

REVIEW

Recent developments in the use of bone morphogenetic protein in orthopaedic trauma surgery

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ABSTRACT

Delayed healing and non-union remain common problems in the treatment of open tibial shaft fractures. Additional surgical treatments may be required to facilitate healing. The efficacy of recombinant human bone morphogenetic protein-2 (rhBMP-2), as an adjunct to the standard of care, has been investigated in the BMP-2 Evaluation in Surgery for Tibial Trauma (BESTT) study. This prospective, randomised, multicentre, controlled study included 450 patients with acute, diaphyseal, open tibial fractures. A significant reduction in the risk of secondary intervention was observed in the 1.50 mg/mL rhBMP-2 group compared with the standard of care

alone group ($p = 0.0005$). In a subgroup analysis of 331 patients with Gustilo–Anderson grade IIA or IIB open tibial fractures, using data combined from the BESTT study and a study conducted at 10 level I US trauma centres, a significant reduction in the incidence of secondary autologous bone graft procedures was observed with 1.50 mg/mL rhBMP-2 compared with the standard of care ($p = 0.0005$). The influence of fracture gap on the re-operation rate has also been examined in the BESTT study. In the 1.50 mg/mL rhBMP-2 group, patients with a 0 mm fracture gap had significantly less re-operations compared with those patients with a greater than 2 mm gap ($p = 0.048$).

Introduction

The treatment of open tibial shaft fractures remains problematic due to non-union and delayed healing. A retrospective review of 104 consecutive tibial shaft fractures revealed that the relative risk (RR) of developing non-union in an open fracture was 8.2 [confidence interval (CI) 2.9–10.5]¹. Analysis of 100 tibial shaft fractures showed that healing time for open fractures was longer compared with closed fractures (14 ± 4.9 weeks versus 11.3 ± 3.2 weeks)². Furthermore, an open tibial shaft fracture has been identified as a predictor of re-operation (RR 4.32, 95% CI 1.76–11.26), following operative management³.

The extent of soft tissue trauma, osteosynthesis failure and infection all impact on fracture healing and

union. More severe soft tissue trauma is associated with greater difficulty in healing⁴. A longer healing time has been observed in those patients with the more severe Gustilo–Anderson type injuries^{5,6}, a classification scheme for open fractures, irrespective of the type of fixation⁷. Implant failure was responsible for re-osteosynthesis in more than 40% of patients, in a series of 23 re-osteosyntheses of the tibial shaft⁸. A significant association between open fractures and infection has also been observed⁹.

Bone morphogenetic proteins, their receptors and signalling components are expressed in human fracture callus¹⁰. Therefore the possibility of stimulating fracture healing has been investigated using recombinant human bone morphogenetic protein-2 (rhBMP-2; dibotermin alfa).

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Christian Drosten



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