

TRI-CALCIUM PHOSPHATE CERAMICS AND ALLOGRAFTS AS BONE SUBSTITUTES FOR SPINAL FUSION IN IDIOPATHIC SCOLIOSIS : COMPARATIVE CLINICAL RESULTS AT FOUR YEARS

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The authors present the results of a comparative study of two series of posterolateral arthrodeses for scoliosis performed using COTREL DUBOUSSET instrumentation.

Fifty-four consecutive patients underwent surgery for idiopathic scoliosis using the same technique. Thirty received a graft consisting of a mixture of cortico-cancellous autologous and allogenic bone frozen at -80°, and 24 patients were grafted with a mixture of cortico-cancellous autologous bone and sticks of tricalcium phosphate (TCP, Biosorb, SBM, Lourdes, France). All patients were seen at three, six and twelve months, then once a year for at least four years with clinical and radiological evaluation at each visit.

At the final follow up visit, no radiologic signs of pseudoarthrosis were found in either group with a minimum follow-up of 4 years. The appearance of bone callus was considered satisfactory at 6 months in all cases ; moreover callus seemed to be more important in the TCP series, although this assessment was subjective. TCP resorption was total after 2 years, while allograft fragments were visible on x-rays after 2 years. Minor mechanical complications occurred but did not influence the results. Loss of correction was 8% of that initially obtained in the allograft group and 2% in the TCP group. Loss of correction did not progress after 6 months in the TCP group and after 2 years in the allograft group.

Based upon this experience, the use of synthetic bone substitutes such as TCP would appear to be a valuable alternative to allografts in posterolateral spinal arthrodesis for idiopathic scoliosis, and it would eliminate the risk of viral contamination inherent to allograft implantation. To our knowledge, there have been no previous comparative studies concerning the use of tricalcium phosphate versus allograft in the literature

Key words : idiopathic scoliosis ; multiple level fusion ; allograft ; tricalcium phosphate.

Mots-clés : scoliose idiopathique, arthrodesè étagée, allogreffe, phosphate tricalcique.

INTRODUCTION

Pseudarthrosis is a major cause of failure in the surgical treatment of idiopathic scoliosis. To avoid this, arthrodesis requires the use of large quantities of graft tissue. Autologous bone graft from spinal processes and iliac crests often provides insufficient quantities ; other sources must therefore be found.

A number of bone substitutes are presently available. Allografts have been widely studied in recent years by DODD *et al.* (11), RECHT *et al.* (28), FABRY (15). they provide a structure favouring growth and leading to satisfactory results in spinal surgery as reported by FABRY (15) and RECHT *et al.* (28).

Because of the risk of viral contamination (HIV, hepatitis, prions, etc...), we have preferred to use synthetic substitutes over the last eight years ; these contain no proteins and are microbiologically safe. Hydroxyapatite and tricalcium phosphate (TCP), which have been studied intensively over the last twenty years would appear to present acceptable properties as regards biocompatibility (30). In their porous form, they facilitate cellular penetration and allow for bone integration (14).

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Hydroxyapatite is generally considered to be non — or only slightly resorbable, while tricalcium phosphate is resorbed by a cellular pathway, leaving newly formed bone tissue. When used for spinal arthrodeses, the quality of grafts obtained has been found to be satisfactory in animals by FLATEY *et al.* (14), NASCA *et al.* (25, 26), and DACULSI *et al.* (7) and in humans by BUCHOLZ *et al.* (1) in fractures of the lower limb and in lumbar arthrodeses for fractures by HUSSON *et al.* (18) or in spinal fusions by PASSUTTI *et al.* (27).

The aim of this study was to assess the quality of bone fusion obtained with tricalcium phosphate ceramics used for treatment of idiopathic scoliosis. In view of the difficulty of evaluating this parameter, a comparative study was undertaken. We present our experience after four years follow-up, and compare the results of tricalcium phosphate grafts with those obtained using allografts for the same indications.

PATIENTS AND METHODS

Between 1986 and 1992, 54 consecutive patients with idiopathic scoliosis had surgery by the same senior surgeon (JCLH). All patients underwent the same anaesthetic protocol and were operated according to the technique of COTREL and DUBOUSSET (CDI) (4) with perioperative monitoring of evoked somesthetic and motor potentials. After the deformity had been reduced, the graft bed was prepared by decortication according to the technique of MOE (23) and GOLDSTEIN (17). Posterolateral grafting was performed by inserting graft tissue under the rods and into the articular facets.

