BMP2 Accelerates Healing and Prevents Infection in 2 Porcine Critical Sized Defect Models

Todd O. McKinley, MD*; Melissa Kacena, PhD; Paul J. Childress, PhD; Jeffrey Anglen, MD, FACS; Tien Gabriel Chu, PhD; Austin Wininger; Karl D. Shively, MD; Roman Natoli, MD*
Indiana University School of Medicine, Indianapolis, IN, United States

Purpose: Severely injured limbs with segmental bone defects (SBDs) frequently develop nonunions and infections. Adjunctive therapies to facilitate bone healing and prevent infection have been repeatedly explored to treat SBDs. Bone morphogenetic protein 2 (BMP2) has been shown to facilitate healing in SBDs and has also been shown to have direct effects on T-cells. Several clinical studies have suggested that BMP2 can mitigate infection. Here we report the effects of BMP2 on promoting bone healing and preventing infection in 2 novel porcine critical sized defect (CSD) models.

Methods: 16 Yucatan Minipigs (YMPs) were subjected to 25-mm SBDs resected from the midtibial diaphysis. The SBDs were stabilized with a statically locked custom porcine intramedullary nail (IMN). Eight pigs were treated with a saline-impregnated collagen sponge placed in the defect and 8 pigs received an identical sponge impregnated with BMP2. Eight additional YMPs were subjected to a 40-mm SBD from the midtibial diaphysis. The SBDs were stabilized with an 8-hole 3.5 compression plate on the lateral surface and an 8-hole one-third tubular plate applied to the anteromedial tibial surface (ORIF [open reduction and internal fixation]). Four pigs had saline-impregnated collagen sponges and 4 pigs had BMP2-impregnated sponges. The IMN pigs were sacrificed at 6 months postsurgery and the ORIF pigs were sacrificed 3 months after surgery. Three trauma- trained orthopaedic surgeons measured mRUST [modified Radiographic Union Scale in Tibial fractures] scores on serial radiographs made at monthly intervals.

Results: All 8 IMN YMPs treated with BMP2 healed (mRUST at 6 months: 15.1 ± 1.0) in contrast to only 1 of 8 YMPs treated with saline (mRUST 6 months: 9.2 ± 2.4; $P < 0.00001$). Three of 4 BMP2-treated YMPs with ORIF healed (mRUST 3 months: 14.3 ± 1.0) in contrast to 0 of 4 ORIF YMPs treated with saline (mRUST 3 months: 8.3 ± 1.2). One BMP2-treated ORIF YMP had catastrophic hardware failure 1 week after surgery and was sacrificed. Mean mRUST score at 2 months in the BMP2-treated pigs was 12.3 ± 1.9 in the IMN group and 13.2 ± 1.3 in the ORIF group, demonstrating rapid healing effects of BMP2 in both models. Seven of 8 YMPs treated with saline and IMN developed surgical site infections that occurred from 28 days to 173 days after surgery. In contrast, only 1 of 8 BMP2-treated YMPs with IMN had an infection 120 days after surgery. Likewise, 3 of 4 of the saline-treated ORIF YMPs had wound infections in contrast to 0 of 3 BMP2-treated YMPs after ORIF.

Conclusion: BMP2 was effective in promoting rapid SBD healing. In addition, infections were minimized in the BMP2 groups. The infections in saline-treated animals were delayed and potentially resulted from nonunion and limb instability. This new porcine CSD model may be an effective model to study SBD interventions.