Distraction Osteogenesis with Bone Morphogenetic Protein Enhancement: Facial Cleft Repair in Humans

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Introduction

This paper demonstrates the use of recombinant human bone morphogenetic protein (rhBMP-2) for enhancement of consolidation during distraction osteogenesis in humans. Three patients with facial bone discontinuity defects underwent distraction surgery. Two patients had nonunions treated with rhBMP-2. One patient had application of rhBMP-2 at the time of distraction osteotomy. All of the sites successfully consolidated. In a previous study, Boyne and Chin showed the efficacy of rhBMP-2 enhancement of alveolar distraction sites in non-human primates. This report demonstrates the combined use of distraction osteogenesis and bone morphogenetic protein in human maxillofacial reconstruction.

Materials and Methods

Recombinant human bone morphogenetic protein (rhBMP-2) is manufactured by Genetics Institute and is distributed by Medtronic as Infuse. In each application, the rhBMP-2 was prepared at 1.5mg per cc. An absorbable collagen sponge (ACS) was used as a carrier creating a rhBMP-2/ACS device. In this series, three application protocols were used. In one case, the rhBMP-2 was placed into the distraction gap after full transport was achieved. In a second case, the docking site was closed by distraction and then the rhBMP-2 placed. In a third case, the rhBMP-2 was placed at the time of osteotomy in both the distraction site and the docking site. Follow up evaluation was done by postoperative radiographs.

Results

Case 1. A 2 year old presented with a Tessier 7 cleft dividing the face
from the commissure through the ear (fig 1). The left mandible was severely hypoplastic and there was substantial soft tissue hypoplasia of the left face. A modified Zurich distractor (KLS-Martin) was used. After a 5 day latency period, the distractor was opened 1 mm per day for 30 days. The distraction process established a 30mm regeneration chamber. Forty-five days postoperatively, plain radiographs showed continuous, bone-like opacity across the distraction site (fig 2). When the site was surgically explored at 49 days postoperative, the distraction chamber was found to be empty (fig 3). There was a thin layer of dense tissue on the medial aspect of the chamber. Disengagement of the distraction device confirmed the segments were not stable. Bone morphogenetic protein, 12mg carried on an absorbable collagen sponge was placed into the regeneration chamber (fig 4). Computed tomography was performed at 3 and 6 months post treatment with rhBMP-2. The CT studies confirmed three-dimensional consolidation of the site (fig 5,6). No local or systemic adverse effects were noted.

Case 2. A second child with a midline facial cleft, Tessier 0, presented with a missing premaxilla (fig 7). Horizontal, bifocal distraction transported bilateral alveolar segments into the midline. Bilateral Liou distractors (KLS-Martin) were used. After a 5 day latency period, the distractors were activated at 1mm per day for 15 days. Orthodontic appliances guided the segments in a curvilinear path. The segments docked in the midline (fig 8). The
Docking site developed a non-union with deficiency of adjacent bone (fig 9). 30 days after the completion of the distraction, the sites were re-entered. The distraction sites were completely consolidated but the midline docking site had osseous discontinuity, thinness of the adjacent bone, and a patent soft tissue cleft in the midline. The defect was managed by elevating and advancing gingival flaps to create a chamber. The chamber was lined with rhBMP-2 in collagen sponges and the central portion filled with rhBMP-2 (fig 10). Osseous union was confirmed by follow-up radiographs (fig 11).

Case 3. A third patient presented with a 20 mm segmental defect in the maxilla. Prior attempts to repair the site with bone grafting had failed. A segmental osteotomy created a transport disk containing a single premolar. The segment was transported horizontally using a Liou distractor. At the time of surgery, rhBMP-2 was placed into the minimally displaced distraction osteotomy. A second rhBMP-2/ACS device was placed into the docking site at the time of the osteotomy. Following a 5 days latency, the segment was transported at 1 mm per day for 12 days. The distractor was left in place for 30 days and then removed. Post-operative radiographs confirmed osseous union.

Discussion

Given the nature of these deformities and proposed treatment, the potential risk for incomplete union was substantial. In case 1, the magnitude of the
transport distance was extreme in comparison to the pretreatment bone mass. Given the severity of the deformity, additional mandibular lengthening surgery can be expected in the future. In the second case, rhBMP-2 was used to consolidate the docking site and augment the width of the adjacent bone for placement of dental implants. In the past, docking sites have typically required secondary surgery to achieve a union. The third case uses rhBMP-2 at both the distraction site and docking sites. In contrast to case 1 and 2, Case 3 administers the rhBMP-2 at the time of distraction osteotomy. The effect of the rhBMP-2 must persist for weeks to be useful in this case. In all cases, the use of rhBMP-2 allowed satisfactory healing without the need to harvest autogenous tissue.

Conclusions

Nonunion following distraction osteogenesis is an inherent risk. Some clinical situations are predisposed to develop unions that are structurally unsatisfactory or lack sufficient volume for dental eruption. Docking sites do not form predictable unions and often require a second procedure to achieve osseous continuity. Large transports distances of narrow ossicles often form thin regenerates. Sites compromised by prior surgery or pathosis may form bone poorly. These three clinical situations may benefit from rhBMP-2 application. This paper demonstrates three approaches to integrate rhBMP-2 into distraction surgery.

Future

Additional research is needed to determine the best specific proteins, timing of administration, dosage, carrier, and distraction protocol to take full advantage of morphogenetic protein enhancement.

References