Injury, Int. J. Care Injured (2005) **36S**, S47—S50

ELSEVIER

INJURY
INTERNATIONAL JOURNAL OF THE CARE OF THE INJURED

www.elsevier.com/locate/injury

Clinical applications of BMP-7 The UK perspective

Peter V. Giannoudis *, **Christopher Tzioupis**

Academic Department of Orthopadic and Trauma Surgery, School of Medicine, University of Leeds, St. James's University Hospital, Beckett Street, Leeds LS9 7TF, UK

Accepted 25 July 2005

KEYWORDS
BMP-7;
OP-1;
Non-union;
UK perspective

Summary Treatment of fracture non-union is a challenging situation in skeletal surgery. Since the discovery of bone morphogenetic proteins (BMPs) by Urist preclinical research as well as clinical trials has shown the efficacy of these molecules in bone healing enhancement. Recombinant bone morphogenetic protein became available in UK during August 2001. We evaluated the type of indications and the efficacy of BMP-7 in a variety of clinical conditions including persistent fracture non-unions, augmentation of periprosthetic fracture treatment and osteotomies, enhancement of fracture healing following acetalular reconstruction, distraction osteogenesis, free fibular graft and arthrodesis of joints. Out of 653 cases, the overall success rate was 82% (535 cases). No local or systemic adverse effects were encountered.

The role of BMP's as a bone stimulating agent is safe, well established and could be considered as a power adjunct in the surgeon's armamentarium for the treatment of these challenging clinical conditions.

Introduction

Fracture healing is a multi-stage cascade of biological events involving the interaction of several cell types with local and systemic regulatory factors at the fracture site through complex intra and extra-signalling pathways.[4,5,21]

Despite the advances made in our philosophy of stabilisation of fractures, implant developments and biological fixation techniques, non-union following bone fractures represents an infrequent but serious local complication. Of the approximately 5.6 million bone fractures in the United States each year, up to 10% do not heal and require further treatment.[18]

While it is now accepted that non-union of the fractures is of multi-factorial nature, with the developments made in the field of molecular biology, molecular medicine and genetics, a lot of attention has been recently given to the healing environment at the molecular level.

Bone morphogenetic proteins (BMPs) are a group of widely studied signalling molecules with a vital role in the development of many body tissues, including the skeleton.[19,21,23] The molecular basis of their action has been the subject of intensive research activity in recent years leading to

* Corresponding author. Tel.: +44 113 2066460; fax: +44 113 2065156.
E-mail address: pgiannoudi@aol.com (P.V. Giannoudis).

0020-1383/$ — see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.injury.2005.07.035

a growing understanding of their fundamental action at a cellular level.[20] The key role of BMPs in bone healing has lead to a growing interest in their potential for use as a biological response modifier, to speed fracture consolidation and bone regeneration in situations where this might not naturally or reliably occur.[2,8,24]

Osteogenic protein-1 (OP-1) (BMP-7) is a powerful BMP with a strong osteoinductive capacity manufactured using recombinant DNA techniques.[8] The therapeutic potential of recombinant human BMP-7 (rhBMP-7) has been well documented in several animal experiments and clinical trials of critical-sized segmental bone defects, osteochondral defects, spinal fusion and distraction osteogenesis.[6,9,10,15,16]

The aim of this study was to document the clinical applications and the efficacy of osteogenic protein-1(OP-1) in the United Kingdom.

Clinical applications—The UK perspective

Patients and methods

Between May 2001 and November 2004, six hundred and fifty three (653) patients were treated with recombinant BMP-7 (OP-1) in several UK centres. Such details were analysed as the anatomical location of the application, whether it was an elective orthopaedic procedure or trauma related, the type of the original injury, the number of additional procedures carried out prior to BMP-7 administration with or without augmentation with cancellous autologous bone graft and whether the BMP-7 was used in isolation or in combination with either autograft or allograft.

Table 1 Type of procedures in which rhBMP-7 was used

UK clinical applications	%
Free fibula graft	0.3
Periprosthetic fractures	0.4
Osteotomies	3.2
Acetabular reconstruction (Hip revision)	3.3
Distraction osteogenesis	8.8
Open fractures	9.3
Arthodesis	14.2
Non-unions	60.5

Following hospital discharge, patients were followed up in the orthopaedic outpatient clinic having routine clinical and radiological assessment. Successful end points of treatment were defined as the accomplishment of both clinical and radiological union. Clinical union was defined as pain free full weight bearing and no further surgical intervention whilst radiological union as evidence of new bone bridging the fracture site on more than one radiological view (evidence of presence of bone healing by direct or indirect means in at least two planes on X-ray).[10] The mean follow up after the application of rhBMP-7 was 15.3 months (range 12—27).

Results

The type of cases and surgical procedures where OP-1 was used included non-unions, augmentation of periprosthetic fracture treatment and osteotomies, enhancement of fracture healing following acetalular reconstruction, distraction osteogenesis, free fibular graft and arthrodesis of joints (Table 1). The distribution of clinical applications of OP-1 is shown in Fig. 1.

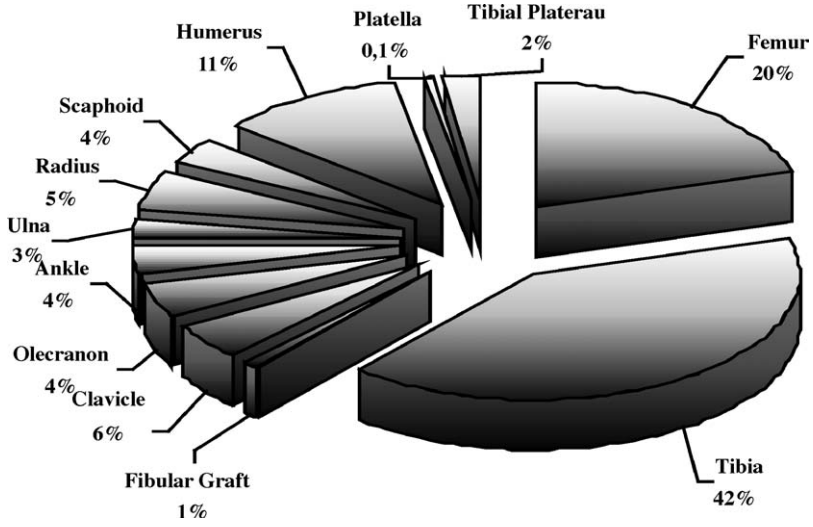

Figure 1 Anatomical distribution of non-union in UK cases.