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Autologous bone grafts vs bone graft substitutes in fracture healing in a tertiary care hospital of North India: A comparative study

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Abstract

Today as a result of rapid urbanization and mechanization there has been a rapid increase in the rate of trauma. As a result of this the treatment of post-traumatic conditions such as delayed unions, non-unions, malunions and other problems has become very challenging. In most cases it is possible to treat a fracture by restoring the alignment and stable fixation of the bone. However, in many cases additional measures such as bone grafting or bone transport are required to bring about bone healing or fill defects. This study will be comparing the efficacy and complications of bone grafts and bone graft substitutes and determining if bone graft substitutes are a worthy alternative to the conventional autologous bone graft.

Keywords: Autologous bone grafts, bone graft substitutes, fracture healing, tertiary care hospital

Introduction

Today we live in the age of speed. Be it machinery or high-speed vehicles. With the increasing sophistication and modernization there has been an exponential increase in trauma. Not only trauma but today we seen more of high energy trauma and injuries. Therefore, an orthopedician today has to deal with many more comminuted, compound type of fractures associated with at times severe crushing of the soft tissues. Problems such as nonunion, delayed union have become much more common. Most of these fractures require intervention in the form of either autologous bone grafting or other techniques. Bone grafts have been the gold standard to promote fracture healing. Since the days of Hippocrates in ancient Greece, it has been recognized that bone has considerable potential for regeneration and repair, Hippocrates is also credited with the concept that naturally occurring endogenous substances are superior therapeutic agents for clinical care ^[1]. In modern times surgeon Job van Meekeren in 1668 transplanted a dog's skull to an injured soldier, this was one of the first accounts of the successful use of an allograft ^[2]. Currently, fresh autologous bone is the most effective graft material for clinical use. It is limited by the fact that it is at times inadequate for large osseous defects, is associated with significant risk of post-operative morbidity and also is not able to fabricate a functional shape from the transplanted tissue^[3].

Autogenous bone is regarded as the gold standard for bone materials as it provides the three elements necessary to generate and maintain bone: scaffolding for osteo-conduction, growth factors for osteo-induction and progenitor cells for osteo-genesis ^[4, 5]. However, this graft is limited in quantity and may not be adequate for filling large cavity lesions. Harvesting autologous graft has its own limitations. It is another operation by itself with additional loss of blood and prolonged anesthesia time ^[6]. The conventional alternative to autograft has been allogenic bone obtained either from cadaveric donors or from donors undergoing total hip arthroplasty. Although it provides a good, natural, bony scaffold, allogenic bone carries certain risks. Specifically, despite the extensive testing of the donor and the bone obtained, a risk of both bacterial and viral transmission from the donor material to the host remains ^[7]. Also in some areas of the world, the practice of allogenic bone transplantation is culturally unacceptable ^[8]. Several methods of reconstructing bone defects are available namely using autograft, allograft, Demineralized Bone Matrix (DBM), Hydroxyapatite Calcium Phosphate (CP, TCP), autologous bone marrow aspirates, Bone Morphogenetic Proteins (BMP), and several other related growth factors (VEGF, PDGF, etc.) ^[9].

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There have been studies comparing bone grafts and bone graft substitutes for fusion in spine and metaphyseal bones defects. To our knowledge there have been very few studies comparing the use of Bone grafts vs substitutes done for the Indian population, therefore we aim to study the efficacy of Autologous/Autogenous bone grafts vs the bone grafts substitute ChronOS®, Synthes (Beta Tricalcium phosphate) in fracture healing in a tertiary care hospital in Northern India. This study was undertaken to evaluate and analyze the results of fracture healing and also study the occurrence of any complications that may arise. It was hoped that this study will help us in guiding the use of bone graft substitutes so that we can avoid the morbidities associated with bone grafting.

Material and Methods

This prospective study was carried out in the department of Orthopedics, Christian Medical College and Hospital, Ludhiana, Punjab. It spanned 12 months and compared the efficacy of autologous bone graft vs against Bone graft substitute Chron OS (beta tricalcium phosphate). All patients with acute long bone fractures, delayed union or nonunion were included in the study. The patients were divided into two groups. Group 1 had 18 patients in whom Chron OS (beta tricalcium phosphate) bone substitute was used. Group 2 had 20 patients in whom the standard of care was autologous bone graft being taken from iliac crest. Randomization was not done due to financial, cultural and social reasons. Therefore, the patients in the Chron OS group were those patients who could afford the additional cost and/or had no other objections to its use. This consecutive prospective cohort series was statistically analyzed.

Inclusion criteria was patients in the 1) age group of 18 to 65 years, with acute fractures where bone grafting is indicated (e.g. comminuted fractures) or 2) with delayed unions and non-unions of fractures, and 3) 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.

All the included patients either had an acute fracture requiring bone graft, a delayed union (no evidence of bone healing at the fracture site by six months), a non-union (no evidence of fracture healing on three consecutive monthly radiographs made more than six months after the fracture), implant failure or malunited fracture which required correction. All the nonunions were atrophic.

