

Efficacy of calcium sulfate plus decompression bone in lumbar and lumbosacral spinal fusion: preliminary results in 40 patients

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Objective: To compare the efficacy of calcium sulfate pellets plus bone obtained from decompression with fresh autologous iliac crest bone in lumbar and lumbosacral spinal fusion with decompression. **Design:** A prospective randomized clinical trial. **Setting:** Four tertiary care centres in Halifax, NS. **Patients:** All were consenting, skeletally mature and suffering from degenerative disc disease or spondylolisthesis. The first 40 patients from a single test centre are reported; 32 of these had completed 1-year follow-up. **Interventions:** Posterolateral lumbar or lumbosacral spinal fusion with spinal canal decompression and randomized placement of test material (decompression bone plus an equal volume of calcium sulfate pellets) on one side and control material (autologous posterior iliac crest bone of equal volume to the test material) on the contralateral side, which allowed subjects to act as their own control. **Outcome measures:** Assessment of bone formation by radiographic evaluation at 6 and 12 months after fusion by an independent musculoskeletal radiologist blinded to the placement of test material. **Results:** At 6 and 12 months after fusion, 78% and 88% of patients, respectively, showed bone formation at the test site that was 75% to 100% of, equal to or more than that at the control site. Increases in bone formation at 6 and 12 months were almost identical at both sites. Smoking status, patient gender or age, instrumentation used and volume of graft used were not predictive of outcome. **Conclusions:** Calcium sulfate pellets plus decompression bone provided bone formation equivalent to autologous iliac crest bone in a majority of patients. Calcium sulfate pellets plus decompression bone may provide a viable alternative to autologous iliac crest as a graft material for spinal fusion.

Objectif : Comparer l'efficacité des implants de sulfate de calcium associés à un greffon osseux prélevé par décompression à l'efficacité d'un greffon d'os autologue frais prélevé sur la crête iliaque dans la fusion des vertèbres lombaires et lombosacrées avec décompression. **Conception :** Étude clinique randomisée prospective. **Contexte :** Quatre centres de soins tertiaires à Halifax (N.-É.). **Patients :** Tous les sujets étaient à maturité squelettique, souffraient d'une maladie dégénérative des disques ou de spondylolisthésis et ont donné leur consentement. On rend compte des 40 premiers patients d'un seul centre d'essai, dont 32 ont terminé le suivi d'un an. **Interventions :** Arthrodèse postérolatérale du rachis lombaire ou lombosacrée associée à une décompression du canal vertébral, et distribution au hasard du matériau à l'essai (greffon osseux prélevé par décompression plus un volume égal d'implants de sulfate de calcium) d'un côté et du matériau témoin (un volume d'os autologue provenant de la crête iliaque postérieure égal à celui du matériau à l'essai) du côté controlatéral, méthode qui a permis à chaque sujet d'être son propre témoin. **Mesures de résultats :** Évaluation de la formation osseuse au moyen d'un examen radiographique effectué à l'insu 6 et 12 mois après la fusion par un radiologue indépendant et spécialisé en évaluation de l'appareil musculosquelettique. **Résultats :** Lors des évaluations à 6 et à 12 mois après l'arthrodèse, on a constaté sur le site du matériau à l'essai de 78 % et 88 % des patients, respectivement, une formation osseuse qui représentait de 75 % à 100 % de celle observée sur le

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site de contrôle, l'égalait ou encore la surpassait. Les augmentations de la formation osseuse enregistrées à 6 et à 12 mois étaient presque les mêmes aux deux sites. Le statut de fumeur, le sexe ou l'âge du patient, les instruments utilisés et le volume du greffon transplanté ne permettaient pas de prévoir l'issue du traitement. **Conclusions :** Les implants de sulfate de calcium associés à un greffon osseux prélevé par décompression ont entraîné une formation osseuse qui équivalait chez la majorité des patients à celle attribuable à l'os autologue prélevé sur la crête iliaque. Le recours aux implants de sulfate de calcium associés au matériau osseux obtenu par décompression pourrait constituer une solution de rechange viable à l'utilisation d'os autologue de la crête iliaque à titre de greffon pour la fusion des vertèbres.

