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New Approaches to the Pharmacotherapy of Neuropathic Pain: Cannabinoids

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Disclosures

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Abstract and Introduction

Cannabinoids

The potential role of cannabinoid agents in the management of neuropathic pain has attracted considerable interest. The discovery of cannabinoid receptors 1 and 2 and the development of specific cannabinoid receptor agonist and antagonist ligands, as well as encouraging results from preclinical studies, point to a role of cannabinoids as a therapeutic modality. However, although animal work continues to suggest that cannabinoids may be useful for neuropathic pain, results in clinical studies have always been controversial. A few years ago, a meta-analysis examining cannabinoids failed to find convincing evidence of analgesic activity beyond that of weak opioids.[68] By contrast, the following randomized controlled trials published on the subject, showed that cannabinoid δ-9-tetrahydrocarnabinol/cannabidiol oromucosal spray[69,70] or dronabinol taken by mouth,[71] produced a significant decrease in the mean intensity of pain and in sleep disturbance in patients with central neuropathic pain due to multiple sclerosis, as well as in patients with chronic neuropathic pain of mixed origin. These results were replicated in an uncontrolled open-label extension study, which confirmed the benefit at 2-year follow-up of the oromucosal spray.[72] However, the important issue with the use of cannabinoids is adverse effects. In the two studies using oromucosal spray, the proportion of patients experiencing adverse events were 89[69] and 91%,[70] and 18% of patients withdrew owing to an adverse effect.[70] The proportion of adverse events was 96% for dronabinol use and 17% of patients had their doses reduced for intolerable adverse events.[71] In the three studies, the main adverse events were gastrointestinal and neuropsychological. Furthermore, driving regulation and legislation might limit cannabinoid utility in some European countries.

Finally, a recent randomized controlled trial compared the effect of nabilone, an oral synthetic cannabidoid, with dihydrocodeine in patients with chronic neuropathic pain of mixed origin and found that dihydrocodeine provided even better pain relief than nabilone and had slightly fewer side effects, although no major adverse events occurred for either drug.[73]

In summary, despite a putative role in central neuropathic pain associated with multiple sclerosis,[32] cannabinoids should not be considered as a first option in the treatment of neuropathic pain because of a debatable benefit–risk profile. The association between long-term use and precipitation of psychosis or schizophrenia is of particular concern.[32]

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