ORIGINAL RESEARCH PAPER

Orthopedics

USE OF β-TRICALCIUM PHOSPHATE (CHRONOS®, SYNTHES) IN COMMINUTED VS NON-COMMINUTED LONG BONE FRACTURES FOR FRACTURE HEALING

KEY WORDS: β-tricalcium phosphate (ChronOS®, Synthes), bone graft substitute, comminuted fracture, fracture union.

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ABSTRACT

Background: Bone graft substitutes are a group of substances available to us today, which are now being increasingly used to enhance/ stimulate bone healing. The reason for this is because they obviate the need for an additional procedure, decrease operative time and are not associated with any donor site morbidity. We endeavored to find out if -tricalcium phosphate (ChronOS®, Synthes) as a substitute gave better union rates in comminuted long bone fractures as against using them in simple fractures which had gone into nonunion, or delayed union, and to compare the complications that occurred.

Methods: This study was a retrospective review of prospectively collected data of patients that underwent bone stimulating procedures using ChronOS® (-tricalcium phosphate) in cases such as nonunion, delayed union or acute comminuted fractures. There were 38 patients, who underwent bone enhancing procedures within a 1-year period, of which in 18 patients ChronOS® was used. Of the 18 patients, 10 were comminuted fractures and 8 were simple fractures the outcomes assessed were union time, comparison of union for each indication and occurrence of any complications or the need for secondary procedures.

Results: The results showed that at 3 months signs of union were evident in both groups. 80% (8 out of 10) of the comminuted fractures and 87.5% (7 out of 8) of the simple fractures went on to unite. 2 patients in the comminuted fracture group and one patient in the simple (non-comminuted fracture) group went on to non-union.

Conclusion: ChronOS® is a viable alternative to autograft in comminuted fractures as well as non-unions, delayed unions and the management of small bone defects. It completely eliminates donor site morbidity associated with autografts in addition to decreasing the operative time.

INTRODUCTION:

There has been a rise in trauma and trauma related deaths in India in the recent times, especially the past two decades. One of the reasons seems to be the ever increasing two- wheelers in India which are the most vulnerable(1,2). Today India accounts for at 73% of deaths due Road traffic accident in South east Asia. India has only 1% of the world's vehicles, but accounts for 6% of the world's road traffic accidents(3). With a significant burden of trauma, most orthopedic surgeons in India see complex injuries including open, comminuted fractures which require bone stimulation in the form of bone grafting or other methods.

The treatment of delayed unions, non-unions and management of skeletal bone defects is complex and challenging and adds to the morbidity. The "gold standard" for managing such cases has been autologous bone graft(4,5). The autologous bone grafts have all the components required to promote bone healing. They are osteoinductive (stimulate bone formation through osteoprogenitor cells), osteoconductive (provide a scaffold on which the bone can grow) and the most essential osteogenic property (inherent capacity to form osteoblasts and its precursors). However the autologous grafts have associated with major complications such as abdominal hernia, and minor complications such as superficial seromas and infection, in addition to the extra operative time that is required to harvest it(6–8). The next most common choice was allograft, especially in North America, with abundance of bone banks. However these have gone into disrepute due the risk of infection and disease transmission(9). The allograft is primarily osteoconductive and to some extent osteoinductive due to the demineralized bone matrix (DBM).

To address the disadvantages of using autograft and allografts, the synthetic bone graft substitutes have become more popular over the past few decades. Among the synthetic bone graft substitutes the calcium phosphate-based biomaterials (e.g. hydroxyapatite, calcium phosphate-based cements and ceramics) and recombinant bone morphogenic proteins (rh-BMP-2 and 7) are most widely used. Of these biomaterials tricalcium phosphate (β- TCP) cement/ ceramics are available in India.

In the present study we used ChronOS®, (β- TCP) from Synthes™. We hypothesized that using ChronOS® in acute comminuted fractures versus delayed union and non-unions would give rise to similar union rates. Logic dictates that since bone graft substitutes have no osteogenic potential (only osteoconductive), therefore they should be ineffective in delayed and non-unions as compared to its use in acute comminuted fractures. So, through this comparison we wanted to find out if this was the case, this study could guide us in exploring the use of bone graft substitutes in non- unions, and delayed unions.