Over 200 000 patients undergo spinal fusion in North America annually.¹ The goal of spinal fusion is to stabilize the aggravating motion segments and thus relieve the patient's symptoms. Fresh autologous iliac crest bone, the standard material used for bone grafting has limitations, including donor site morbidity, increased operative time and blood loss, and availability.²⁻⁷ Allograft bone has produced disappointing results in clinical trials of lumbar arthrodesis, and transmission of viral contaminants remains a problem.^{4,6,8,9}

Synthetic grafting substitutes to date have shown poor resorption and some may induce an antigenic response in the host. Calcium sulfate is another alternative. It has shown promising results in bony procedures since 1892.¹⁰ OsteoSet (Wright Medical Technologies, Arlington, Tenn.) calcium sulfate pellets are composed of medical grade calcium sulfate, which acts as an osteoconductive matrix. Because of its composition and crystalline structure, its rate of resorption is consistent with that of new bone growth.¹¹

Current research is focused on the efficacy of OsteoSet pellets combined with bone obtained from decompression compared to the use of fresh autologous iliac crest bone in posterolateral lumbar and lumbosacral spinal fusion with decompression. Our hypothesis is that OsteoSet pellets plus decompression bone will provide spinal fusion equivalent to that of a similar amount of autologous iliac crest bone graft. If this is the case, several advantages may be realized.

Methods

Informed consent was obtained

from all participants in keeping with the requirements of the Queen Elizabeth II Health Sciences Centre Ethics Review Committee. Although this project is a multicentre clinical trial, the results herein are the preliminary findings of the first 40 subjects (27 men, mean age 48 years, [range from 25-74 years]) to undergo the procedure at a single test centre. They include all those enrolled at that centre. At the other 3 centres, the study had not progressed to the point of 6-month outcomes, precluding inclusion of these subjects in the analysis. Subjects included all consenting, skeletally mature individuals from the time of study onset suffering from degenerative disc disease or spondylolisthesis for which conservative treatment had failed. Patients were included in the study if they required instrumented or noninstrumented posterolateral lumbar or lumbosacral spinal fusion with spinal canal decompression and had not undergone an operation of this nature previously. Patients were excluded if they had any contraindications as listed in the OsteoSet labelling. These were as follows: severe vascular or neurologic disease, uncontrolled diabetes, severe degenerative bone disease, pregnancy, hypercalcemia or abuse of drugs or alcohol.¹²

The test protocol utilized subjects as their own controls. Subjects received posterolateral lumbar or lumbosacral spinal fusion with decompression. In the usual fashion, the operative site was exposed and canal decompression performed. Bone obtained from the decompression was combined with an equal volume of OsteoSet pellets, and this comprised the test material. A volume of autologous iliac crest bone graft equal to the

OsteoSet plus decompression bone was obtained from the patient's posterior iliac crest, serving as the control material. The graft bed at the fusion site was then prepared in routine fashion. Placement of the graft materials, either on the left or the right, was determined at this time by opening a sealed ballot containing a randomized indication of the side of placement for test material. Posterior iliac crest autograft was placed on one side, thus serving as the control side. The opposite side received OsteoSet pellets plus autograft from the spinal decompression, serving as the test side.

Posteroanterior and lateral lumbar spine radiography was carried out postoperatively and during standard follow-up visits at 3, 6 and 12 months postoperatively to evaluate the fusion.^{4,13-18} At 6 and 12 months, evaluation was performed by an independent musculoskeletal radiologist blinded to the side on which the test material was placed. The development of new bone mass was quantified and compared on radiograph using 2 methods.

- Method A. Viewing the posteroanterior radiograph with the lateral radiograph as a reference, the radiologist assessed the spine for the presence of new bone mass. If new bone was apparent, the mass on that side was compared with the mass on the other side. The side bearing the larger mass was noted and the side bearing the smaller mass was graded as a percentage of the larger side as follows: 0 to 24%, 25% to 49%, 50% to 74%, 75% to 100%, or equal. For example, if the left side of the spine showed new bone formation with an estimated area of 8 cm² and the

right side showed an estimated area of 5 cm², then the left side would be noted as the larger side and the right would be graded in the category 50% to 74%.

- Method B. Viewing the posteroanterior radiograph with the lateral radiograph as reference, the radiologist assessed the spine for the presence of new bone mass. If new bone mass was apparent, the outline of this mass on either side of the spine was obtained. These outlines provided area measurements, which were quantified by placing the outlines over graph paper and totalling the 1 mm² areas within the outlines, allowing comparison between the outlines.

All 40 patients were assessed 6 months postoperatively. At the time the 12-month findings were assessed, follow-up for 6 patients was less than 12 months, 1 patient had been lost to follow-up and 1 patient could not be scored because the radiologist felt that instrumentation obscured any potential bone mass, negating adequate assessment. Thus, 32 patients were assessed at 12 months after fusion.

The 2 methods of analysis were examined for intraobserver reliability during evaluation of the 12-month radiographs. Both methods were performed by the same musculoskeletal radiologist during 2 sessions, with an interval of 1 month between sessions. Each subject's results were recorded using both methods during the 2 sessions. Re-

sults that were found to be the same for both sessions were reported as a percentage of the total number of results. This percentage was reported for both methods of analysis and represents the intraobserver reliability (repeatability) of the assessment.

Quantification of the fusion masses at 6 and 12 months provided measures of change in size over time. Documentation of patient and operative information permitted evaluation with respect to gender, age, smoking history, instrumentation and volume of graft material used.

