Paper - Basic Science

Paper Session: Quantifying Fracture Healing

Are Bone Turnover Markers Useful Surrogate Measures of Fracture Healing After Intramedullary Fixation of Tibia and Femur Fractures?

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Purpose: Bone turnover markers (BTMs) have been promoted as promising surrogate markers of fracture healing. We sought to describe the changes in BTMs during fracture healing, and determine if vitamin D supplementation would alter fracture healing metabolism.

Methods: Adult patients aged 18-55 years receiving an intramedullary nail for a tibial or femoral shaft fracture were invited to participate in a randomized controlled trial comparing varying doses of vitamin D3 supplementation to placebo. Participants received active or placebo loading doses at injury and 6 weeks, and doses daily for 3 months. Treatment allocation was double-blinded, and included 4 treatment arms: (1) 150,000 IU loading doses, (2) 4000 IU daily, (3) 600 IU daily, or (4) placebo. Serum concentrations of CTX (C-terminal telopeptide of type I collagen, a bone resorption marker) and PINP (N-terminal propeptide of type I procollagen, a bone formation marker) were measured at baseline, 6 weeks, and 12 weeks post-injury. Clinical fracture healing was assessed at 3 months by the treating surgeon. The change in BTMs over time was analyzed relative to each participant's baseline concentration. Mixed effects linear models were used to determine the mean difference in BTM concentrations between participants who achieved fracture healing within the 3-month study period versus those who did not. Additional models explored the effect of vitamin D3 supplementation on the BTM concentrations.

Results: 101 participants were enrolled with a mean age of 27 years (standard deviation [SD] 8). Both CTX and PINP concentrations changed over time, with maximal mean differences observed at 6 weeks in all treatment groups. Additionally, both BTMs had higher concentrations at 6 weeks among patients who healed within 3 months of injury versus those who did not heal during the study period: CTX mean difference 0.29 (95% confidence interval [CI]: 0.01 to 0.57, P = 0.04) and PINP mean difference 57.2 (95% CI: 8.3 to 106.4, P = 0.02). Vitamin D3 supplementation appeared to decrease CTX activity compared to placebo (–0.28 mean difference; 95% CI –0.59 to 0.02; P = 0.08). Vitamin D3 supplementation had no effect on PINP (P = 0.58).

Conclusion: CTX and PINP concentrations increase during acute fracture healing. Vitamin D3 supplementation may cause a decreased bone resorption marker response, but does not affect the bone formation marker. Given the early association between the 6-week BTM concentrations and 3-month clinical fracture healing, CTX and PINP appear to be potential surrogate markers of fracture healing.

OTA Grant