The first 30 patients (22 females, 8 males ; mean age, 21 yrs, range 13-26) were operated on between 1986 and 1990 (Table I). Fusion involved a mean of 12 vertebrae. These patients received grafts consisting of a mixture of equal parts of autologous cortico-cancellous bone (from spinous and transverse processes) and allografts frozen at -80°C (A group)). A subsequent group of 24 patients (18 females, 6 males : mean age 20 yr. (range 14-40) were grafted between 1990 and 1992 using a mixture of equal parts of autologous cortico-cancellous bone from spinous and transverse processes and sticks of tricalcium phosphate (Biosorb, SBM, Lourdes, France) (STCP group).

The mean number of vertebrae fused was 11 in the second group. The two groups of patients were matched

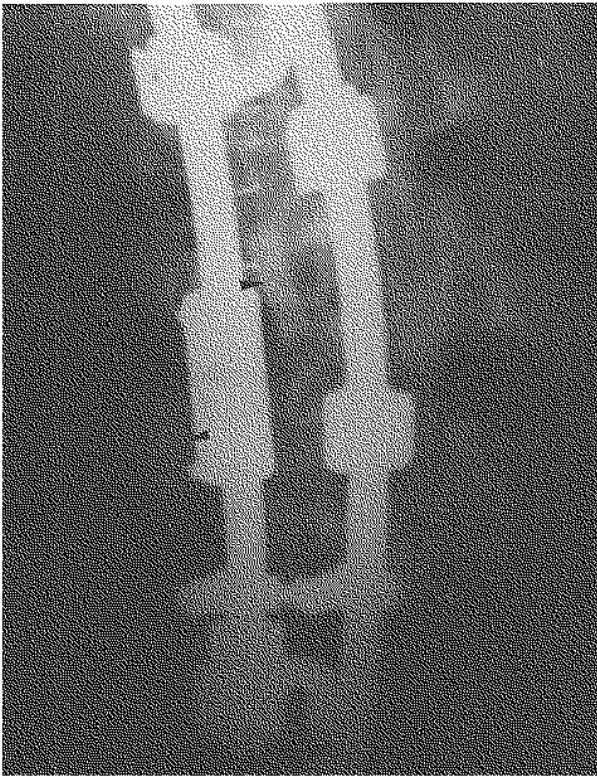
for age, sex, and indications (Table I). Deformation was measured using the Cobb angle determined from standing x-rays of the spine. Before intervention, AP and lateral xrays were taken with the patient bending, to determine the level of mobile disks and to choose the superior and inferior vertebral limits according to the technique of COTREL and DUBOUSSET (4). Apical vertebral rotation was measured using the technique of NASH and MOE (26).

External immobilisation was not used after operation. Two daily sessions of physiotherapy were programmed, with relaxing massage and respiratory rehabilitation. All patients were seen at 3, 6 and 12 months post-operatively then once a year for at least 4 years. At these visits, any signs indicating the possible existence of pseudoarthrosis were noted, either clinical (symptoms of pain or deep infection) or radiological (aspect and volume of the fusion mass, evidence of debris, evolution of the Cobb angle). When possible, histologic analysis was performed on biopsies.

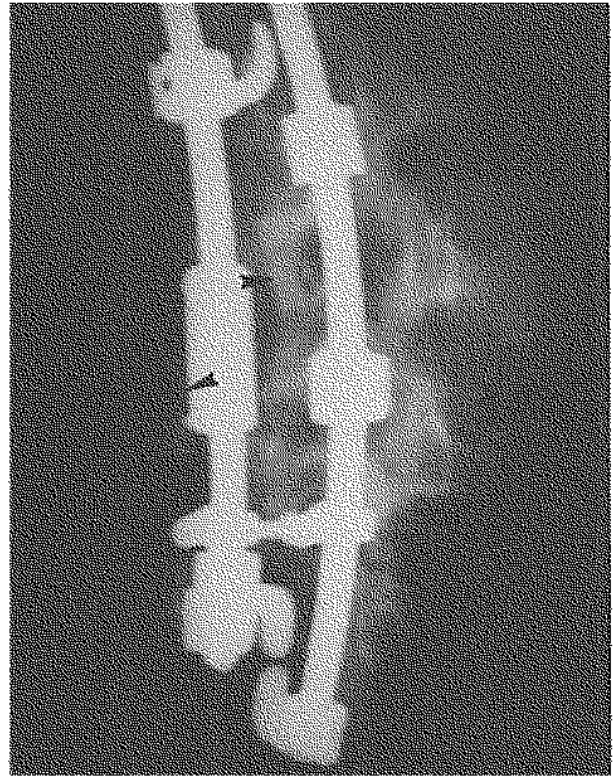
The accuracy of measurement was estimated to be $\pm 3^{\circ}$ owing to deformation and rotation of the vertebral bodies on the major curves. Evolution of less than 3° was therefore considered as insignificant. The results are presented as arithmetic means of the data. To monitor the evolution observed over time, the loss of correction between two follow-up visits was measured. This loss was expressed in degrees, then as a percentage of the difference from the initial value (post-operative correction). Finally, the number of cases with a loss of correction superior or equal to 3° was noted for each group.