MATERIALS AND METHODS:

This was retrospective study of a prospectively collected data in the department of Orthopedics, Christian Medical College and Hospital, Ludhiana, Punjab. Our study spanned 12 months and consisted of adult patients (18 -65 yrs.) who had sustained comminuted long bone fractures, or had a delayed union or non-union of fracture. Chron OS (- tricalcium phosphate). There was a total of 38 patients who underwent bone stimulating procedures. Out of these patients in 18 patients Bone graft substitutes were put. All of these patients were those patients who opted for Bone graft substitute after detailed discussion with them including the risks, benefits and the likelihood of reoperation and need for further surgeries, in case of failure. These 18 further divided into two groups. Group 1 included patients with comminuted fractures (acute) who were treated with ChronOS® and Group 2 consisted of patients with simple fractures most of which were either delayed unions or non-unions. Randomization was not done. This consecutive prospective cohort series was statistically analyzed.

Inclusion criteria was:

1. age group of 18 to 65 years,
2. acute, comminuted fractures for group 1

3. simple fractures for group 2
4. delayed unions and non-unions of fractures for group 2
5. bone defects less than 5 cm.

Patients excluded were those with:

1) pathological fractures
2) conditions when both bone graft and the substitute are used together (composite graft),
3) infected non-unions
4) gap non-union,
5) patients who had received Bone marrow injections one year prior and one year after the procedure and gap non-union with bone gap of over 5cm were taken as exclusion criteria.

The patient's data that were included in this study were those with acute comminuted long bone fractures, a delayed union (no signs of healing even after 6 months), non-union (no progress of fracture healing on X-rays for 3 consecutive months taken after 6 months) or a bone defect less than 5cm.

The data was recorded prospectively at the time of admission and included the patient demographics, the pattern of fracture (comminuted or simple), site of fracture (diaphyseal or metaphyseal), weather bone grafting was immediate or delayed, the occurrence of any complications both the grafted site and the donor site.

Clinical assessment to assess union included the assessment of pain at the fracture site and the presence of any abnormal mobility of the fracture. All patients were clinically examined by both the authors at each of the 3 monthly follow ups till a period of 1 year or till the bone had united.

Radiological assessment also was also done during the same time as the clinical assessment. The X-rays were seen together by both the authors independently and then together to bring about objectivity. The parameters that were seen were the presence of callus at the fracture site and bridging trabeculae across the fracture site. A fracture was said to be fully united if 3 out of 4 cortices showed callus and bridging trabeculae.

The variables were coded and entered into a Microsoft Excel computer program. Data were analyzed using the Stata version 8 and Epi Info 2003.

RESULTS AND ANALYSIS:

This study compares bone healing with the synthetic bone substitute (ChronOS®, Synthes) in patients with acute comminuted long bone fractures versus those with delayed, nonunion, malunion and bone defects less than 5 cm.

Patients from the ages of 18-65 years were recruited for the study. Patients were followed up at 3, 6, 9 and 12 months or till full union.

There was a total of 18 patients underwent bone graft substitutes for inducing fracture healing. These were further divided into 2 groups, 10 of whom had comminuted fracture, and 8 of whom had simple non-comminuted fractures.

Table 1. Demographics in either groups

	COMMINUTED FRACTURES	SIMPLE FRACTURE
Males	8 (80%)	7 (87.5%)
Females	2 (20%)	1 (12.5%)
Mean age(years)	40.8	32

Majority of patients in both the groups (80% in the group with comminuted fracture 87.5% males in the group with simple fractures) were males. The average age in the comminuted fracture group was 40.8 yrs. as compared to 32 yrs. in the simple fracture group both the groups had a majority of patients who had sustained closed fractures following their injuries (80% patients with comminuted fractures had sustained closed fractures, while all patients with simple fractures had closed fractures). Most patients in both the groups had sustained closed fractures, (non-comminuted fractures had all closed fractures as against 80 % of those who were in the comminuted fracture group).

Lower limb injuries were more common in both the groups; however, they were significantly more common in the comminuted fracture group (90% vs 62,5 % in the non-comminuted fracture group). Diaphyseal fractures were common in both the groups (70% in comminuted fracture group and 100% in the simple fracture group).