The data was recorded prospectively at the time of admission and included patient demographics, fracture pattern (comminuted or non-comminuted), site of fracture (either metaphysis or diaphysis), indication for using bone graft or bone substitute, type of graft used, immediate or delayed grafting, graft site complications, donor site complications.

Table 2: Comparison between open/closed fractures in autologous and ChronOS® Groups with mean union time of fracture

Fracture Type open/closed	Autologous	Union (Months)	ChronOS®	Union (Months)	P values
Open	8	8	2	10	0.0933
Closed	12	5.5	16	9	0.042
P value	0.044		P value		0.3114

It was found that in autologous group, closed fracture united faster (at 5.5 months) as compared to open fractures (8 months) and this was statistically significant with a p value of 0.044. This difference was not significant in the ChronOS® group. On

The clinical assessment included the presence of 1) any pain at the fracture site or 2) abnormal mobility at the fracture site.

The radiological assessment included the 1) presence of callus, 2) bridging trabeculae across the fracture site.

Data were analyzed with independent tests as well as chi square test. The null hypothesis was that the two groups were similar. A p value of <0.05 was considered to represent a significant finding. The variables were coded and entered into a Microsoft Excel computer program. Data were analyzed using the Stata version 8 and Epi Info 2003.

Result & Analysis

This study compares bone healing with standard autologous bone graft versus the synthetic bone substitute (ChronOS®, Synthes) in patients with acute long bone fractures and in those with malunion, delayed or nonunion.

Majority (90% in autologous and 83.3% in the ChronOS® group) of the patients were males. There was no statistically significant (p value-0.164) difference between the two groups. Majority of patients presented with road traffic accident (80% in the autologous and 94.4% in the ChronOS® group) in both the groups, the next most common presentation was history of fall (15% in the autologous and 5.56% in the ChronOS® group). The p-value (0.12) showed that the groups were similar. The majority of Autologous bone grafts and bone graft substitutes were done for patients with closed fractures. The number of patients in each group was not identical. This difference between the two groups was found to be statistically significant with a p-value of 0.0485. This study had 11 patients with non-comminuted fractures that underwent autologous bone grafting while in the Chron OS® group majority (10) had comminuted fractures, however, the difference between the two groups was not found to be statistically significant with a p value of 0.25.

Table 1: Distribution of patients according to indication of bone grafting

Indications	Autologous		ChronOS®		p-value
	No.	%	No.	%	
Comminution	1	5	7	38.89	
Delayed Union	15	75	6	33.33	
Non-Union	3	15	4	22.22	
Others	1	5	1	5.56	
<i>p-value</i>					0.038

It was found that the commonest indication for autologous grafting was delayed union (in 75% cases), while the commonest indication of ChronOS® insertion was comminution. There was one patient in the autologous group (5.26%) who had a malunion at 12 months. One patient in the autologous group had infection at the graft site prior to 3 months for which incision and drainage was done.

In the ChronOS® group there was one infection which was seen radiologically at 12 months for one of the non-union cases.

comparing the union time of closed fractures in between the ChronOS® and the autologous group we found that closed fractures in the autologous group united faster with a statistically significant difference (p-value of 0.042).

Table 3: Site of fracture in each group (ChronOS® and autologous grafts) compared with mean union time and failure rates

Site of Fracture	Autologous Grafts	Union Time	Failure	ChronOS®	Union Time	Failure	P value
Diaphysis	17	6	2	15	9	2	0.0411
Metaphysis	3	6	0	3	11	0	-
P value					0.9		

On comparing the union time in diaphysis and metaphysis in autologous and ChronOS® groups it was found that fractures in the diaphysis, united earlier in the autologous group compared to those in the ChronOS® group and this was found to be statistically significant with a p-value of 0.0411.

Discussion

Autologous Iliac Crest Bone graft has been long since been considered the gold standard in terms of bone graft material, more importantly it provides the three essential properties required for bone healing i.e. osteo-genic, osteo-inductive and osteo-conductive property. However, there has been a constant search for alternative materials for bone healing, due to donor site morbidity associated autografts and risk of transmission of diseases (HIV, HCV and HBsAg) with allograft use. Bone graft substitutes are gaining in popularity due to the above reasons. Since there is a paucity of literature comparing bone grafts vs substitutes, we decided to compare autologous bone graft vs substitutes in a north Indian population. In this study the patients were grouped based on the mechanism of injury in each of the ChronOS® and the autologous groups. It was found that majority of patients had sustained a road traffic accident (80% in the autologous and 94.4% in the ChronOS® group). The second most common cause was fall from height (15% in the autologous and 5.56% in the ChronOS® group). None of the other studies has listed/distributed their patients according to the mechanism of injury. No definite conclusion which could be drawn. In our study population majority (90% in autologous and 83.3% in the ChronOS® group) of the patients were males in both groups which was similar to most other studies [10], however a randomized controlled trial by Bajammal *et al.* however had an equal number of males and females [11]. Majority of patients in the study had sustained a road traffic accident (80% in the autologous and 94.4% in the ChronOS® group). The study showed that in the autologous group most patients had non-comminuted fractures while in the ChronOS® group majority (10 patients) had comminuted fractures. However, the difference between the two groups was not found to be statistically significant. In the autologous group 40% (eight) patients' group had sustained a fracture both bones of the leg while 33.3% (Six) in the ChronOS® group had a fracture shaft of femur.