RESULTS

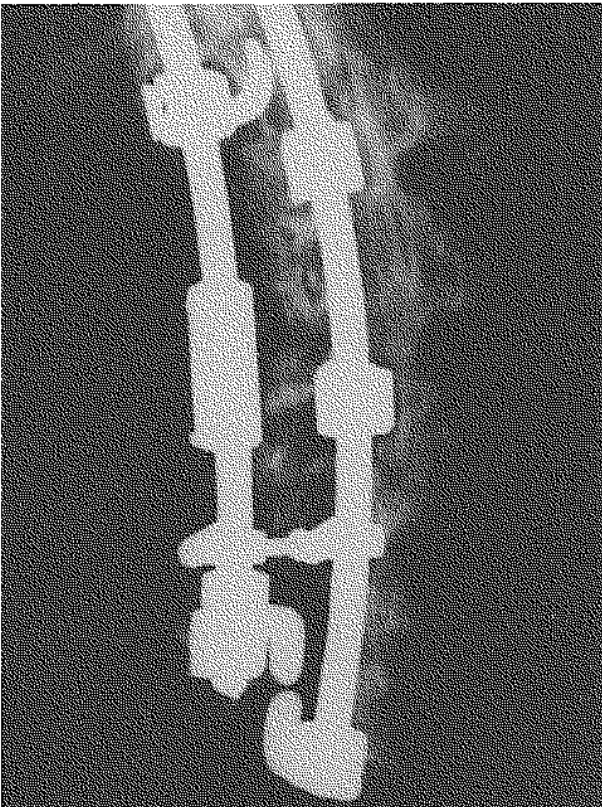
Results were analysed separately in the two groups. No signs of deep pain or deep infection were noted in either group at any time during follow-up. There were no respiratory, vascular or digestive complications. One case of intercostal neuralgia in a patient with an 80° thoracic scoliosis regressed 4 weeks after operation. No unequivocal radiologic signs of pseudoarthrosis were noted. The appearance of the bone callus was considered satisfactory at 6 months in all cases, in both groups, but was larger in STCP, although this assessment was subjective. Resorption of the ceramic implants in the STCP group became evident at 12 months (Fig. 1), and was complete after 2 years. In the SA group, fragments of allograft were visible on