Bone graft substitute was used on an average 1 month following the index procedure in the comminuted fracture group and 7months following the index procedure in the non-comminuted fracture group. The substitute was introduced to the fracture site either by opening it or by introducing it percutaneously by small incisions. 3 out of 10 patients (30%) underwent percutaneous graft insertion in the comminuted group as compared to 3 of 8 in the closed fracture group (37.5%).

Table 2: Union rates and average time to union in both the groups at the end of the study

	COMMINUTED FRACTURES	SIMPLE FRACTURE
union	8 (80%)	7 (87.5%)
non-union	2 (20%)	1 (12.5%)
Earliest appearance of callus (in months)	3	3
Average time to union(months)	11.1	8.8

The average union time was lesser for the simple fracture group as compared to comminuted fracture group (11.2 months in comminuted fracture group as compared to 8.8 month in the simple fracture group).

The outcomes for fracture union were assessed by the average union time and the appearance of callus. 2 patients (20%) in the comminuted fracture group did not unite and required secondary grafting procedures using autologous bone grafts, the simple fracture group had 1 patient (12.5%) who did not unite. In all the fractures that united in both the groups the callus and sings of union could be seen at 3 months. 2 of the 10 (20%) in the comminuted fracture group underwent complete graft resorption at the time the fracture was labelled as united. While only 1 patient ` (12.5%) in the simple fracture group underwent full resorption of the graft.

DISCUSSION:

This study was designed to test the efficacy of bone graft substitute β-TCP (ChronOS®,Synthes) in fracture healing in comminuted long bone fractures and comparing its use in simple fractures. This data revealed that in this particular population both the groups were skewed towards having more males in each group and most of them had sustained these fractures secondary to road traffic accidents. Bajammal et. al. in 2008 conducted a metanalysis on the use of calcium sulfate bone cement and 14 other studies were analyzed in this metanalysis all of which had a demographic data with equal number of males and females(10). While Chapaman et. al study on Collagen phosphate ceramic with a bovine collagen carrier had a majority (69%) males in their study population(11).

Our study showed that the comminuted fracture group had more 20% open fractures, while none of the simple fractures were open fractures. It corroborates with the fact that most

comminuted fractures are of higher energy and are more likely to be open than the simple fractures which would occur with a lower energy. Both the Chapaman's study of 1997 and the BESTT-ALL included open and closed fractures in their study but their impact on the outcomes were not studied(12).

Our study found that the bone graft substitute procedure was done on an average 1 month following the index procedure, while in the simple fracture group this duration was found to be 7 months, this showed that primarily the fracture comminution dictated the bone graft substitute procedure as against the development of a delayed union or a non-union was the major indication of bone graft substitute in the simple fracture group. The study by Chapman et. al studied the treatment of acute long bone fractures with collagen composite bone graft substitute, however they did not define the criteria of bone grafting in acute long bone fractures, they compared this with autologous graft and found on significant difference between the 2 groups, This was similar to our findings as in the comminuted group 80% (8 out of 10 fractures) and in the simple fracture group 87.5%(7 out of 8) achieved union.

The mean union time however was 11.2 months for the comminuted fracture group as compared 8.8 months for the simple fracture group. These results were as expected as comminuted fractures took longer to unit; however, the ultimate union rates were not very different between the groups. The first appearance of callus was seen in both the groups at 3 months.

Both the comminuted and non-comminuted fractures had very good union rates in long bone fractures following ChronOS® insertion, we did not use any composite material to get osteogenic potential. What was a surprise was that the non-unions and delayed unions also went on to unite. Many studies have shown that the union rates comparing bone graft substitutes are similar when compared to the gold standard Autogenous grafts(13–15).

LIMITATIONS:

The sample size was very small to draw any definite conclusion. There was no randomization of the patients. The indication of bone grafting in the comminuted fracture group was not very well defined.

CONCLUSION:

Most of the available literature like the study by Chapman does not give us clear cut indications for the need for grafting in acute long bone fractures. This study demonstrates that the use of ChronOS® as a bone graft substitute provides good union rates in both comminuted acute fractures as well as non-unions and delayed unions, in long bones without the need composite grafts such as bovine collagen or bone marrow injections, or BMP which provide the osteoinductive and to some extent osteogenic potential needed for union. However, more studies with larger sample sizes and randomized controlled trials are required to give us more clarity on this subject.

