“Oral Transmucosal Cannabidiol Oil Formulation as Part of a Multimodal Analgesic Regimen: Effects on Pain Relief and Quality of Life Improvement in Dogs Affected by Spontaneous Osteoarthritis”

Review by: Gary Ritcher, M.S., D.V.M., C.V.C., C.V.A.

1. The study specifically looked at the efficacy of transmucosal CBD in conjunction with an anti-inflammatory drug (NSAID or prednisone). While the authors acknowledged it in the discussion section, it is difficult to evaluate how much of the CBD preparation was absorbed transmucosal and how much was swallowed. This doesn’t change the results of the study but, as the study specifically stated the CBD absorption was transmucosal, it does bring into question if oral administration of CBD would achieve the same effect.

2. The authors make a very important statement in this paper in that anti-inflammatory drugs do not fully alleviate chronic pain. Because our patients are non-verbal, many veterinarians and pet owners assume pain is relieved if they see improvement on conventional therapy. Both veterinarians and pet owners need to be aware that improvement on therapy does not necessarily mean the animal’s pain is completely gone. We need to be diligent at evaluating patients and exploring other treatment options, such as CBD, to achieve better chronic pain control.

3. The dose of CBD used in the study was 2 mg/kg BID, which is consistent with the doses used in other animal studies. As a practical matter, 2 mg/kg BID is a very expensive dose of CBD for larger dogs. Given that larger dogs are very prone to OA and associated chronic pain, it needs to be acknowledged that 2 mg/kg CBD BID may not be practical for many pet owners. In these cases, veterinarians should recommend a lower, more affordable dose such as 0.5 mg/kg BID and monitor for effect. The dose can be titrated up to effect over time.

4. The authors noted the CBD preparation used had minimal, but not absent, levels of other cannabinoids. They did not mention terpene content at all. This brings into question whether the entourage effect had any impact on the study results. Were the results purely due to the effects of CBD or did small amounts of other cannabinoids and/or terpenes contribute to the analgesia noted?

5. The authors made two key points regarding the concurrent use NSAIDs and CBD. First, they noted that the use of CBD may allow for reduced doses of anti-inflammatory drugs, thus alleviating some of the possible negative aspects of the pharmaceuticals such as GI, renal, and

hepatic effects. Secondly, the authors noted that COX2 inhibitors may slow the breakdown of CBD, allowing it to provide a longer duration of analgesia**.**

Take-home message:

1. Although it is not 100% clear the CBD in this study was absorbed transmucosal or a combination of transmucosal and GI, the results showing increased pain relief and increased quality of life when using CBD and pharmaceuticals for OA concurrently. This is something every practitioner should consider when treating patients with chronic pain.

2. Despite the studied dose of CBD being 2 mg/kg BID, lower dosages of CBD can be effective. Although not discussed in this paper, practitioners may find broad or full spectrum cannabis extracts to be more effective than CBD isolates alone due to the entourage effect. This is important due to the cost of treatment for large dogs at high doses of CBD.

Review by: Conny Mosley, DMV, DACVAA, CVA

1. This study looked at the efficacy of adding a CBD isolate to a multimodal OA treatment plan. The 12 weeklong study had some good aspects and some limitations. I appreciated the thorough introduction and discussion about the challenges within OA treatments. Even though Amitriptyline is not a drug that is commonly chosen in North America due to its potential side effects and lack of evidence for efficacy, the combination of an NSAID with gabapentin and an additional pharmaceutical drug is often used to treat OA. It was good to see somewhat of a standardized treatment protocol, although I think in this case it would have been nice to stay within either an NSAID or a steroid, especially because of the added variation of dosing reduction.

2. There were a few too many variations in such a small number of dogs per group, which was not captured adequately by the statistics and assessments. Unfortunately, no pharmacokinetic evaluation was done to support some of the hypothesis made by the authors. My biggest concerns are the subjectivity of assessment in particular considering the fact that owners were not blinded for the additional CBD. Also baseline numbers were not equivalent (dogs in control group appear to be worse off than in CBD group) and the changes seem inconsistent.

3. Table 3 is very important to look at to see those trends and differences. Using only one assessment tool (owner questionnaire) unfortunately also reduced outcome due to higher potential for placebo effect and limited objectivity. I was surprised to see that the control group hardly had improvements with the introduction of an NSAID, which makes me question the validity of its ability to pick up on any changes.

Take-home message:

We gained some very good insight from this study (and I am very grateful, that the authors provided us with this important information from publishing their clinical study.) Some of the things I really appreciated were:

1. There is a potential for the ability of reducing NSAIDs when used in conjunction with CBD (although this should be confirmed with a follow up study that includes pharmacokinetic data).

2. Reducing the NSAID dose without CBD appears to be not effective for treatment (specific data was not provided of how many dogs needed to have an increased dose again but looking at table 3 it appears that at week 4 (T3) the results seem to be worse for many dogs (which is when they reduced the dose by another 50%).

3. A CBD isolate appears to be effective when used in conjunction within a multimodal regimen and does not appear to cause side effects including bloodwork. The dose of 2mg/kg for an isolate is consistent with other studies but could also benefit from pharmacokinetic data for to further evaluate absorption/bioavailability as the author's statement about oral versus TM was extrapolated from other drugs (dexmedetomidine). It would be good to know for sure, if this was a true isolate (I presume it was?) as they only mentioned the very small amount of other minor cannabinoids, but did not say anything about terpenoids?