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β -tricalcium phosphate as a bone substitute for dorsal spinal fusion in adolescent idiopathic scoliosis: preliminary results of a prospective clinical study

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Dedicated to Prof. Hartmut Zippel, MD,
Head of the Orthopedic Clinic in the
Charité Hospital, where all the surgery
was done

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Abstract The aim of this study is to evaluate the ability of β -tricalcium phosphate (TCP) in granular form to achieve dorsal spondylodesis in adolescent idiopathic scoliosis (AIS). Twenty-eight patients underwent surgical correction and were followed up for 13 ± 8 (range 6–33) months. Posterolateral grafting was performed, using either autograft bone mixed with allograft bone ($n=19$; “bone group”) or autograft bone mixed with 25 g TCP ($n=9$; “TCP group”). Patients were followed by clinical examination, X-rays and computed tomographic (CT) scans to measure bone mineral density. Fusion involved 12 ± 1 (range 10–14) vertebrae. The segments were fused after 6 ± 1 months in both groups according to the radiographs. No pseudarthrosis was observed. Bone mineral density was 430 ± 111 (range 273–629) mg/cm^3 in the TCP group versus 337 ± 134 (range 130–669) mg/cm^3 in the bone group. Resorption of TCP was complete on the

radiographs after 8 ± 2 (range 6–10) months. Based upon the results of this small preliminary study, the use of TCP appears to be a valuable alternative to allografts for application in the spine, even when large amounts of bone are needed.

Keywords Scoliosis · Spinal fusion · Bone substitutes · Bone regeneration

Introduction

Despite modern fixation techniques, pseudarthrosis is a major cause of failure in the surgical treatment of idiopathic scoliosis. To avoid this, dorsal spondylodesis requires the use of large quantities of bone graft. Autologous bone graft from spinal process and iliac crest often provides insufficient quantities. In addition, morbidity after harvesting bone from the pelvis is considerable [1, 7].

Allograft bone from bone banks carries known risks of bacterial contamination and viral transmission [2, 5].

Because of these problems, there is an increasing interest in biodegradable osteoconductive ceramic bone graft substitutes. These materials must fulfil certain properties [1, 13]: compatibility with surrounding tissues, chemical stability in body fluids, compatibility of mechanical and physical properties, ability to be produced in functional shapes and to withstand the sterilization process, reasonable cost of manufacture and reliable quality control.

Fig. 1 **A** Posteroanterior and **B** lateral radiograph of an idiopathic adolescent scoliosis ("bone group"), before and after surgery

Calcium phosphate ceramics, whose composition is similar to that of mineral bone, are known to be safe and non-allergenic, with good bone bonding capacity. They have been explored and used as substitutes for bone graft in orthopaedic, maxillofacial and dental operations over the last 30 years. Hydroxyapatite (HA) is generally considered to be only slightly resorbable, while tricalcium phosphate (TCP) is resorbed by a cellular pathway, leaving newly formed bone tissue [3, 19]. When used for spinal arthrodesis, the quality of grafts obtained has been found to be satisfactory in animal models and in human spinal fusion [4, 8, 9, 12, 14, 15].

In previous studies of treatment of idiopathic scoliosis with synthetic bone substitutes, blocks or sticks of TCP composites were used (biphasic ceramic TCP/HA [15, 17], composite collagen/TCP [11]). The aim of this prospective study is to evaluate the performance of TCP in granular form in human dorsal spine fusion and to assess the quality of bone fusion obtained in the treatment of adolescent idiopathic scoliosis.

