

Manicourt D-H, Brasseur J-P, et al. Role of Alendronate in Therapy for Posttraumatic Complex Regional Pain Syndrome Type I of the Lower Extremity. Arthritis Rheum 2004;50(11):3690-3697.

Design: Randomized clinical trial

Population/sample size/setting:

- 40 patients (20 men, 20 women, mean age 45) treated for CRPS-I involving the lower extremity in the rheumatology department of a university hospital in Belgium
- All patients had symptoms after a trauma not associated with nerve damage and not confined to the distribution of a single peripheral nerve, with pain scores >40 on a scale from 0-100, allodynia and hyperalgesia in the diseased area, with skin changes and regional osteoporosis on plain x-ray; all patients had high uptake on a 3 phase bone scan
- Exclusion criteria were previous bisphosphonate treatment or sympathetic nerve blocks, ineffective calcitonin treatment within 1 week of study entry, peptic ulcer, diabetes, hypothyroidism, or renal/hepatic/cardiovascular disease

Main outcome measures:

- Study was divided into a double blind phase lasting 8 weeks and, after a 4 week washout period, an open label phase lasting 8 weeks to which all participants were invited
- Randomized to alendronate 40 mg each morning (n=20) or identical appearing placebo (n=20)
- Outcomes were measured at baseline and at weeks 4, 8, and 12
- The outcomes were spontaneous pain VAS on a 100 point scale, pressure tolerance measured with a dolorimeter, edema measured by the ratio of the circumferences of both legs (midpatellar, ankle, foot), and mobility measured by a goniometer
- Only 1 patient (in the alendronate group) withdrew due to upper GI intolerance; 1 placebo patient had nausea and heartburn but did not withdraw
- IN the placebo group, a small change from baseline was observed at week 12, but not earlier; in the alendronate group, a large reduction in pain scores was observed at 4, 8, and 12 weeks (4 weeks after discontinuing alendronate)
- Pressure tolerance was increased in the alendronate group at 4, 8, and 12 weeks, but did not change in the placebo group
- Edema decreased in both groups by a similar amount
- Mobility increased more in the alendronate than in the placebo group
- Urinary levels of type I collagen N-telopeptide decreased in the alendronate group after 8 weeks, but did not change in the placebo group
- After the 12 week point, 12 patients from each group volunteered for the 8 week open-label phase of the study; during this period, patients who had been in the placebo group improved their pain VAS, pressure tolerance, and joint mobility scores; the patients who had been in the alendronate group continued to improve in their pain, pressure tolerance, and mobility measurements

Authors' conclusions:

- At a daily dose of 40 mg (the dose generally used for Paget's disease), alendronate effectively treats post-traumatic CRPS of the lower extremity

Comments:

- Randomization appears to have been done in a way that produces a low risk of bias
- The primary outcome is not clearly stated; presumably, it was the spontaneous pain VAS scores
- The results are stated qualitatively in the text (no tabular display), and graphically in Figures 2, 3, and 4; visually, there appears to have been a large effect of alendronate, but the scores must be approximated by visual inspection of the figures
- Table 1 (baseline values of selected variables) states that none of the between-group differences were statistically significant, but the disease site (alendronate: 2 knee and 18 foot/ankle, placebo: 8 knee and 12 foot/ankle) is statistically significant (chi square with 1 degree of freedom is 4.8, p-.028)
- Success rates (proportion with 50% pain reduction) are not reported and cannot be calculated from the data presented; however, the success rate (from Figure 2) must have been high in the alendronate group

Assessment: Adequate for evidence that alendronate can effectively reduce lower extremity pain and pressure sensitivity in CRPS-I with positive bone scintigraphy