

Use of the Analgesic, Anti-inflammatory and Neuroprotectant Supplement Palmitoylethanolamide in the Tarsal Tunnel Syndrome

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Editorial

Tarsal tunnel syndrome (TTS) is an entrapment neuropathy. Conservative treatment options include anti-inflammatory drugs not always lead to resolution, and although results of surgical decompression are good in selected patients, postoperative fibrosis can lead to recurrence of complaints. However, clinical studies in this field are pilot trials only, both for decompression techniques as well as for conservative interventions, and only few patients were evaluated in each trial. If one would select a treatment based on sufficient clinical studies, data in other compression syndromes should be considered.

We will discuss such data for palmitoylethanolamide (PEA), a natural compound available as a supplement with an excellent safety profile [1]. PEA has been studied since the 1957 of last century as an anti-inflammatory and analgesic drug in many hundreds of pharmacological studies and in more than 30 clinical trials, in a total of around 6000 patients. PEA's efficacy and safety in nerve compression syndromes has been evaluated in nerve compression syndromes such as sciatic pain and pain due to carpal tunnel syndrome, in a total of 8 clinical trials and more than 1000 patients [2]. As the often-prescribed co-analgesic pregabalin appeared to be ineffective in a compression syndrome such as sciatic pain, PEA should be considered as an alternative treatment option for the treatment of nerve compression syndromes [3].

Nerve compression syndromes have different clinical manifestations, dependent on the localization of the compressed nerve, but they share identical pathogenesis and pain symptomatology. Research has shown that nerve pressure causes an inflammation of the nerve. Such a neuritis progresses into a more chronic pathological state due the induction of a number of cascades of chemical inflammatory reactions, and PEA can inhibit such cascades [4]. PEA is effective in various animal models of nerve compression, such as sciatic nerve ligation. PEA administered in such models decreases inflammation and pain. Repeated treatments with PEA even reduced the presence of intraneural edema and macrophage infiltrate and led to neuro-regeneration, such as a significantly thicker myelin sheath, an increased axonal diameter, and an increased number of nerve fibers [5]. These data support the use of PEA in nerve compression syndromes, and the active dose-range in most of the models was 10-30 mg/kg bodyweight. The vicious circle of inflammation, increasing pain and nerve degeneration thus can be halted by PEA.

In a double blind, placebo controlled study a high dose and a low dose of PEA was evaluated after three weeks of treatment. In this pivotal trial in six hundred and thirty-six patients suffering from pain due to radicular compression of the sciatic nerve were included. The decrease of pain was largest in the high dose group and significantly better than low dose and placebo, with more than 50% pain reduction

[6]. The numbers needed to treat (NNT) of PEA at week 3 was 1.5. The number needed to harm (NNH) must be at least in the hundreds, but for the time being not calculable due to the absence of serious and troublesome side effects leading to drop-outs in clinical trials [7]. In a controlled study in 26 patients the carpal tunnel syndrome PEA reduced pain and significantly improved the compression-induced reduction of median nerve latency time [8]. In a second study in 40 patients following a group-controlled randomized design in diabetic patients suffering from carpal tunnel syndrome, with pain, PEA significantly improvement pain and all neurophysiological parameters measured improved on PEA [9].

PEA belongs to an entire new class of analgesic products, devoid of addiction potential and drug-drug interactions so far have not been documented. This co-analgesic is easy to administer (in daily dose up to 1800 mg) and is available in 400 mg capsules containing pure PEA free from excipients. The optimal dose seems 1200 mg/day. The risk-benefit balance favours its inclusion in the therapeutic armamentarium of chronic pain and in nerve compression syndromes such as the tarsal tunnel syndrome. PEA can be administered both as a standalone analgesic as well as part of a pharmacological cocktail during multi-drug therapy.

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