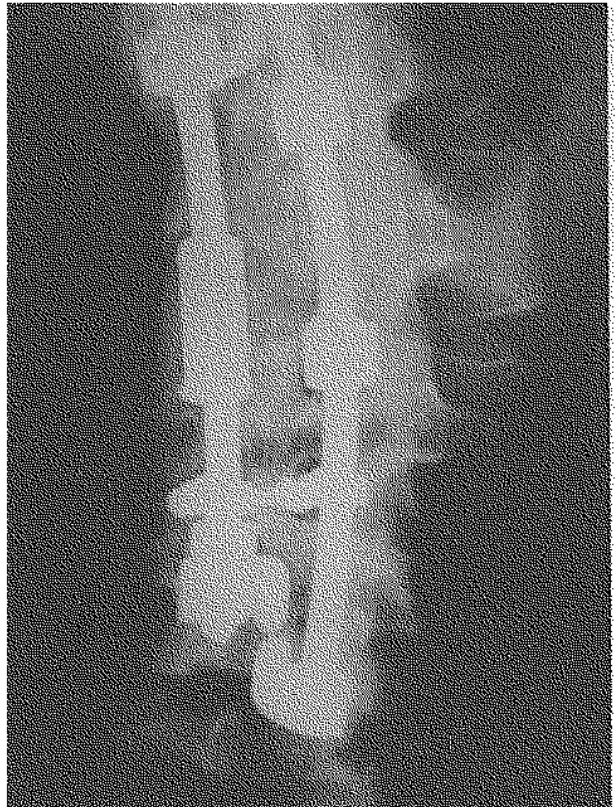
A



B

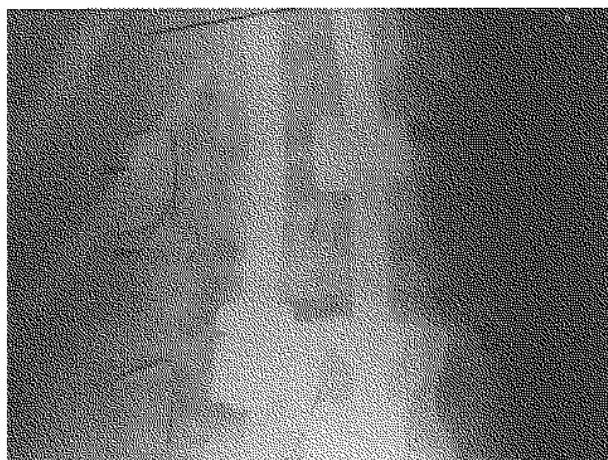


C
(6 months)

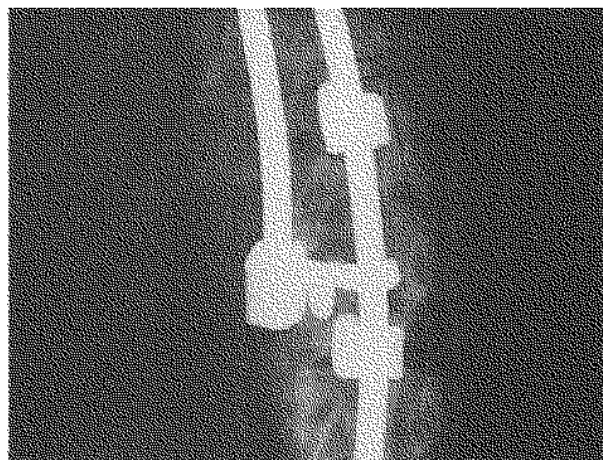


D
(11 months)

Fig. 1. — Evolution of the TCP resorption between the post-operative period and the last follow-up (15 days (A), 3 months (B), 6 months (C), 11 months (D)). There is complete resorption at 11 months in this patient (20 years old at last control).



A



B

Fig. 2. — Evolution of the allograft between the post-operative period and the last follow-up (15 days (A), 24 months (B)). There is incomplete resorption at 24 months.

x-rays taken after 2 years (Fig. 2); this was not the case in the STCP group.

Complications

A. In the SA group, there was one case of superior cervicalgia due to re-balancing of the spine above the operated segment, and 5 cases of pain due to protuberant hardware (hooks, transverse devices (D. T.)). One case required early reoperation to change a sublaminar hook which had come out of its notch on day 5 due to technical error during insertion: once it was changed, the clinical course was uneventful. Finally, there was one case of superior rupture of a DT two years after operation without loss of correction or pain (fortuitous discovery on x-ray).

B. In the STCP group, there was one case of persistent lumbo-sacral radicular pain in a 40-year-old woman treated for lumbar scoliosis with instrumentation to L4. There was one case of superior cervicalgia and 5 cases of pain due to protuberant hardware (hooks, transverse devices (DT)), one of which involved pain at the level of the residual gibbosity. In one case, the pedicular screw broke after one year, owing to the absence of a protective hook

under the lamina of the corresponding vertebra; the screw was removed, a hook was inserted with a subsequently uneventful clinical course and rapid return to work.

CORRECTION

Post-operative correction

Correction was measured in three planes. In the coronal plane (Table I), mean initial correction in the SA and STCP groups was 44 and 36%, respectively. In the sagittal plane, mean correction was not significant with respect to thoracic cyphosis. On the other hand, correction was comparable for lumbar lordosis, with values close to 30% (+ 11). Finally, measurements of the correction of rotation were so poorly reproducible that no exploitable data could be obtained.

