

# Pamidronate in complex regional pain syndrome: effective therapy in CRPS

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Complex regional pain syndrome (CRPS) is a debilitating disorder of which the underlying pathogenesis is poorly understood. Often, after trivial trauma, patients develop severe signs of pain and autonomic dysfunction in the affected limb leading to substantial loss in quality of life. Women are more often affected than men.

CRPS is mostly monophasic but some patients develop a relapsing remitting course.<sup>1</sup> A small group of patients develop chronic symptoms that can be so severe that ultimately amputation appears to be the sole solution. Two forms of CRPS can be distinguished: type I and type II. Different from CRPS type II, in type I no nerve damage can be demonstrated.

Although the underlying pathogenesis is not well known, inflammation is often considered the hallmark of the disease, but central sensitisation is probably also important. Dirckx et al. indicated the importance of mast cells in the pathogenesis of the disorder.<sup>2</sup>

In the past, various anti-inflammatory treatments have been tried with varied success. Remarkably, in a meta-analysis by Wertli et al., not immunosuppression but drugs usually used in disorders of calcium and bone metabolism appeared to be most effective in reducing pain.<sup>3</sup> Especially bisphosphonates were able to reduce pain in both early and longstanding disease. The effect of bisphosphonates is thought to be twofold. Bisphosphonates exert an effect on bone cells but probably also work in an anti-inflammatory manner. Other drugs that have been tried include anti-TNF, thalidomide and mannitol.

Although most cases of CRPS appear to be associated with trauma, CRPS can also develop after stroke. Petchkrua et al. calculated the incidence of CRPS after stroke to be 1.56%.<sup>4</sup>

In the current issue of the journal, Eun Young et al. describe the effect of treatment with pamidronate on

patients with CRPS type I following stroke and compare the effect with that of a two-week, high-dose corticosteroid treatment.<sup>5</sup> The results showed pamidronate to be as effective as corticosteroids to reduce pain in this group, but corticosteroids were somewhat better at reducing swelling. In their discussion, the authors suggest to use pamidronate in patients whose dominant symptom is pain and to combine pamidronate with steroids in those who suffer from severe swelling. As the authors state, corticosteroids have substantial side effects in a group of patients with cardiovascular disease. Alternatives for corticosteroids are available. In a very small study, anti-TNF treatment appeared to reduce symptoms as well.<sup>6</sup> However, anti-TNF treatment is expensive. Combining anti-TNF with pamidronate might be more interesting when human studies corroborate the findings in animal studies that anti-TNF might protect the brain from ischaemic damage.<sup>7</sup>

For now, pamidronate appears to be the drug of choice in both post-traumatic and post-stroke CRPS type I. However, as with many illnesses, therapy should not be restricted to only providing medication. A multidisciplinary approach involving pain management, physiotherapy and cognitive behavioural therapy next to drug treatment is most likely to benefit patients.

## REFERENCES

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