Editorial comment

Improving pain treatment in children

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In this issue of the Scandinavian Journal of Pain, Brown and co-workers publish a randomized controlled trial comparing amitriptyline and gabapentin for the treatment of complex regional pain syndrome (CRPS) type I and neuropathic pain in children.1 There is an urgent need for well-performed trials in paediatric pain to guide clinical practice, and this study is the first randomized trial to compare first-line drugs for these conditions in the paediatric population.

1. Complex regional pain syndrome (CRPS)

CRPS is a condition characterized by spontaneous and evoked pain, oedema, changes in skin colour and temperature and trophic changes in the distal extremities. CRPS type I typically occurs after minor trauma without affecting the nerves, whereas type II is associated with nerve damage, but CRPS may occur irrespective of the nerve innervation territory.2 The diagnostic criteria for CRPS include continuing pain disproportional to any inciting event, at least three of sensory (hyperesthesia or allodynia), vasomotor, sudomotor or trophic symptoms and at least one sensory, vasomotor, sudomotor or trophic sign.3 The pathophysiology is complex and may include both inflammatory and central sensitization mechanisms.2 CRPS may also affect children and adolescents, in particular girls.4 CRPS has a relatively good prognosis in children, and many have spontaneous resolution after some months although it is also reported that pain persists into adulthood in some patients.4

2. Neuropathic pain

Neuropathic pain is pain caused by a lesion or disease of the somatosensory nervous system.5 It includes phantom pain, postherpetic neuralgia, painful polyneuropathy, posttraumatic nerve injury pain and central pain related to multiple sclerosis, stroke or spinal cord injury. In contrast to CRPS, neuropathic pain is distributed in an area consistent with the nervous system lesion, and there should be negative sensory signs in the same neuroratomically plausible area.6 Neuropathic pain in children is rare and differs from the forms seen in adults.7 In children, neuropathic pain mainly occurs following trauma, surgery or cancer. Even though the incidence of pain following nerve trauma is lower in children than in adults, it can still be severe and difficult to treat, and more focus on neuropathic pain in children is therefore needed.7

3. Treating pain in children

Treatment recommendations for CRPS and neuropathic pain differ. However, in both conditions, the underlying disease should be treated whenever possible. In many cases, the treatment of chronic pain is symptomatic and should balance effects and side effects. Often a multidimensional treatment approach is used, including both pharmacological and psychological treatments. For CRPS, exercise and physical therapy are the most important treatments, while pharmacological treatments can be used to facilitate mobilization and training. Recent treatment recommendations for neuropathic pain in adults include tricyclic antidepressants, serotonin-norepinephrine reuptake inhibitors, pregabalin and gabapentin, including extended release forms as first-line treatments, while tramadol, strong opioids, lidocaine 5% patches, capsaicin 8% patches, and botulinum toxin A are second- and third-line treatment options.8

There are no evidence-based treatment recommendations for CRPS and neuropathic pain in children and the treatment is based on recommendations for adults. Therefore, the study by Brown et al. is a very important contribution to the field. The current study investigated the effect of amitriptyline 10 mg at bedtime compared with gabapentin 900 mg/day in three divided doses for CRPS type I (n = 20) and neuropathic pain (n = 14) in children.1 Secondary outcomes were sleep disability and adverse events. Both amitriptyline and gabapentin significantly decreased pain for a treatment period of 6 weeks, with no statistically significant difference between the two drugs (p = 0.71). Both drugs also improved sleep to the same degree. There were very few adverse events related to the study medication. The very important and highly clinically relevant message from the study is that there is no difference in effects and side effects.
effects between gabapentin 900 mg and amitriptyline 10 mg in this paediatric population. As the authors also note, it is important to take into account the low number of patients, and it is possible that differences between the two drugs could be identified in a larger population, but recruitment to such a trial is very challenging.

The leading question is if the drugs are actually better than placebo? From clinical trials in adults, we know that placebo responses can be very high, with up to 50% pain reduction or more after placebo treatment. Of particular concern in relation to the particular study is that there is a good prognosis of CRPS in children and with the inclusion of patients with a pain duration of only 1 month, spontaneous recovery over the 6-week period of the trial is expected. Furthermore, the large age span (7–18 years) and thus presumably a large variation in weight in this population raise the question if the dosages used were therapeutic in all subjects as they will be lower than recommended in a large proportion of the study population [9]. The research team did not find it ethical to add a placebo treatment, which is very understandable, but the result is that it leaves us with this open question. Despite the limitations, the study presents a daily clinical problem and provides valuable information on the comparative efficacy of two drugs commonly used for treating neuropathic pain and CRPS.

Conflicts of interest

The authors declare no conflict of interest related to this Editorial comment.

References