A significantly large number of the patients in both groups had diaphyseal fractures, as against metaphyseal fractures which were very small in number. The most common indication being comminution for ChronOS® insertion while Autologous bone grafting was done for patients with a delayed union usually at 2 to 3 months or for a nonunion as late as over five months.

This study showed that autologous grafts united faster (30% at 5 months) as against none in the ChronOS® group. There was a significant difference between absorption rates of the graft with 50% of ChronOS® not being absorbed at the end of the fracture union. This study found that 40% patients had fractures that united by 6 months, 70% by 9 months and 85% by 12 months in the autologous group. In the ChronOS® group at 6 months only one fracture had united (5.56%), at 9 months 7 more fractures and at 12 months 7 more fractures had united (83.3%). Russel *et al.* in 2008 compared autologous bone graft and endothermic calcium phosphate and found no significant difference in the

union times [12]. The BESTT-ALL study group by Jones *et al.* in 2006 studied union times between autograft and a composite graft (BMP-7) in tibial fractures [13]. They found that the rates of healing between the two groups were statistically equivalent. Friedlander *et al.* in 2001 concluded that 81% of the fractures in the bone graft substitute group (BMP-7) and 85% of the fractures in the autograft group had successful outcomes [14] as compared to our study groups which had 85% of the patients in the autologous group and 83.3% in the ChronOS® which went on to achieve union.

In the ChronOS® group one patient (5.56%), had pain. At 3 months 3 patients (15.79%) in the autologous group and 2 patients (11.11%) in the ChronOS® complained of pain. At the end of 6 months none of the patient complained of pain. On comparing the union time at 3, 6, 9 and 12 months it was found that the autologous grafts united faster than the ChronOS® (i.e. 8 fractures in the autologous group as compared to only one in ChronOS® group at 6 months). In this study 18 patients (94.74%) in the autologous group and 16 patients (88.89%) in the ChronOS® group showed callus formation and signs of union at final follow up. There was one patient in the autologous group (5.26%) who had a malunion at 12 months. One patient in the autologous group had infection at the graft site few days post-operatively for which incision and drainage was done. In the ChronOS® group there was one patient who had infection of ChronOS® which was seen radiologically at 12 months for one of the cases of nonunion.

It was also found that in the age groups of 31-40 and 41-50, it took longer for the fractures to unite in the ChronOS® group, while patients in the autologous group in the above-mentioned age groups had their fractures uniting faster. It was found that closed fractures in autologous group united faster (at 5.5 months) as compared to open fractures (8 Months). Closed fractures in the ChronOS® group took longer to unite (5.5 months in the autologous as compared to 9 months in the ChronOS®). These were statistically significant findings which were different from other similar studies which found no difference in the union times (10,12,14). Non-comminuted fractures in autologous group united faster (5 months as compared to 9 months in ChronOS®).

The fractures of the metaphysis in the ChronOS® group took longer than the diaphyseal fractures. These results can be explained by the fact that the two metaphyseal fractures in the ChronOS® group had defects which had to be filled up and as discussed union was reported later in the ChronOS® because of late resorption of the graft. When used for management of delayed union and nonunion, in the autologous group the fractures united faster (by 6 months) as compared with the ChronOS® group (9 months). This was found to be statistically significant.

Limitations

There were some limitations in the study like no randomization was possible in this study, allocation of patients to each group was done on the patient's ability to afford ChronOS®, radiological interpretation was done by different surgeons at different follow ups therefore resulting in inter observer variation, the number of metaphyseal fractures was too small to

draw any inference from and the sample size in this study was small therefore the results of this study were not similar to other studies.

Conclusion

To our knowledge, the present study represents one of the few studies comparing autologous bone rafts versus bone graft substitutes in long bones. This study demonstrated that bone graft substitutes are a viable alternative to classical autologous bone graft, without the morbidity associated with harvesting of the graft. The use of substitutes is especially useful in cases of bone defects, especially metaphyseal defects, and defects where a large amount of graft is required. Our study demonstrated good union rates using bone graft substitute (ChronOS®) as compared to the gold standard Autologous graft. Most of the available bone graft substitutes today are expensive and at times out of reach of the average Indian patient. However, more studies with a larger sample sizes like randomized controlled trials are required to validate the efficacy of substitutes.

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