Percutaneous autologous bone marrow injections for delayed or non-union of bones

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ABSTRACT

Purpose. To evaluate 12 patients with delayed or non-union of bones treated with bone marrow injections.

Methods. 6 men and 6 women aged 15 to 70 (mean, 45) years underwent bone marrow injections for delayed union (n=2) or atrophic non-union (n=10) of the ulna (n=6), femur (n=3), humerus (n=2), or metacarpal (n=1). Bone marrow was aspirated from the anterior iliac crest and injected to the delayed and non-union sites. Two injections were given for children and adolescents, and 3 for adults. The interval between the injections was 6 to 8 weeks. The amount of bone marrow injected was 30 to 40 ml for long bones and 20 ml for metacarpals.

Results. Ten of the 12 delayed or non-union of bones healed after bone marrow injections. The mean time for callus formation was 5.8 (range, 3–10) weeks, for clinical union was 7 (range, 4–12) weeks, and for radiological union was 16 (range, 10–24) weeks.

Conclusion. Multiple injections of low-volume bone marrow can be used for treatment of delayed or non-union of bones.

Key words: bone marrow; bone matrix; injections; platelet-rich plasma

INTRODUCTION

The process of fracture healing involves interplay of various biomechanical and biological factors.1 Inadequate mechanical stability and biological environmental may result in non-unions. Hypertrophic non-unions result from inadequate mechanical stability with abundant callus formation, whereas atrophic non-unions are characterised by little or no callus formation secondary to poor biological response.2 The biological environment can be improved by introduction of materials with osteogenic, osteoinductive, and osteoconductive properties, and thus autografts are the gold standard for the treatment of non-union.3 Nonetheless, bone grafting is associated donor-site morbidity.4 Percutaneous bone marrow grafting and injections is less invasive,5–10 while also being osteogenic and

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osteoinductive. We evaluated 12 patients with delayed or non-union of bones treated with bone marrow injections.

MATERIALS AND METHODS

Between March 2004 and August 2010, 6 men and 6 women aged 15 to 70 (mean, 45) years underwent bone marrow injections for delayed union (n=2) or atrophic non-union (n=10) of the ulna (n=6), femur (n=3), humerus (n=2, Fig. 1), or metacarpal (n=1, Fig. 2). The fractures were the result of high- (n=6) or low- (n=6) velocity trauma; there was no open fracture or infected non-union. All the fractures were grossly stable. The mean time since injury was 9 (range, 5–53) months.

Non-union was defined as no progression of bone union after 6 months. Clinically, delayed union was indicated when there was pain and tenderness on stress at the fracture site, whereas non-union was indicated when no pain and movement was elicitable at the fracture site. Radiologically, delayed union was indicated when the fracture site was clearly visible but the ends were not sclerosed, whereas non-union was indicated when the fracture site was visible with ends sclerosed.

Patients were placed in a supine position and under general anaesthesia. The procurement procedure was similar to that used for bone marrow transplant by haematologists and oncologists. A 2-mm incision was made at the level of anterior iliac crest, and a bone marrow aspiration needle was introduced into the cancellous part of the iliac crest in between the inner and outer tables, down at a depth of 6 to 7 cm. Bone marrow was aspirated in small volumes to avoid dilution by peripheral blood, using a 10-ml plastic syringe. After one full turn, the trocar was withdrawn 1 cm toward the surface and the same process repeated until the desired volume was obtained.

Under fluoroscopic control, the bone marrow was then injected (via the same trocar) into the gap and bone ends (Fig. 3). Two bone marrow injections were given for children and adolescents, and 3 for adults. The interval between the injections was 6 to 8 weeks. The amount of bone marrow injected was 30 to 40 ml for long bones and 20 ml for metacarpals.

Patients were discharged on the same day and followed up at weeks 3 to 4 to assess callus formation and clinical and radiological union. Mobility was not restricted.
Ten of the 12 delayed or non-union of bones healed after bone marrow injections (Table). The mean time for callus formation was 5.8 (range, 3–10) weeks, for clinical union was 7 (range, 4–12) weeks, and for radiological union was 16 (range, 10–24) weeks. There was no complication, except that most patients felt mild discomfort at the donor and injection sites. The remaining 2 cases were failures. In a 50-year-old female cigarette smoker with non-union of a mid-shaft ulnar fracture, callus formation was delayed and did not lead to clinical or radiological union. In a 56-year-old chronic alcoholic man with non-union of a right proximal humeral fracture, he first underwent fixation with a plate, which was removed 4 months later. There was no sign of bone union, and the patient underwent intramedullary nailing 3 months later and was followed up for 18 months, but non-union persisted. The patient then underwent Exogen (ultrasound) treatment without much effect. 15 months later, the nail was replaced with a plate and bone grafts, but this too failed. 17 months later, bone marrow injections were attempted but eventually failed.

The incidence of non-unions is estimated to be about 2.5%, and can increase to 13 to 16% in the presence of an open fracture and soft-tissue injury.16–18 Bone grafting involves surgery at the donor and non-union sites for graft harvesting and transplantation.4,19–22 Percutaneous autologous bone marrow injection is minimally invasive and can promote bone healing for stable atrophic non-union. The concentration of colony-forming units needed to stimulate bone healing has been reported.9 A one-off bone marrow injection is suggested, but its success rates varied.6–10 Other methods to address non-union that have limited success include use of demineralised bone matrix (DBM),23 recombinant bone matrix protein (rhBMP),24,25 and platelet-rich plasma.26,27 The DBM is osteoinductive and osteoconductive and can stimulate new bone formation via endochondral ossification.23 However, it necessitates surgery at the non-union site and its outcome is unpredictable, as the quality of DBM depends on the patient’s age and health status of donors, processing and sterilisation of products, and bioassays.28 Similarly, the use of rhBMP necessitates surgery at the non-union site, and there are few such
studies for non-unions in humans. Platelet-rich plasma can be administered percutaneously, but centrifugation is needed and its osteogenic potential has not been established in human models, despite varied success rates in animal models. In terms of costs, bone marrow and platelet-rich plasma can be obtained from the patient, whereas a vial (4 ml) of rhBMP costs around £3000, and a vial (2.5 ml) of DBM costs £286.

In earlier studies for non-union of the tibia, a copious amount (100 to 150 ml) was used for one-off injection at the fracture site. This large volume decreases the concentration of osteoblast progenitor cells owing to dilution of the bone marrow with peripheral blood. It is suggested that one-off 20 ml injection of concentrated bone marrow (from 120 ml of bone marrow aspirate) can provide predictable bone healing stimulation. In the current study, frequent injections of small volumes of crude (non-centrifuged, non-concentrated, non-diluted) bone marrow over a 12-week period also achieved good bone healing for non-union of various bones. Our approach obviated the need for centrifuging the bone marrow aspirate and could be used in district-level hospitals.

The limitations of the current study were the small patient number and the absence of laboratory evidence of minimum colony-forming units in the sample used. The outcome of bone marrow injection is operator and patient dependent, as they determine the stem cell concentration of aspirate. The need to undergo general anaesthesia on 2 to 3 occasions is a drawback, but postoperative functional limitation is minimal. Bone marrow injection is a minimally invasive, almost complication-free, day-surgery procedure for treating delayed or non-union of bones. It should be considered prior to more extensive surgical options like autologous bone grafting.

**DISCLOSURE**

No conflicts of interest were declared by the authors.

**REFERENCES**