Materials and methods

Between October 1998 and April 1999, 28 patients with idiopathic adolescent scoliosis were operated. There were 22 female and 6 male patients with an average age of 14.5 ± 1.6 (range 10–17) years. The hospital stay was 14 ± 3 (range 10–23) days. We carried out a dorsal spondylodesis with USS-titanium implants (Mathys Medical, Ltd) (Fig. 1). The surgical procedure for operative correction of the scoliosis was performed analogously to the rod rotation procedure of Cotrel and Dubousset. All operations were performed by one surgeon (M. M.). No anterior release or anterior fusion was considered to be necessary. Convex side rib hump resection was

Fig. 2 Mixture of β -tricalcium phosphate (TCP) and morcellised autologous bone

added in 24 patients during the operation. Posterolateral grafting was performed with two sorts of graft: autograft bone mixed with allograft bone ($n=19$; "bone group") and autograft bone mixed with 25 g TCP (chronOS, Mathys Medical, Ltd) ($n=9$; "TCP group") (Fig. 2, Fig. 3).

In both patient groups, perioperative antibiotics were given. The patients were mobilized without corset, starting on the 2nd postoperative day.

Patients were followed up for 13 ± 8 (6–33) months. Clinical examination and posteroanterior and lateral radiographs of the spine in standing position were carried out preoperatively and postoperatively at 3 months, 6 months, 1 year and 2 years.

The evaluation of the patient records and radiographic measurements were performed by an independent observer (S.H.). For each patient, the intraoperative blood loss, the duration of surgery and complications were recorded. From the posteroanterior view we measured not only the Cobb angles of the thoracic major curve and the lumbar secondary curve, but also the rotation of the apex and the sagittal profile (kyphosis T4–12 and lordosis L1–5) according to Pedriolle [16]. To measure bone mineral density, all patients underwent one computed tomographic (CT) scan at 11 ± 8

Fig.3 Idiopathic adolescent scoliosis, instrumented with USS, before (A) and after (B) augmentation with autologous bone and β -tricalcium phosphate (TCP)

Fig.4 Computed tomographic (CT) scan 3 months after dorsal instrumented spondylodesis with good coverage of the metal implants with autologous bone/ β -tricalcium phosphate (CP)

Fig.5 CT scan 8 months after dorsal instrumented spondylodesis ("TCP group") shows homogeneous bone formation between the transverse process and the measurement results of the bone mineral density (418 mg/cm^3)

(range 3–33) months (Fig. 4, Fig. 5). The CT scans were carried out by one radiologist (K.B.), who was not informed of the aim of the study. To reduce the radiation exposure of the patients, only one vertebral level was scanned. It was agreed to use the setting of the instrumentation resulting in darker images (setting C1=800, W1=2000), thus reducing the artifacts and emphasising bone.

Results

The distribution of age, gender, type of scoliosis according to King as well as the stay in the hospital were similar in the two groups (Table 1). Significant correction of the spine was achieved by surgery in both groups. No differ-

Table 1 Comparison of the bone and β -tricalcium phosphate (TCP) group according to patient age (mean $\pm$ SD with range in parentheses), gender, type of scoliosis (King classification) and stay in hospital

	Bone group	TCP group
Age (years)	14.3 $\pm$ 1.7 (10–17)	14.8 $\pm$ 1.5 (12–17)
Gender	14 girls, 5 boys	8 girls, 1 boy
King type 2	10	5
King type 3	7	2
King type 4	2	2
Days in hospital	14.1 $\pm$ 3.1 (10–21)	13.9 $\pm$ 4.0 (10–23)

Table 2 Comparison of preoperative and follow-up measurements of the thoracic major curvature, the lumbar secondary curvature, the thoracic and lumbar rotation at the apex of the curvature, and the thoracic kyphosis and lumbar lordosis between the β -tricalcium phosphate (TCP) and the bone group (all measurements expressed in degrees with mean $\pm$ SD, and minimum and maximum values in parentheses)

* $P < 0.01$; ** $P < 0.05$; n.s._{pre} (not significant): all compared with preoperative values

