Specific Outcome Measures (CSOMs) or Caregiver Reported Outcome Measures (CROMs) and their use deserves some focus here. During our history taking we can often identify these behaviours and work with the client so they understand that we are using these as outcome measures at our next consultation. I tend to identify 3–5 behaviours. I recommend reading further on this topic, by Innes.[1] In this article Prof Innes highlights why CROMs should become part of our routine.

The author suggests that the everyday use of CROMs would bring benefits to animals with chronic health conditions and improve the impact that our profession can have on animal welfare.

In addition to these pain behaviours we can also use various metrology instruments – examples being the Canine Brief Pain Inventory (CBPI) (osteoarthritis pain & cancer pain), Liverpool Osteoarthritis in Dogs (LOAD)(OA), Feline Musculoskeletal Pain Index (FMPI).

To me, a huge part of outcome measures is my physical exam. In that initial consultation we are documenting where the pain is. Of course the pain we detect is not always the primary source of pain and we may be identifying areas of secondary compensation, for example muscular pain. At each and every visit we go back to basics and use that physical exam to support what the owner and the pain scores are telling us. The caveat to this are those patients where examination is not possible due to a behavioural presentation where pain could be a factor and this increases the emphasis on the use of tools to measure pain.

Quality of Life as an Outcome
Pain is a contributor to quality of life (QoL). Using an assessment tool that directs us to consider quality of life therefore makes sense in these complex cases. Vetmetrica is an online health-related quality of life instrument that measures QoL across four domains in dogs and three domains in cats.

We Now Know What We Are Measuring, So What Next?
Armed with the ability to measure the impact of our intervention, we need to provide some rationale around which analgesic to use.

Where Is the Pain Coming From?
An understanding of pain aetiology can help us narrow down the pain type. We consider pain types as three broad categories, as per the International Association for the Study of Pain definitions.

Nociceptive/Inflammatory
Pain that arises from actual or threatened damage to non-neural tissue and is due to the activation of nociceptors.

Note: This term is designed to contrast with neuropathic pain. The term is used to describe pain occurring with a normally functioning somatosensory nervous system to contrast with the abnormal function seen in neuropathic pain.

Analgesic choices include NSAIDs, grapiprant, anti-NGF products, opioids.

Neuropathic
Pain caused by a lesion or disease of the somatosensory nervous system.

Note: Neuropathic pain is a clinical description (and not a diagnosis) which requires a demonstrable lesion or a disease that satisfies established neurological diagnostic criteria.

Analgesic choices include gabapentin or pregabalin.

Nociplastic
Pain that arises from altered nociception despite no clear evidence of actual or threatened tissue damage causing the activation of peripheral nociceptors or evidence for disease or lesion of the somatosensory system causing the pain.

Note: Patients can have a combination of nociceptive and nociplastic pain

Nociplastic pain is poorly recognised/defined in dogs and cats. That doesn't mean that it doesn't exist, it simply means we are likely to be missing it.

Do We Need an Imaging Diagnosis?
Recent information teaches us that owners of dogs with OA are more likely to comply with treatment recommendations where a radiographic diagnosis has been achieved. The definition

Figure 1: Ace Vets Ltd

of neuropathic pain from IASP uses the term 'demonstrable lesion' which suggests we should pursue diagnostics. From a clinical perspective, it is of course far easier to treat effectively if we understand our diagnosis.

Starting a Pain Trial
With clear outcome measures defined and hopefully an understanding of pain type, we can choose an analgesic for our pain trial. As a very general rule, we should provide analgesia for a reasonable period of time before attempting to judge efficacy. There is limited evidence in this area and we make recommendations here, rather than hard and fast rules. Where possible we should use licensed options. The concept of a pain ladder is illustrated in figure one using arthritis as an example. We start with licensed options, following on with drugs that have evidence of efficacy, and work up the ladder. Higher up the ladder we have options that may have less evidence and are not licensed.

Non-steroidal Anti-inflammatory Drugs (NSAIDs)
This is the one area where we have firm evidence regarding onset and efficacy. We see an effect from NSAIDs within 7 days. In one study[2] examining enflicoxib (Daxocox) in dogs with OA, pain scores continued to decrease from day 0 to day 42.

- Recommendation – prescribe for 30 days then reassess.

Anti-nerve Growth Factor (NGF) Products

- Frunevetmab – in work by Gruen *et al.*[3] there was an improvement in CSOMs with treatment at day 28, which increased at day 56.
- Recommendation – ask cat owners to report CSOMs back to you at 28-day intervals
- Bedinvetmab – significant improvements in CBPI scores were noted at day 28 in dogs treated with bedinvetmab[4]
- Recommendation – owners often report a positive effect within 7 days. Full effect likely to be seen at 8-week time point.

Gabapentinoids (not licensed)
With initial prescription of gabapentin we often see sedation in gabapentin naive patients. There are few studies evaluating the analgesia associated with gabapentin, especially with chronic pain. I now recommend starting low (5mg/kg BID) and titrating up to 10mg/kg TID to avoid sedation. That process will take one month.

- Recommendation – prescribe for 30 days then reassess in cases where we are suspicious of neuropathic pain.

Amantadine (memantine) (not licensed)
In the Lascelles *et al.* study[5] amantadine was administered in conjunction with meloxicam for three weeks, and then the dogs were reassessed. This doesn't mean amantadine takes 3 weeks to work, it simply reflects the fact that the assessment interval was 3 weeks.

The NMDA antagonists are chosen where central sensitisation is suspected. If a peripheral driver is responsible for central sensitisation (ie: OA) then analgesics directed at that peripheral driver should also be used (ie: NSAIDs, anti-NGF).

- Recommendation – prescribe for at least 21 days then reassess in cases where we are suspicious of central sensitisation.
- Recommendations for memantine follow those of amantadine – for more info: www.zeropainphilosophy.com

Ketamine (not licensed for chronic pain)
The rationale for using ketamine is where we suspect central sensitisation. Central sensitisation can occur in all pain types and one source[6] suggests using ketamine to evaluate whether the patient could be experiencing central sensitisation. Further studies are required in dogs to create an evidence base around this recommendation.

- Recommendation – trial ketamine in the individual as a single injection with a view to this lasting one month. Inform the client that they may see an effect within days and it could last one month.

Our chronic pain cases do present us with challenges. A pain trial can be rewarding and help us improve quality of life in our patients. By following these key steps of considering what the pain driver is likely to be, using an outcome measure and selecting a rational analgesic you are informed to take a logical approach to pain trials.

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