Loss of correction over time

Data concerning the evolution of the correction over time are shown in Tables I-III and Figures 3-5. In the SA group, 10 cases (33%) had a significant loss of correction at the most recent follow-up. Of these, the loss of correction in 4 was apparent at six months, with no further deterioration, 4 patients had loss of correction between

Table I. — Analysis of data according to the type of curve and the type of implant ;
T.o.C. : Type of Curve — Th : Thoracic — Th-L : Thoraco-lumbar — L : Lumbar —
D.M. : Double Major — N : Number of patients — (Min-Max)

		Cobb Angle (degrees) STCP group					
T.o.C	N	Preop	Postop	1 month	1 year	2 years	4 years
Th	13	66 (20-108) N=13	44 (12-80) N=13	44 (12-80) N=13	44 (22-65) N=13	44 (12-80) N=13	44 (12-80) N=13
Th-L	7	64 (42-105) N=7	35 (12-65) N=7	36 (12-65) N=7	36 (12-65) N=7	36 (12-65) N=7	36 (12-65) N=7
L	2	52 (45-60) N=2	23 (12-35) N=2	25 (15-35) N=2	25 (15-35) N=2	25 (15-35) N=2	25 (15-35) N=2
D.M.	2	50/79 N=2	39/63 N=2	39/64 N=2	39/64 N=2	39/64 N=2	39/64 N=2
Total	24	64 N=24	41 N=24	42 N=24	42 N=24	42 N=24	42 N=24

		Cobb Angle (degrees) SA group					
T.o.C	N	Preop	Postop	1 month	1 year	2 years	4 years
Th	12	65 (45-85) n=12	38 (20-60) n=12	38 (20-60) n=12	39 (20-60) n=12	39 (20-60) n=12	39 (20-60) n=12
Th-L	8	60 (36-72) n=8	32 (18-50) n=8	35 (18-50) n=8	35 (18-50) n=8	36 (18-50) n=8	36 (18-50) n=8
L	5	51 (33-65) n=5	27 (15-50) n=5	29 (15-62) n=5	31 (15-62) n=5	31 (15-62) n=5	31 (15-62) n=5
D.M.	5	64/72 n=5	35/42 n=5	37/42 n=5	37/42 n=5	37/42 n=5	37/42 n=5
Total	30	63 n=30	35 n=30	36 n=24	37 n=24	37 n=24	37 n=24

Table II. — Mean loss of correction between two visits ;
N : Number of patients — d° : degrees — % : percentage

Follow-up	TCP			Allografts		
	N	d°	%	N	d°	%
Post-Op ; 6 months	2	-0,5	-1,8	4	-1,2	-4,6
6 months ; 1 year	0	0	0	4	-0,6	-2,1
1 year ; 2 years	0	0	0	2	-0,2	-0,7
2 years ; 4 years	0	0	0	Q	0	0
Total	2	-0,5	-1,8	8	-2,0	-8,0

Table III. — Patients showing loss of correction
at latest follow-up ;
N : Number of patients — % : Percentage of patients

T.o.C	TCP		Allografts	
	N	%	N	%
Th	0	0	2	17
Th-L	1	14	4	50
L	1	50	3	40
D.M.	0	0	1	20
Total	2	8	10	33

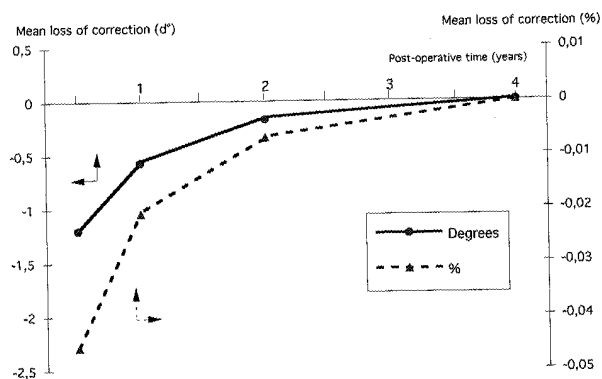


Fig. 3. — Mean loss of correction versus post-operative time in patients grafted with allografts.

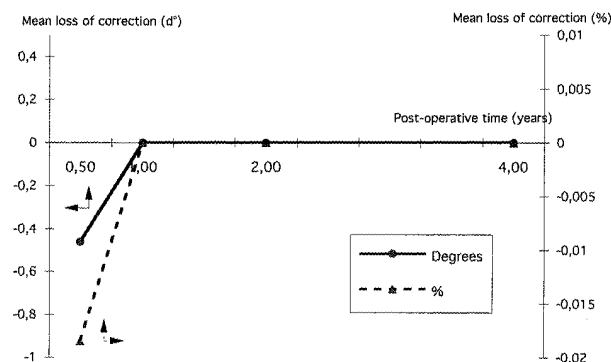


Fig. 4. — Mean loss of correction versus post-operative time in patients grafted with TCP.