Results

Evaluation of the methods of analysis showed an intraobserver reliability of 70% for Method A and 67% for Method B. Differences in final results were minimally affected despite this level of repeatability. Outcomes (test-side performance compared to control side) differed by 3% between sessions for both methods. Despite this, the difference was so minor that both reports would be classified similarly, in favour of either the test or the control side. The results from the session providing the less favourable outcomes (the lower values) of the 2 sessions for OsteoSet performance are reported.

Bone mass formation at the site of test material placement was considered "equivalent" to the bone mass at the control site if the test material bone mass was in the category of 75% to 100% of, equal to, or better

than the control side. We arbitrarily categorized the results in this manner because in our opinion the test material would show clinical promise if it produced a bone mass at least 75% as large as that of the control material.

Results obtained from Method A indicated that 78% of patients at 6 months and 88% at 12 months produced bone formation at the test site graded as equivalent to that at the control site. Results for both methods of analysis are reported in Table 1.

The average bone mass formation measured by Method B was equal for both graft materials (Table 2). Both sites noted continued improvement in bone mass size over time, the test material increasing an average of 9.18 cm² and the control material an average of 8.44 cm² from 6 to 12 months after fusion.

The differences in OsteoSet bone mass formation in relation to patient gender, age and smoking history, instrumentation, and volume of graft used were analyzed using Method A (Tables 3 to 7). The data obtained at 6 months were divided into the results from the total group of 40 patients and the results from the 32 whose follow-up data were also available at 12 months.

Since this was a preliminary report of only 40 patients from one of the test centres, and there was no compelling evidence to stop the trial, statistical analysis was not performed in order to maintain statistical power at the conclusion of the study.

Discussion

OsteoSet, calcium sulfate, is an osteoconductive material that allows

Table 1

Results of the Two Methods Used to Assess Bone Mass Formation (32 Patients*)

Method/assessment time, mo	OS + DB mass in relation to ICA mass, no. of patients				Result, %†
	Greater than	Equal to	≥75%	Less than	
Method A					
6	8	7	10	7	78
12	8	7	13	4	88
Method B					
6	13	5	4	10	69
12	11	5	13	3	91

OS + DB = OsteoSet pellets plus decompression bone, ICA = iliac crest autograft.

*The total group of 40 patients was assessed at 6 mo. The respective results for these were as follows: Method A — 11, 9, 11, 9 and 78%; Method B — 15, 6, 6, 13 and 68%.

†The percentage of patients in whom OS + DB showed bone mass formation greater than, equal to, or ≥75% of ICA bone formation.

Table 2

Size of Bone Mass in 32 Patients As Measured by Method B

Assessment time, mo	Size, cm ²	
	OS + DB	ICA
6	8.09	8.81
12	17.27	17.25

OS + DB = OsteoSet pellets plus decompression bone, ICA = iliac crest autograft.

ingrowth of blood vessels and osteogenic cells while it resorbs in aqueous media without generating dissolution products that could impede bone formation. The composition and crystalline structure of the medical grade calcium sulfate used to make OsteoSet pellets were designed so that its resorption rate corresponds with the rate of new bone growth.¹¹

Results should be interpreted realizing that there are study limitations. The operative procedure involved placement of different graft materials on either side of the spine at the level to be fused. It is essential to consider that the success of any bone graft or graft substitute may vary according to the particular environment. This environment will be altered owing to the testing of 2 different materials on opposite sides of the same spine at the same time. It is possible that, should the autograft heal faster, the slower healing OsteoSet would be affected. This effect may be positive in

that the autograft fusion may stabilize the spine and permit additional healing of the graft material on the other side.

However, the effect may be negative, as the autograft fusion causes stress shielding of the other side predisposing the OsteoSet to increased resorption. Certainly these remarks would be applicable in reverse: should the OsteoSet heal faster, the autograft side could be similarly affected. Unfortunately, although it is understood that the effect of one graft on the other is important, the nature of the effect is unknown.

Also, data acquisition involved a 2-dimensional (area) analysis by plain radiographs of the 3-dimensional bone mass on each side of the spine.

Thus, some information regarding size will be lost during acquisition. The decision to use radiographs was based on the true clinical scenario, in which the orthopedic surgeon relies on these images to evaluate the arthrodesis. Finally, bone mass was assessed rather than fusion mass. To confirm spinal fusion is difficult, expensive and unreliable. The assessment of bone mass instead is based on the true clinical scenario: the plain radiograph.

Although one may suspect that the density as seen on radiograph is greater on the experimental side as decompression bone tends to be cortical and iliac bone cancellous, this difference was not discernible at either the 6- or 12-month assessments.

