Buprenorphine and neuropathic pain

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1. What defines neuropathic pain?
Neuropathic pain is caused by a lesion (permanent or not) or a functional disturbance in either peripheral nerves or in the central nervous system. The main clinical symptoms of neuropathic pain syndromes are the presence of (painful or unpleasant) sensory disturbances (either spontaneous or evoked) as well as spontaneous pain.

2. Why is neuropathic pain difficult to diagnose and treat?
Often patients will fail to mention the presence of these sensory disturbances and physicians often fail to ask for it too. In addition, classical neurological electrodiagnostic investigations will examine the larger (A-beta) nerve fibers which are not mediating the pain signals. Classical neurological tests can not identify disturbances in the small afferent fibers (A-delta and C-fibers) that are part of the pathological process.

3. What treatments are available for neuropathic pain?
In the treatment of neuropathic pain antidepressants and anticonvulsants are often considered as the first line therapies for these conditions. However, in addition, the additive use of analgesics is often necessary (because insufficient analgesia is obtained with the TCAs and anti-convulsants). Moreover, several topical and other systemic therapies (such as NMDA-receptor antagonists, neuroleptics) can be used for the treatment of these painful conditions.

4. Why should opioid analgesia be used in neuropathic pain?
Opioids should be used if treatments with tricyclic antidepressants and/or anticonvulsants fail to show significant analgesic efficacy. In these conditions the addition of a 'general' analgesic is necessary and useful. After trying with class I and II analgesics, class III analgesics should be used if necessary. The addition of opioids to therapy-resistant neuropathic pain syndromes should only be initiated if and when polypharmaceutical approach to a neuropathic pain syndrome still appears to be insufficient.
5. What unique properties does buprenorphine have in neuropathic pain?
It seems, mostly from basic scientific investigations, that buprenorphine has some unique pharmacological and biochemical actions, beside the 'classical' interaction with the mu-opioid receptor. It is not only interacting with other opioid receptors beside the μ-receptor, but has probably also some strong interactions at other cellular and neurological levels. It is the only opioid demonstrating an antinociceptive effect via PTX-insensitive pathways. These characteristics are probably the reason for the increased efficacy of the molecule buprenorphine in the treatment of neuropathic pain syndromes.

6. What is the clinical evidence to support the use of buprenorphine in neuropathic pain?
At this moment, there is still not much clinical data to support the hypothesis of the specific efficacy of buprenorphine in the treatment of neuropathic pain. A few, rather small studies, have nevertheless shown an increased efficacy of buprenorphine in the treatment of typical neuropathic pain conditions (such as postoperative neuralgias). Unfortunately, much of this information is still anecdotal, and larger randomised controlled trials are therefore very much needed to further investigate the potentials of this analgesic drug in the treatment of painful neuropathic conditions.

7. How has buprenorphine performed in clinical usage?
It seems that buprenorphine is performing well in clinical usage, but as earlier mentioned, there is still a lack of randomised controlled trials that have really proven the superior efficacy of buprenorphine in these painful conditions.

8. Is the patch formulation of buprenorphine particularly appropriate for the treatment of neuropathic pain?
The patch formulation of buprenorphine leads to an easier use of buprenorphine in all clinical conditions (and hence to an increased patient compliance of the patients), but has no specific added value as such for patients suffering from neuropathic pain. It is about ease of use (compared to sublingual tablets) and this is identical for all types and kinds of pain patients. As in other forms of pain, the patch formulation avoids the serum peaks and troughs associated with other delivery types - so theory would suggest that the patch offers clinical advantages. The clinical data would suggest this too. Recent case studies by Likar & Sittl have confirmed that transdermal buprenorphine can be highly successful. Another multicentre study in 237 patients confirmed the efficacy of transdermal Buprenorphine in neuropathic pain conditions.

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9. Does the safety profile of buprenorphine affect treatment?
The favourable safety profile of buprenorphine is of course of great clinical importance. It means that we can use this molecule in patient populations that otherwise would be banned from the use of opioid analgesics (e.g. elderly). In addition, the safety profile of this molecule allows us to use it in a treatment scheme with several other pharmaceutical agents, like anti-depressants and anti-convulsants, without having to fear for major side effects.

10. Where next for buprenorphine?
There is still a need for further investigation into the interactions of the molecule of buprenorphine with the different opioid and non-opioid receptor systems. This additional information will probably shed some additional, and interesting, light on the clinical applications of buprenorphine.

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