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Treatment with parathyroid hormone does not enhance clinical resolution and fracture healing of Charcot osteoarthropathy: double blind randomised placebo controlled trial

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Background and aims: There is a growing body of evidence to show that parathyroid hormone (PTH) is an effective anabolic therapy for the enhancement of bone repair, following fracture. The main objective of this study was to investigate whether recombinant human (rh) PTH (1-84) could enhance fracture healing and arrest bone and joint destruction in the acute Charcot foot.
Materials and methods: We carried out a double blind randomised placebo controlled trial in 48 patients with acute Charcot osteoarthropathy. We treated patients with daily subcutaneous injections of rh PTH 1-84 or placebo until clinical resolution of the osteoarthropathy or up to a period of 12 months. All patients received casting therapy and Calcium and Vitamin D3 supplementation. Time to clinical resolution was recorded in months. Serum concentrations of the bone turnover markers amino-terminal propeptide of type I procollagen (P1NP) and carboxyterminal telopeptide of type 1 collagen (CTX) were measured at presentation and then at 3 monthly intervals until clinical resolution or up to a period of 12 months. The rate of change of these bone markers from baseline up to clinical resolution was compared between the active and placebo groups. Semiquantitative bone marrow oedema (BMO) scores and fracture scores were calculated on non-contrast magnetic resonance imaging scans and the rate of change of these scores from presentation and on follow up (at clinical resolution or at 12 months) was compared between the groups.
Results: Logistic regression analysis indicated that there was no statistically significant difference between the active and placebo groups in the percentage of patients with clinical resolution at 6 months (Odds ratio= 0.94; 95% CI 0.30 to 3; P=0.92) and at 12 months (Odds ratio=2.3; 95% CI 0.68 to 7.7; P=0.18). There was no statistically significant difference between the survival (non-resolution patterns) between the active and placebo groups. The log-rank statistic was 0.11 yielding a p-value of 0.74 and the estimated hazard (for resolution) ratio was 1.1 (95% ci 0.57 to 2.1; P=0.78). There was a significant reduction in the serum concentration of P1NP during the study period, (P=0.004). However, the rate of change in P1NP was not significantly different between the active and placebo groups (P=0.13). The serum concentration of CTX remained unchanged from presentation to follow up (P=0.92). Moreover, there was no significant difference in the longitudinal change of this marker between the active and placebo groups. (P=0.25). The total BMO score significantly decreased between presentation and follow up ($p<0.001$). However, the rate of change in the total BMO score was not significantly different between the active and placebo groups (p=0.95). Similarly, although the total fracture score significantly decreased between presentation and follow up (p=0.001), the rate of change in the total fracture score was not significantly different between the active and placebo groups (p=0.55).
Conclusion: This study has shown that treatment with rh PTH does not enhance time to resolution and fracture healing of the acute Charcot foot. Casting therapy remains the mainstay of Charcot foot management.
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