Bone regeneration using uncultured cells of bone marrow aspirate concentrate

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[Objectives]
Regenerative therapy with cultured bone marrow MSCs is associated with uncertainties with regard to the extent of bone regeneration. This technique is expensive and complex. In this study, we examined the bone-inducing ability of uncultured cells of bone marrow aspirate concentrate (BMAC).

Bone regenerative therapy

Cultured cell therapy
Bone Marrow Aspirate (BMA)

Cultural therapy

- Complex Safety? Expensive Uncertainty
- Easy Safe Costeffective

Can we regenerate bone using BMA without culture procedure?

[Methods]

Experiment 1: ectopic bone formation model
Animals: Four adult beagle dogs (male, approximately 10 kg)
Preparation of implant materials
- BMA group: 8-tricalcium phosphate (B-TCP) with BMA anti-coagulant CPD2ml + BMA13ml + B-TCP centrefuge (2500G 15min)
- BMAC group: B-TCP with nonconcentrated BMA anti-coagulant CPD2ml + BMA2ml + B-TCP 2%CaCl2 added to form coagulation.
- TCP group: B-TCP alone

B-TCP was implanted into the back muscle of dogs. Porous B-TCP blocks, 5 × 5 × 5 mm, porous size: 200–400 μm (Ostex, Olympus Terumo Biomedical Co, Japan).
Bone marrow is extracted from the iliac and femur bone.

Cell counts of BMA and BMAC

- BMA group
- BMAC group

Platelet counts and TGF-β concentrations

Histological analysis

- Characteristic of mononuclear cells were analyzed by FACS.
- Selection two levels of sections per sample
- Quantitation of bone formation area

Beta-TCP

The endpoint differences between the groups were analyzed using t-test (p < 0.05).

[Results]

Platelet counts - Fibroinogen and TGF-β concentrations

We compared the number of bone marrow cells that could be cultured for 1 week and collected between the BMA group and BMAC group.

The concentration of TGF-β1 were undetectable or lower than 62.5 pg/ml.

TCP group BMA group BMAC group

In the TCP group, many residual TCP was invagination. The bone trabecula and bone marrow were still immature in both group. In the BMA group, the contour of the alveolar bone crest was well retained. A significant difference was observed between the control group and experimental groups (P<0.05) at 6 and 12 weeks.

In another experiment, β-TCP block with cultured MSCs was implanted into the back muscle of dogs using the same method.

The numbers of cells in BMAC was much less than that of the cultured cells. But the results of BMAC group were better than the cultured one. Therefore, we speculate that the number of MSCs was not the most important factor for bone formation.

In the TCP group, many residual TCP was noted, and the crest width was not sufficiently augmented and the outline of the buccal alveolar plate was depressed with epithelial invagination. The bone trabecula and bone marrow were still immature in both group. In the BMA group, the contour of the alveolar bone crest was well retained. A significant difference was observed between the control group and experimental groups (P<0.05) at 6 and 12 weeks.

Three important factors of regeneration therapy are signal, cells and scaffold. BMAC includes bone marrow stromal cells and BMSCs as cells, fibrin as scaffold, growth factors from BMA or platelets as signal. We think that signal and scaffold factors are more important than cells.