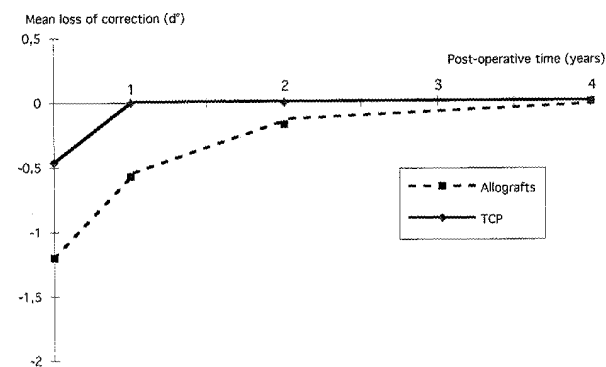


Fig. 5. — Compared loss of correction between patients grafted with allografts or TCP versus post-operative time.

months 6 and 12 with no prior or subsequent evolution; the remaining two patients evolved between years 1 and 2, with no prior or subsequent evolution. Mean loss of correction in the SA group was 2° , i.e. 8% of the initial correction. The losses of correction were significantly more frequent and greater in curves at the thoraco-lumbar and lumbar levels (53% of such curves).

In the STCP group, 2 patients (8%) had a significant loss of correction at month 6, which did not evolve subsequently. No loss of correction was noted in any case after month 6. Total loss of correction at the most recent follow-up visits in the STCP group was 0.5° (2% of initial correction). Here again, there was a higher rate of evolution at the thoraco-lumbar and lumbar levels, both in terms of frequency (22% of curves) as well as amplitude.

DISCUSSION

The aim of the present study was to assess the efficacy of tricalcium phosphate in posterolateral spinal fusion. The most accurate evaluation of grafts quality would ideally take into account both clinical as well as biological elements, such as bone growth, cell penetration and mechanical quality of the graft after explantation. These criteria clearly are not applicable in a human study. Use of CT scan to measure bone density or estimating graft rigidity with dynamic films is not possible, owing to the presence of the metallic devices; these cause interference and obscure the image of the grafted area. Moreover, their rigidity precludes any real estimation of the solidity of the graft tissue itself. Consequently, we decided to assess pseudoarthrosis, as proposed by DAWSON *et al.* (8) by seeking indirect signs indicating a consolidation defect, to the exclusion of any other criteria.

DAWSON *et al.* (8) insist on the difficulty of diagnosing pseudoarthrosis in instrumented idiopathic scoliosis. Like NASCA *et al.* (25), PASSUTI *et al.* (27) and NASH and MOE (26), they note that the presence of deep pain, loss of correction, debris, and radiologically visible pseudoarthrosis are the most frequent markers for the presence of one or several pseudoarthroses.

Pseudoarthroses can often be identified on x-ray. LAUERMAN *et al.* (18) observed them indeed in 68% of 63 patients at one or several levels. We found no such case in our series. However, we used COTREL-DUBOUSSET instrumentation, which is bulky and has two rods; it may therefore be difficult to demonstrate one or several pseudoarthroses radiologically in the presence of this device. We consistently found a homogeneous graft in which the tricalcium phosphate implants were progressively resorbed, leaving behind tissue of the same density as bone. In one case, histologic analysis of biopsies removed at operation two years after scoliosis surgery for a benign subcutaneous tumour confirmed complete disappearance of the tricalcium phosphate and the presence of healthy bone tissue. HUSSON *et al.* (18) report comparable results in 35 patients grafted with tricalcium phosphate during lumbar arthrodeses for fractures.

Pain is one of the most frequent symptoms of pseudoarthrosis according to CUMINE *et al.* (6) and DAWSON *et al.* (8). However, certain cases are painless and can even be totally asymptomatic according to DAWSON *et al.* (8).

Our results reveal respectively 6 (20%) and 7 (29%) patients reporting pain in the SA and STCP groups. Of these, 10 (77%) had elective pain on superficial palpation and this was attributed to protuberant devices causing periodic bursitis, while the other 3 had pain at a level superior or inferior to the last level of the arthrodesis. The latter were attributed to articular overload due to rebalancing of the spine above and below the fixed areas. Therefore, no case of deep persistent pain could be ascribed to a pseudoarthrosis. Moreover, STCP patients did not feel significantly more pain than the others ($p < 0.005$). The absence of deep infection also confirmed the good tolerance of the grafts.

