Thrombopoietin: A Novel Bone Healing Agent

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Critical-size defects in bones do not heal spontaneously and usually require the use of grafts. Unfortunately, grafts have several limitations. To improve bone formation, many clinicians now use bone morphogenetic proteins (BMP), particularly in spinal fusion, fracture healing, and in critical-size defect regeneration. However, multiple side effects of BMP treatment have been uncovered including increased incidence of cancer. Thus, there is great interest in alternatives that allow for safe and effective bone regeneration. Here we show the ability of thrombopoietin (TPO), the main megakaryocyte growth factor, to heal critical-size femoral defects rodents. 5mm or 4mm segmental defects were created in the femur of Long Evans rats or C57BL/6 mice, respectively. The defects were filled with a novel bioabsorbable scaffold which was loaded with recombinant human TPO, BMP-2, or saline, and held stable by a retrograde 1.6 mm intramedullary Kirschner wire (rats) or 23G needle (mice). Xrays were taken every 3 weeks in rats and weekly in mice. Animal were sacrificed at 15 weeks, at which time micro-computed tomography (μCT) and histological analyses were performed. The results observed in mice and rats were similar. The saline control group did not show bridging callus at any time. Both the BMP-2 and TPO groups healed the defect, although bridging callus was evident at earlier times in the BMP-2 groups. However, the TPO groups showed a much more remodeled and physiologic contour on both Xray and μCT. μCT and histological analysis confirms that compared to BMP-2, TPO-treated specimens have a thicker cortex but smaller diameter and smoother contour. TPO appears to restore the original bone contour by stimulating osteoblastogenesis, allowing for periosteal bridging and stabilization to occur, while simultaneously stimulating osteoclast formation. Thus, TPO may serve as a novel bone healing agent.

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