Injury, Int. J. Care Injured (2007) **38**, 1227—1235

ELSEVIER

INJURY
INTERNATIONAL JOURNAL OF THE CARE OF THE INJURED

www.elsevier.com/locate/injury

REVIEW

Bone morphogenic protein and its application in trauma cases: A current concept update

Bagaria Vaibhav [a,*], Patil Nilesh [b], Sapre Vikram [c], Chadda Anshul [d]

[a] *CIIMS Hospital, Nagpur, India*
[b] *Deenanath Mangeshkar Hospital, Pune, India*
[c] *NIIDAAN Hospital, India*
[d] *NIIDAAN Hospital, India*

Accepted 13 December 2006

KEYWORDS
Bone morphogenic protein;
Fracture healing;
Non-unions;
Bone regeneration;
Recombinant {rh}BMP 2

Summary

Background: Bone morphogenic proteins (BMP) have shown tremendous potential in bone formation at fracture sites and at non-union sites. Animal studies and limited human studies have proven their efficacy as an alternative or enhancer of autologus bone graft in bone regeneration. The action of BMP is mediated through receptor kinases and transcription factors called Smads that regulate the expression of target genes. In preclinical studies, it was observed that BMP is relatively devoid of adverse effects and carcinogenicity but further studies are needed to clarify the issue of ectopic bone formation before its extensive use in humans.
Materials and methods: This review article intends to give brief information on biology and basic science of BMP and provide an overview on the current research data on clinical application of BMP in the treatment of fractures and difficult non-unions.
Results: Various studies have shown that BMP holds promise in the management of delayed unions and recalcitrant non-unions. It has also been observed to initiate faster healing resulting in less pain and infection at the fracture site in open fractures. However the role of BMP in fresh fractures is debatable.
Conclusion: Judicious use of BMP in certain clinical scenarios may revolutionise management of non-unions and delayed unions. The major constraints for routine use of BMP are inadequate clinical trials in humans and the need to comprehensively assess the cost-effectiveness and budget impact of BMP.

* Corresponding author at: Department of Orthopedics, CIIMS Hospital, 88/2 Bajaj Nagar, Nagpur 440010, India. Tel.: +91 932 3951 631; fax: +91 712 2236 416.
E-mail address: vaibhavbagaria@rediffmail.com (B. Vaibhav).

0020-1383/$ — see front matter © 2007 Published by Elsevier Ltd.
doi:10.1016/j.injury.2006.12.012

Contents

Introduction

Application of biofactors for bone regeneration has revolutionised the management of fractures and difficult non-unions. Various biological factors, such as bone morphogenic proteins (BMP), fibroblast growth factors (FGF), platelet-derived growth factor (PDGF), insulin like growth factors (IGFs)[36,19,11,7] have been investigated for application in bone regeneration and skeletal repair. Despite remaining the gold standard for most orthopaedic procedures, autologus bone graft suffers from significant disadvantages[4,5,20,35,63] (Table 1) and the search for ideal bone graft continues (Table 2).

Different approaches are being tried to achieve bone regeneration as mentioned in (Table 3).

Dr Marshall Urist in 1965 pioneered the concept of the presence of a substance naturally present in the bone responsible for its regeneration and repair, which he called bone morphogenic protein (BMP) also known as osteogenic protein or OP.[37] Following this, numerous path breaking researches have provided newer insights into the nature of bone biology and the breakthrough in recombinant technology made commercial availability of BMP products a reality.

This review article intends to provide a brief overview on the biology, basic science, safety profile, of BMPs and various preclinical and clinical trials conducted to evaluate the role of BMPs in non-unions and delayed union.

Table 1 Disadvantages of autogenous bone graft

(1) Limited availability
(2) Postoperative pain at the operative site
(3) Potential injury to the lateral femoral cutaneous nerve
(4) Potential injury to superior gluteal artery
(5) Postoperative haematoma
(6) Potential for infection at the operative site
(7) Possibility of the gait disturbance

Bone morphogenic protein classification, character and properties

BMPs are members of the TGF-beta super family. The super family compromises of proteins that are coded for by a 45-gene sequence that has a highly characteristic conserved 7 cysteine motifs in their mature domain. This super family of proteins contains: five isoforms of TGF-beta (TGF-beta 1 through TGF-beta 5), the BMPs, growth differentiation

Table 2 Features of an ideal bone graft substitute

(1) Have results as good as or better than autograft in achieving union
(2) Be cost effective
(3) Have no immunogenicity
(4) Have handling characteristic familiar to surgeon
(5) Resorb with a predictable degradation time
(6) Act locally without any or negligible systemic side effects
(7) Be osteoconductive and osteoinductive with a potential of supplying or attracting osteogenic cells
(8) Not interfere with modern imaging modalities
(9) Produces non-exothermic reaction when implanted so as to prevent heat damage to antibiotics and growth factors