An in vitro and in vivo analysis of fibrin glue use to control bone morphogenetic protein diffusion and bone morphogenetic protein-stimulated bone growth.

Authors: Patel VV, Zhao L, Wong P, Pradhan BB, Bae HW, Kanim L, Delamarter RB

Publication Date: 2006

Abstract:

BACKGROUND CONTEXT: Recombinant human bone morphogenetic protein-2 (rh-BMP2) has become popular for augmenting spine fusion in the lumbar and cervical spine. Concerns exist, however, over bone morphogenetic protein (BMP)-stimulated soft-tissue swelling and bone growth stimulation in areas where bone is not desired, especially as the material "leaks" into such spaces. The most detrimental effects of such leakage might be airway compromise, while heterotopic bone formation into the spinal canal has been reported in animal and human studies. Fibrin glue has been used as a carrier of many osteoinductive materials; however, its efficacy at modulating the clinical effects of BMP are not known. The amorphous nature of fibrin glue makes it a candidate to control diffusion of BMP and possibly limit bone formation by limiting BMP diffusion to areas where such bone is not desired.

PURPOSE: To evaluate the use of fibrin glue to limit BMP diffusion and BMP-stimulated bone growth.

STUDY DESIGN/SETTING: This is an in vitro basic science study and an in vivo prospective randomized animal study.

STUDY SAMPLE: Eighteen Lewis rats.

OUTCOME MEASURES: In vitro study: Enzyme-linked immunosorbent assay measurement of rh-BMP2 concentration in saline. In vivo study: At day 60, rats were evaluated for neurologic deficits before sacrifice. Spines were harvested, and the following studies were performed: 1) manual testing for fusion and bone growth; 2) X-ray evaluation; 3) Micro-computed tomography (micro-CT) scans.

METHODS: In vitro study: Collagen sponges soaked with BMP at two different concentrations were incubated in saline solution with and without encapsulation by fibrin glue. Saline BMP concentrations were measured at consecutive time points. In vivo study: A rat fusion model using rh-BMP2 for fusion has been developed and tested with resultant100% fusion in over 100 rats. Lewis rats were divided into two groups and treated as follows: I: Exposure of L4-L5 transverse processes, decortication, and placement of BMP sponge in the lateral intertransverse space. II: Exposure and decortication as above and placement of fibrin glue before BMP sponge placement.

RESULTS: In vitro study: Peak rh-BMP2 concentrations in saline were 20% and 45% of the maximum possible for fibrin glue encapsulated sponges and controls, respectively, with a more gradual increase to peak concentration in samples encapsulated in fibrin glue. In vivo study: No rats exhibited any neurologic deficits. X-rays revealed at least partial bone formation in all rats. Manual testing of intertransverse fusion spines revealed 100% fusion in rats treated with BMP only, whereas rats treated with fibrin glue before placement of BMP sponges revealed only one possible fusion. Posterior-lateral bone formation was present on X-ray in both groups, and micro-CT imaging revealed bridging bone from transverse processes to the BMP-stimulated bone in the control groups. In spines treated with fibrin glue before rh-BMP2 placement, bone formation could still be seen within the soft tissues; however, bridging bone connecting to the transverse processes was either significantly decreased or not present.

CONCLUSIONS: Fibrin glue can limit rh-BMP2 diffusion. Also, because it limited bone formation at the transverse processes, it can be inferred that fibrin glue can limit bone formation when used to separate areas of desired bone formation from areas where bone formation is not desired.