Loss of angular correction, has been noted with all types of instrumentations, as noted by COCHRAN *et al.* (3), DRUMMOND (13), KOSTUIK (19) and WOJCIK *et al.* (31). It was not significant in our patients during the first post-operative months. Although the reasons for the initial loss of a few degrees remain unclear, these do not automatically suggest pseudoarthrosis. However, is possible that satisfactory, homogenous bone

fusion throughout the grafted levels offer sufficient rigidity such that the curve will no longer worsen significantly. There may be some evolution in the immediate segments above and below the grafted areas by a mechanical overload or "crankshaft" phenomenon, especially in patients not having reached full skeletal maturity as shown by DUBOUSSET *et al.* (5). Owing to the location outside the grafted area, such evolution cannot be attributed to an absence of fusion. It would therefore appear that a good quality arthrodesis is not associated with long-term loss of correction, as DOWELL *et al.* (12) and KOSTUIK (19) have shown. In our series, 2 (8%) patients who received synthetic ceramics had significant loss of correction (1.8% of the whole group) in the first six post-operative months, (mean loss : 0.5°) but thereafter the loss did not progress. Moreover, a significantly higher number of patients (10, i.e. 33%), with allografts had a greater deterioration of the correction which stabilised during the second year. These results are similar to those reported by FABRY *et al.* (15) who compared allograft versus autograft and noted a loss of correction of 5.4° with autograft, versus 3.8° with allograft after one year. They used Harrington's instrumentation, which is less stiff than the CD instrumentation.

Three remarks must be made here. First, loss of correction in the first six months was comparable in the two groups of patients, and also comparable to cases in the series reported by GIOIA *et al.* (16), SPONSELLER *et al.* (29) and DICKSON *et al.* (9), who used autologous bone graft. Therefore, loss of correction does not seem to depend upon graft type, as FABRY *et al.* (15) and RECHT *et al.* (28) have noted comparing autograft and allograft.

Moreover, we did not observe any evolution after the second year, which would seem to indicate that stability is reached in all cases after this time period. This suggests that the arthrodesis was of good quality. Stability seems to be reached after the sixth month with tricalcium phosphate, while 6 patients (20%) in the SA group continued to evolve after this date. Nevertheless, this deterioration occurred more frequently in the thoracolumbar and lumbar regions. In the STCP group, all patients with loss of correction had curves at

this level and 70% of them in the SA group (Table III). The need to perform compression with forceps in the transitional thoraco-lumbar area, as described by GIOIA, M'RABET and DUBOUSSET (16), is probably an explanation for the loss of correction observed at the beginning of our experience with the SA group, at a time when the forceps was not used systematically. We are unable to draw any precise conclusions on this point regarding the lumbar area owing to the small number of cases (2 in the STCP group). The difference in frequency of pain above the levels of fixation noted in the two groups is, however, significant; this could mean that grafts are fused more quickly with tricalcium phosphate, although we have no other evidence to confirm this.

It would seem that there were no cases of pseudoarthrosis at 4 years follow-up in either group. This seems to be confirmed by observations regarding broken devices. Whatever material was used, the need for early reoperation usually indicates a perioperative technical error which must be immediately rectified. This does not appear to increase the risk of pseudoarthrosis. Early breakage may mean that excessive mechanical strain has led to fatigue. Such failure can occur around a pseudoarthrosis, which then behaves like a mobile area generating flexional and torsional stress. Unfortunately, there was one case of breakage of an inferior pedicular screw with a device reaching as low as L3 in the STCP group.

However, this breakage may have been due to the absence of a sublaminar protective hook, as DE PERETTI and ARGENSON (10) have demonstrated in fractures. At no time did we see any mobile area within a reconstruction, again confirming the high quality of vertebral fusion obtained with tricalcium phosphate.

CONCLUSION

In this study, tricalcium phosphate, when used for posterior spinal grafting during instrumentation of idiopathic scolioses, did not give rise to any signs of intolerance or sepsis, nor was it responsible for any atypical complications at four years follow-up. It was progressively resorbed at the site of implantation, and was completely replaced by

radiologically normal bone tissue two years later. There was no loss of correction after six months, nor was there any discernible pseudoarthrosis after four years. These results are comparable to those obtained with cryopreserved allografts, although we found more rapid angular stabilisation with tricalcium phosphate in the thoracic and thoracolumbar regions. However, it has not been possible to confirm this with easily carried out confirmatory tests. In summary, tricalcium phosphate associated with autologous corticocancellous grafts seems to be a valuable alternative to allografts for posterolateral spinal arthrodeses in idiopathic scoliosis.

RÉSUMÉ

J. C. LE HUEC, E. LESPRIT, C. DELAVIGNE, D. CLEMENT, D. CHAUVEAUX, A. LE REBELLER. Céramique de phosphate tricalcique et allogreffes comme substituts osseux dans l'arthrodèse des scolioses idiopathiques.

