Bisphosphonates for pain relief in reflex sympathetic dystrophy?

Reflex sympathetic dystrophy (RSD) is a poorly characterised condition whose various and unpredictable features include pain, tenderness, swelling, vasomotor, and sudomotor changes, involuntary movements, and trophic phenomena.1 Also known by terms such as algodystrophy, Sudeck's atrophy, and complex regional pain syndrome (CRPS) type I, RSD most commonly follows trauma and is distinguished from causalgia (CRPS type II), which is associated with major nerve injury. The pain of RSD may have various qualities but is typically burning, spreads outside the area that has been damaged, and is often accompanied by sensory features, including allodynia and hyperalgesia. Osteoporosis is one of its diverse trophic features. It characteristically spares the articular surfaces and may be spotty, focal, or more widespread than at the site of the causative lesion.1 First recognised radiographically in 1900 by Sudeck,2 abnormalities of bone have subsequently been assessed by isotope, computed tomographic, and magnetic resonance bone scanning, and by bone densitometry. Evidence for a blood-flow-independent inflammatory component in RSD has been accruing3 to support Sudeck's suggestion of a pseudo-inflammatory cause for the osteoporosis he described. Do Sudeck's osteoporosis (atrophy) and these inflammatory changes provide clues to the cause of the pain of RSD and suggest new approaches to its treatment? Although in RSD the presence and extent of the pain and the osteoporosis are variable and seemingly unrelated, treatments that affect the structure of bone are not necessarily those responsible for the rapid pain relief. Rather, pain relief may result from effects on prostaglandin E2 and other nociceptive substances.4

Do the effects of bisphosphonates contribute to understanding the cause of pain in RSD? These drugs bind to bone and inhibit bone resorption by inhibition of osteoclasts, but processes that affect the structure of bone are not necessarily those responsible for the rapid pain relief. Nevertheless the bisphosphonates, currently unlicensed for use in RSD, seem to be well worth further investigation in appropriately controlled, long-term, sufficiently studies, to reach conclusions on their analgesic properties and therapeutic benefits in this disorder.

The use of different drugs, treatment regimens, and methods of assessing pain all make it difficult to reach definitive conclusions from these studies. Furthermore, the trials have each included 23 or fewer patients, patients' underlying conditions (although mostly post-traumatic) have been heterogeneous, some reports have not made clear how many patients had pain relief, and length of follow-up was unstated in some but was less than a year in all studies. Existing data are therefore only preliminary. The bisphosphonates, currently unlicensed for use in RSD, seem to be well worth further investigation in appropriately controlled, long-term, sufficiently studies, to reach conclusions on their analgesic properties and therapeutic benefits in this disorder.