REFERENCES

1. Mathers CD, Loncar D. Projections of Global Mortality and Burden of Disease from 2002 to 2030. Samet J, editor. PLoS Med. 2006 Nov 28;3(11):e442.
2. Ameratunga S, Hijar M, Norton R. Road-traffic injuries: confronting disparities to address a global-health problem. The Lancet. 2006 May;367 (9521) : 1533–40.
3. Seid M, Azazh A, Enquselassie F, Yisma E. Injury characteristics and outcome of road traffic accident among victims at Adult Emergency Department of Tikur Anbessa specialized hospital, Addis Ababa, Ethiopia: a prospective hospital-based study. BMC Emerg Med. 2015 Dec;15(1):10.
4. Ahlmann E, Patzakis M, Roidis N, Shepherd L, Holtom P. Comparison of anterior and posterior iliac crest bone grafts in terms of harvest-site morbidity and functional outcomes. J Bone Joint Surg Am. 2002 May;84-A(5):716–20.
5. Giannoudis PV, Dinopoulos H, Tsiridis E. Bone substitutes: an update. Injury. 2005 Nov;36 Suppl 3:S20-27.
6. Goulet JA, Senunas LE, DeSilva GL, Greenfield MLVH. Autogenous Iliac Crest Bone Graft: Complications and Functional Assessment: Clin Orthop. 1997 Jun;339:76–81.
7. Giannoudis PV, Karadimas EJ, Kanakaris NK. Anterior Iliac Crest Bone Graft Harvesting. In: Giannoudis PV, editor. Practical Procedures in Orthopedic Surgery [Internet]. London: Springer London; 2011 [cited 2019 Aug 4]. p. 51–5. Available from: http://link.springer.com/10.1007/978-0-85729-817-1_17
8. Arrington ED, Smith WJ, Chambers HG, Bucknell AL, Davino NA. Complications of iliac crest bone graft harvesting. Clin Orthop. 1996 Aug;(329):300–9.
9. De Long WG, Einhorn TA, Koval K, McKee M, Smith W, Sanders R, et al. Bone Grafts and Bone Graft Substitutes in Orthopaedic Trauma Surgery: A Critical Analysis. J Bone Jt Surg. 2007 Mar;89(3):649–58.
10. Bajammal SS, Zlowodzki M, Lelwica A, Tornetta P, Einhorn TA, Buckley R, et al. The use of calcium phosphate bone cement in fracture treatment. A meta-analysis of randomized trials. J Bone Joint Surg Am. 2008 Jun;90(6):1186–96.
11. Chapman MW, Bucholz R, Cornell C. Treatment of acute fractures with a collagen-calcium phosphate graft material. A randomized clinical trial. J Bone Joint Surg Am. 1997 Apr;79(4):495–502.
12. Govender S, Csimma C, Genant HK, Valentin-Opran A, Amit Y, Arbel R, et al. Recombinant human bone morphogenetic protein-2 for treatment of open tibial fractures: a prospective, controlled, randomized study of four hundred and fifty patients. J Bone Joint Surg Am. 2002 Dec;84(12):2123–34.
13. Menon KV, Varma HK. Radiological outcome of tibial plateau fractures treated with percutaneously introduced synthetic porous Hydroxyapatite granules. Eur J Orthop Surg Traumatol. 2005 Aug 1;15(3):205–13.
14. Friedlaender ge, Perry CR, Dean Cole J, Cook SD, Cierny G, Muschler GF, et al. Osteogenic Protein-1 (Bone Morphogenetic Protein-7) in the Treatment of Tibial Nonunions. J Bone Joint Surg Am. 2001;83-A Suppl 1(Pt 2):S151–8.
15. Cassidy C, Jupiter JB, Cohen M, Delli-Santi M, Fennell C, Leinberry C, et al. Norian SRS Cement compared with conventional fixation in Distal Radial fractures: A RANDOMIZED STUDY. J Bone Jt Surg-Am Vol. 2003 Nov;85(11):2127–37.