Demineralized bone matrix enhances consolidation during distraction osteogenesis by promoting endochondral bone formation.

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ABSTRACT INTRODUCTION:
Distraction osteogenesis (DO) is a strong tool for bone and tissue regeneration. However, prolonged healing time remains as a major problematic obstacle. Enhancement of bone formation had been tried using various drugs including medesenchymal stem cells (1), bone morphogenetic protein (2) and growth factors (3). So far, these enhancement methods have limitations in terms of accessibility, high cost, short duration of effect and low effectiveness. Demineralized bone matrix (DBM), which is thought to have both osteoinductive and osteoconductive activity, is widely used to enhance bone formation in bone defect or impaired fracture healing (4,5). In this study we examined the effect of DBM on consolidation of bone regenerate during DO.

METHODS:
All animal protocol received prior approval by the institutional animal care and use committee.

Animal Model
The immature rabbit tibial DO model was used. After the application of bilateral monofixator using K-wires, meticulous osteotomy was done. Tibiae were elongated at a rate of 1mm twice a day for 10 days (total 20 mm length-gain) after 4 days of latency period. At the end of distraction (POD14), animals received DBM 100mg (DBX®, MTF, Edison, NJ) percutaneously (DBM group, n=12) (Fig.1) or were left without further procedure (CON group, n=12). Another 18 animals which underwent DBM injection were allocated to histologic examinations to evaluate temporal histological changes following DBM injection.

Fig. 1. Rabbit tibial DO model and percutaneous injection of DBM

Analytic Parameters
In DBM group and CON group, plain radiographs were taken every week. Pixel analysis of digitized plain radiograph was performed using ImageJ program. At post-distraction 3rd and 6th weeks after sacrifice, bone DEXA and micro computerized tomography (μCT) studies were conducted to determine bone mineral density (BMD) in the regenerate and adjacent host tibiae. Pixel data and BMD of the bone regenerate was normalized by data from ipsilateral tibial bone. For histologic analysis, decalcified bone section was stained with hematoxylin & eosin (H&E stain) and Safranin O & fast green stain.

RESULTS SECTION:
Pixel analysis of the digitized plain radiographs shows that higher density values in DBM group during early consolidation period and density became similar between two groups after 4 weeks of consolidation (Fig.2). Regenerate BMD was higher in the DBM group when compared with that in CON group at post-distraction 3rd weeks (Fig. 3). Quantitative analysis using μCT revealed larger trabecular bone volume, higher trabecular number and less trabecular separation in the DBM group versus CON group. Cross-sectional area and cortical thickness at post-distraction 6th weeks, assessed using μCT, was greater in the regenerates of DBM group compared with CON group. Histological evaluation revealed higher trabecular bone volume and trabecular number in the regenerate DBM groups (Fig.4). New bone formation was apparently enhanced, via endochondral ossification, at the site and in the vicinity of the injected DBM (Fig.5). DBM was slowly absorbed but remained until postoperative 6th weeks after injection.

Fig. 2. Relative pixel density of distraction gap on digitized plain radiographs

Fig. 3. Relative BMD of bone regenerate in the distraction gap

Fig. 4. Histologic evaluation of distraction gap at post distraction 3rd week (H&E stain)

Fig. 5. Endochondral ossification in the vicinity of the injected DBM

DISCUSSION:
DBM administration into the distraction gap at the end of distraction period leads to significantly greater regenerate bone area, trabecular number and cortical thickness in rabbit’s tibial DO model. These data suggest that percutaneous DBM administration at the end of distraction period or early consolidation period may stimulate regenerate bone formation and consolidation in the clinical situation with delayed bone healing during DO.

REFERENCES:

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