

Histological Examination of the Effects of Thrombopoietin Mimetic Peptide (TMP) and High-Fat Diet on Femur Fracture Healing

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Background and Hypothesis:

In the US, 11.3% of the population are diabetic. Impaired bone healing is a complication of diabetes that dramatically impacts quality of life. Thus, it is imperative to find effective, low-risk treatments for patients that can accelerate fracture healing. We propose treatment of femur fractures using a thrombopoietin (TPO) analogue, TMP, will expedite healing, reduce adverse side effects compared to FDA-approved BMP-2, and improve quality of life of diabetic fracture patients.

Experimental Design or Project Methods:

Tie2^{CreERT+} mice were bred with Mpl^{fl/fl} mice to generate mice in which the TPO receptor (Mpl) was deleted in cells of the endothelial lineage (Tie2 expressing cells) following tamoxifen induction (3 consecutive daily 10mg/kg doses). Tie2^{CreERT+}; Mpl^{fl/fl} and Tie2^{CreERT+}; Mpl^{+/+} mice served as experimental and control mice, respectively. Eight-week-old male mice of both genotypes were placed on a low-fat diet (LFD) or high-fat-diet (HFD) for 12 weeks. One week prior to surgery, mice were injected with tamoxifen to induce Cre-recombination. Mice were then subjected to femur fracture and treated with saline or TMP (33nmol/kg/day) for the first week post-surgery. Mice were euthanized at 1-, 2-, and 4-week post-surgery and injured femurs were isolated for histological evaluation of the fracture callus size and composition.

Results

To date only Tie2^{CreERT+}; Mpl^{fl/fl} specimens have been processed. As expected, untreated HFD mice exhibited impaired fracture healing compared to similarly untreated LFD mice. As would also be expected, no differences were observed in fracture healing histological parameters between saline and TMP treated Tie2^{CreERT+}; Mpl^{fl/fl} mice at similar time points post-surgery.

Conclusion and Potential Impact:

While ongoing, this study explores the efficacy of using thrombopoietic agents for fracture healing in type 2 diabetes. If promising, thrombopoietic agents could replace, BMP-2 treatment, and may improve the quality of life for individuals experiencing impaired fracture healing.