Table 3

Comparison of Test Material (OS + DB) and Control Material (ICA) According to Gender in 32 Patients*

Assessment time, mo	Male, n = 22	Female, n = 10
6	73	90
12	91	80

OS + DB = OsteoSet pellets plus decompression bone, ICA = iliac crest autograft.
*Values are the percentage of patients with OS + DB equal to or better than ICA.
The total group of 40 patients was assessed at 6 mo. The respective results for these were as follows: male, n = 27, 74%; female, n = 13, 85%.

Table 5

Comparison of Test Material (OS + DB) and Control Material (ICA) According to Smoking History in 32 Patients*

Assessment time, mo	Smokers, n = 12	Nonsmokers, n = 20
6	67	85
12	83	90

OS + DB = OsteoSet pellets plus decompression bone, ICA = iliac crest autograft.
*Values are the percentage of patients with OS + DB equal to or better than ICA.
The total group of 40 patients was assessed at 6 mo. The respective results for these were as follows: smokers, n = 14, 57%; nonsmokers, n = 26, 89%.

Table 4

Comparison of Test Material (OS + DB) and Control Material (ICA) According to Age in 32 Patients*

Assessment time, mo	Age group, yr			
	<40, n = 14	41-50, n = 8	51-60, n = 4	>60, n = 6
6	71	75	75	100
12	86	75	100	100

OS + DB = OsteoSet pellets plus decompression bone, ICA = iliac crest autograft.
*Values are the percentage of patients with OS + DB equal to or better than ICA.
The total group of 40 patients was assessed at 6 mo. The respective results for these were as follows: age <40 yr, n = 16, 69%; 41-50 yr, n = 10, 70%; 51-60 yr, n = 5, 80%; >60 yr, n = 9, 100%.

Table 6

Comparison of Test Material (OS + DB) and Control Material (ICA) According to Instrumentation in 32 Patients*

Assessment time, mo	Instrumentation, n = 23	No instrumentation, n = 9
6	78	78
12	83	100

OS + DB = OsteoSet pellets plus decompression bone, ICA = iliac crest autograft.
*Values are the percentage of patients with OS + DB equal to or better than ICA.
The total group of 40 patients was assessed at 6 mo. The respective results for these were as follows: instrumentation, n = 27, 81%; no instrumentation, n = 13, 69%.

Table 7

Comparison of Test Material (OS + DB) and Control Material (ICA) According to Volume of OsteoSet Used in 32 Patients*

Assessment time, mo	≤10 mL OsteoSet, n = 17	>10 mL OsteoSet, n = 15
6	76	80
12	94	80

OS + DB = OsteoSet pellets plus decompression bone, ICA = iliac crest autograft.
*Values are the percentage of patients with OS + DB equal to or better than ICA.
The total group of 40 patients was assessed at 6 mo. The respective results for these were as follows: ≤10 mL OsteoSet, n = 22, 73%; >10 mL OsteoSet, n = 18, 83%.

Furthermore, the OsteoSet pellets were not visible, suggesting complete resorption by 6 months. Density of bone mass was not felt to affect measurements for either method of quantification.

OsteoSet plus decompression bone was observed to be equivalent in a majority of patients at 6 months, and this outcome improved to at least 88% of patients at 12 months. Using evaluation Method A, 25% of patients actually had superior results with the OsteoSet and decompression bone over the current standard iliac crest bone grafting method. Furthermore, the development of visible bone mass on posteroanterior radiographs at 6 and 12 months was seen to approximately double for OsteoSet, in parallel with the autologous bone. Significant progression was noted in bone mass formation from 6 to 12 months. This magnitude of change may be a valuable parameter with which to assess outcome. Lack of clinical correlation and length of follow-up place this insight beyond the scope of our paper, but this parameter is certainly worthy of further analysis.

Smoking appeared to be a clear predictor for worse outcomes at 6 months, but results improved for smokers at 12 months. Similarly, whereas patient gender and age, instrumentation and volume of graft material used appeared to be suggestive factors in determining outcome at 6 months, the differences became less apparent at 12 months. Therefore, not only does OsteoSet provide results comparable to autologous bone, these results continue to improve over time and appear not to be influenced by major patient factors.

Conclusions

OsteoSet plus decompression bone may provide a viable alternative

to fresh autologous iliac crest bone as a graft substitute in posterolateral lumbar and lumbosacral spinal fusion. In a majority of patients it provided bone mass at the site of spinal fusion that was equivalent in amount to the same volume of autologous iliac crest bone on the contralateral side. Elimination of bone graft harvesting could facilitate improvements in spinal fusion surgery through changes in surgical technique, leading to decreased morbidity, operative times and blood loss, improved outcomes, and consequently to a decrease in hospital stay and patient care costs. Further research is required to confirm these advantages, and assessment of the success of OsteoSet alone in spinal fusion is also required.

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