Les auteurs présentent les résultats d'une étude comparative de deux séries d'arthrodèses postéro-latérales pour scoliose réalisées en utilisant une instrumentation de Cotrel-Dubousset. La greffe était constituée par un mélange d'autogreffe et d'allogreffe ou de céramique de phosphate tricalcique (TCP). La qualité de la fusion a été examinée en fonction de critères cliniques et radiologiques. Il n'existe pas dans la littérature d'étude comparative semblable entre allogreffe et phosphate tricalcique.

Cinquante-quatre patients ont été opérés en utilisant la même technique pour scoliose idiopathique. Trente ont reçu une greffe constituée d'un mélange à parts égales d'os cortico-spongieux autologue et d'allogreffe congelée à -80°C (SA), et 24 ont été greffés avec un mélange d'os cortico-spongieux autologue et de bâtonnets de phosphate tricalcique (STCP) (Biosorb, SBM, Lourdes, France). Tous les patients ont été revus à 3, 6, 12 mois puis une fois par an pendant au moins 4 ans, avec évaluation clinique et radiologique. Au dernier contrôle, aucun signe de pseudarthrose radiologique n'était noté avec un suivi minimal de 4 ans dans les deux séries. L'aspect du cal était considéré satisfaisant à 6 mois dans tous les cas,

cependant il semblait plus volumineux dans le groupe TCP, bien que cette impression soit subjective. La résorption du TCP était totale après deux ans, alors que des fragments d'allogreffes étaient toujours visibles sur les radiographies après deux ans. Quelques complications mineures sont survenues mais n'ont pas influencé les résultats. La perte de correction était de 8% par rapport à la correction post-opératoire dans le groupe des allogreffes, et de 2% dans le groupe STCP. Cette perte de correction ne progressait pas après 6 mois dans le groupe STCP et après deux ans dans le groupe SA.

Considérant le risque de contamination virale inhérent aux allogreffes, l'emploi de substituts synthétiques comme le TCP est une alternative intéressante aux allogreffes pour réaliser des arthrodeses postéro-latérales dans le traitement des scolioses idiopathiques.

SAMENVATTING

J. C. LE HUEC, E. LESPRIT, C. DELAVIGNE, D. CLEMENT, D. CHAUVEAUX, A. LE REBELLER. Tricalciumfosfaat keramiek en allogreffes als beensubstituten bij spinale fusie in idiopathische scoliose.

De auteurs stellen de resultaten voor van een vergelijkende studie van 2 reeksen van posterolaterale artrodese voor scoliosis met Cotrell-Dubousset instrumentatie.

Vierenvijftig opeenvolgende patiënten werden geopereerd met dezelfde techniek. Bij 30 werd een ent materiaal bestaande uit een mengsel van corticocancelluze autologe en allogene botfragmenten diepgevroren op -80°C gebruikt. Bij 24 werd een mengsel van corticocancellus bot en tricalciumfosfaatstrookjes (TCP, biosorp, SBM, Lourdes, France) gebruikt.

Alle patiënten werden teruggezien na 3, 6 en 12 maanden en vervolgens 1 x per jaar tot minimum 4 jaar met klinische en radiologische evaluatie bij elk bezoek.

Bij de laatste follow-up werd radiologisch geen enkel teken gevonden van pseudartrosis in geen van beide groepen met een minimum follow-up

van 4 jaar. Het aspect van de botcallus was als bevredigend beoordeeld op 6 maanden bij alle gevallen. Callus leek eerder meer belangrijk te zijn bij de TCP-reeksen, alhoewel deze beoordeling subjectief was.

TCP-resorptie was volledig na 2 jaar, terwijl allogreffragmenten zichtbaar bleven op radiografie ook na 2 jaar. Mineure mechanische complicaties vonden plaats doch zonder invloed op het resultaat.

Een correctieverlies van 8% van de initieel bekomen correctie in de allogreffegroep en 2% in de TCP-groep werd vastgesteld. Na 6 maanden was er geen verlies meer van correctie in de TCP-groep en na 2 jaar in de allogreffegroep.

Met deze ervaring, lijkt het dat een synthetisch botvervangmiddel zoals TCP een waardevol alternatief voor allogreffes in posterolaterale spinale artrodese voor idiopathische scoliose blijkt te zijn. Het zou het risico op virale besmetting inherent aan allogreffes vermijden. Voor zover bekend werden geen voorafgaande studies met het gebruik van tricalciumfosfaat vergeleken met allogreffes.

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