The Efficacy of Synthetic Bone Graft Substitutes

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Summary

One of the most difficult challenges in orthopaedics is the treatment of large bone voids or defects. While autografts have traditionally been considered a standard treatment, this procedure has been associated with complications such as increased incidence of pain, nerve injury, arterial damage, harvest site fracture, hematoma, infection, and compromised patient function. Synthetic bone graft substitutes, including STRUCSURE™ CP (Smith & Nephew, Inc., Memphis, TN, USA), have been developed as an effective alternative to grafting. Evidence suggests that these materials may support improved fracture reduction outcomes, reduced pain, and improved postoperative patient function. The utility of STRUCSURE CP has been verified in unpublished clinical case studies, including fixation of tibial plateau and proximal humeral fractures, with good results at a follow-up of up to 2 years.

Introduction

One of the most difficult challenges in orthopaedics is the treatment of large bone voids or defects. The need to fill a bone void can arise following a traumatic injury, or it may be necessary during revision total joint arthroplasty. One of the more common occurrences in trauma is following compression fracture [1]. Here, depressed cortical bone fragments can destroy the underlying cancellous bone, creating a void following reduction [2]. Untreated, these voids can result in subsidence, which significantly increases the risk of reduction collapse, postoperative pain, posttraumatic arthritis, and loss of function [2, 3].

The standard treatment for bone voids has traditionally been autograft [1, 4]. Because these grafts are obtained from the fracture patient, they have been found to support excellent results [2, 4, 5]. Alternatively, cadaveric allografts have also been utilized successfully [2, 5-7]. While both grafting techniques are effective and suitable for specific cases, complications associated with these procedures have led to the development of alternative synthetic bone graft substitutes. Available experimental and clinical evidence suggests that these synthetic osteoconductive biomaterials may support the regeneration of new bone at the administration site, while reducing patient morbidity and improving functional outcomes [2, 5, 8].
Standard Bone Grafting

Autografts are typically harvested from non-essential bone such as the iliac crest or fibula. The primary benefit of this technique is that transplant of host tissue provides vital bone and marrow cells to the fracture site, in addition to an osteoconductive scaffolding that promotes further bone ingrowth [4, 5, 9-11]. However, this procedure is associated with a significant risk of complication. Autograft is a secondary surgical procedure that can exacerbate postoperative patient morbidity [2, 5, 8]. Increased incidence of pain, nerve injury, arterial damage, harvest site fracture, hematoma, infection, and compromised patient function are all common complications that have been reported in the literature [2, 5, 8, 12-15]. Furthermore, the supply and quality of autograft is inherently limited. The amount of suitable graft that can be harvested from the host patient may not be sufficient for filling large or numerous bone voids [5]. Additionally, this procedure is expensive, with an average cost of approximately $4,154.00 USD [16].

During cases where suitable autograft may be unavailable, allograft has also been successfully utilized [2]. A key advantage of allograft is that there is an increased relative supply. However, allograft inherently does not provide any autogenic bone growth factors. In addition, allograft can increase the risk of disease transmission from donor to patient, and can increase the rate of non-union and long-term graft failure due to tissue incompatibility [4, 6, 17, 18].

Synthetic Bone Graft Substitutes

Recently developed synthetic bone graft substitutes (BGS) are an attractive alternative to grafting. BGSs are a class of materials created from biologically inspired ceramics, commonly including calcium sulfates and calcium phosphates. A key benefit of a BGS is that there is no risk of undue postoperative patient morbidity, disease transmission, or infection following administration [2]. Further, BGSs are easily stored, sterile, and readily available in an essentially unlimited supply [5]. As previously noted, this is a particularly important consideration during the treatment of large or numerous bone voids.

STRUCSURE® CP Bone Graft Substitute

STRUCSURE® CP (Smith & Nephew, Inc., Memphis, TN, USA) is an injectable, self-setting calcium phosphate BGS intended to be placed into bony voids or gaps of the skeletal system that are not intrinsic to the stability of the bony structure. This synthetic BGS consists of a powder component and an aqueous solution component. The powder component is a mixture of calcium phosphate and hydroxypropyl methylcellulose (HPMC). Calcium phosphate provides an osteoconductive scaffold that facilitates bone healing and formation [19]. HPMC is a polymer that changes the rheology of the material for a smooth injection, allowing STRUCSURE CP to have a paste-like viscosity so it can be injected immediately after mixing, and enabling suitable wettability and porosity [20, 21]. The liquid component is a sodium phosphate solution.

The material is prepared for administration by mixing the powder and the liquid, initiating the hardening of the BGS. Specifically, STRUCSURE CP has been found to undergo a chemical reaction to form calcium-deficient apatite (CDA), which is similar to natural bone when compared using x-ray diffraction [19]. Over time, the CDA crystals increase in size and undergo physical entanglement and intergrowth, contributing to the favorable mechanical properties of the product [22].

There are disadvantages to other commonly-encountered BGS materials, such as calcium sulfate and hydroxyapatite (HA). Calcium sulfate has a very fast dissolution rate of approximately 4-12 weeks, which is faster than the rate of bone growth [19]. HA, on the other hand, is known to be resistant to resorption and can take years to be remodeled [23].

After 24 hours at body temperature (98°F) and in vivo conditions, STRUCSURE CP is fully hardened and reaches a compressive strength of 24 MPa, which is similar to that of cancellous bone (4-12 MPa) [24, 25]. The general strength of settable synthetic BGSs is sufficient to support a reduced risk of bone fragment
displacement and subsidence [26]. Additionally, STRUCSURE CP has been found to have a full range of pore sizes, ranging from less than 10 µm to over 100 µm [27]. Variation in pore size is important for cell infiltration and transport of nutrient to the cells, with pores larger than 100 µm considered necessary for proper vascularization and bone colonization [28].

The Clinical Performance of Calcium Phosphate Bone Graft Substitutes

A recently completed meta-analysis provides insight into how calcium phosphate BGSs perform, and discusses the benefits of using these materials over conventional treatments (with or without autogenous bone grafts) [2]. The primary objective of this analysis was to compare the clinical performance of an injectable calcium phosphate BGS against control fracture treatments, consisting of autograft or fixation with no bone graft. The authors performed a comprehensive review of the fracture literature, identifying all published randomized control studies and relevant papers in national orthopaedic meeting proceedings. Results of this meta-analysis demonstrated a statistically significant improvement in the patients treated with a calcium phosphate BGS. There was a 68% improvement in fixation stability for BGS-treated patients, as compared to patients treated with autograft (p < 0.05). Further, when compared against patients receiving no graft, BGS-treated patients reported a lower prevalence of pain at the fracture site (p < 0.05).

A statistical comparison of functional outcomes was not possible in the meta-analysis. However, the authors noted that three of the identified studies did cite statistically significant improvements in postoperative patient functional scores following treatment with BGS [29-31]. The utilization of STRUCSURE CP during the fixation of proximal humeral and tibial plateau fractures, procedures that are similar to those previously analyzed [2], is illustrated in Figures 2 and 3.

Conclusion

While bone grafting has long been considered the standard treatment for addressing bone voids, there is evidence demonstrating that synthetic BGSs, including STRUCSURE CP, are versatile osteoconductive materials that can be successfully used in a wide range of procedures. Furthermore, published literature suggests that these materials may support improved clinical outcomes following administration.
References


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