	Bone group	TCP group	Significance
<i>Preoperative values</i>			
Thoracic major curvature	53 $\pm$ 8 (36–66)	54 $\pm$ 10 (46–72)	$P = 0.87$ (n.s.)
Lumbar secondary curvature	31 $\pm$ 11 (0–45)	35 $\pm$ 8 (19–43)	$P = 0.38$ (n.s.)
Thoracic rotation (apex)	25 $\pm$ 8 (5–35)	18 $\pm$ 4 (10–25)	$P = 0.02$
Lumbar rotation (apex)	7 $\pm$ 6 (0–20)	6 $\pm$ 5 (0–15)	$P = 0.38$ (n.s.)
Thoracic kyphosis (T4–12)	29 $\pm$ 13 (9–48)	17 $\pm$ 14 (2–43)	$P = 0.03$
Lumbar lordosis (L1–5)	37 $\pm$ 16 (5–45)	38 $\pm$ 14 (21–60)	$P = 0.87$ (n.s.)
<i>Follow-up values</i>			
Thoracic major curvature	17 $\pm$ 6 (8–30)*	16 $\pm$ 6 (7–23)*	$P = 0.73$ (n.s.)
Lumbar secondary curvature	8 $\pm$ 7 (0–22)*	7 $\pm$ 6 (0–16)*	$P = 0.73$ (n.s.)
Thoracic rotation (apex)	16 $\pm$ 10 (0–30)*	11 $\pm$ 4 (5–15)**	$P = 0.27$ (n.s.)
Lumbar rotation (apex)	2 $\pm$ 5 (0–15)**	6 $\pm$ 6 (0–15) n.s. _{pre}	$P = 0.15$ (n.s.)
Thoracic kyphosis (T4–12)	22 $\pm$ 9 (6–34) n.s. _{pre}	22 $\pm$ 8 (8–32) n.s. _{pre}	$P = 0.99$ (n.s.)
Lumbar lordosis (L1–5)	37 $\pm$ 10 (19–50) n.s. _{pre}	28 $\pm$ 6 (21–36) n.s. _{pre}	$P = 0.08$ (n.s.)

Table 3 Comparison of patients' blood loss (intraoperative and postoperative; mean $\pm$ SD with range in parentheses), number of patients who received blood transfusion (autologous and blood from blood bank) and operation time between the two groups

	Bone group (n=19)	TCP group (n=9)	Significance
Blood loss (ml)	1793 $\pm$ 486 (900–2600)	1850 $\pm$ 524 (1100–2400)	n.s.
Intraop. blood loss (ml)	1207 $\pm$ 506 (400–2000)	1150 $\pm$ 476 (700–1800)	n.s.
Postop. blood loss (ml)	612 $\pm$ 209 (200–3000)	678 $\pm$ 248 (200–1000)	n.s.
Blood transfusion (no. of patients)	16	6	n.s.
Only autologous blood	12	4	
Blood from bank	4	2	
Operation time (min)	181 $\pm$ 29 (135–240)	186 $\pm$ 46 (135–290)	n.s.

Fig. 6 Measurements of bone mineral density (BMD in mg/ccm) in the bone group and in the β -tricalcium phosphate (TCP) group, and logarithmic regression analysis of the values (filled circles bone group, open circles TCP group, thick line bone group trend line, thin line TCP group trend line)

Fig. 7 **A** Anteroposterior and **B** lateral radiographs, immediately (*left*) and 6 months (*right*) after surgery, showing β -tricalcium phosphate granules resorption and formation of solid bone fusion

ence according to the amount of the correction of the thoracic major curve, the lumbar secondary curve, the thoracic rotation, the thoracic kyphosis or the lumbar lordosis was observed between the two patient groups (Table 2). Comparison of the preoperative and follow-up measurements of lumbar rotation demonstrated a significant correction in the bone group, but was not observed in the TCP group.

Blood loss during the operation and after surgery, transfusion of blood (autologous blood or blood from the

bank) and the operation time were recorded (Table 3). No significant differences were seen between these parameters. Three of 19 patients (15%) in the bone group and 3 of 9 patients (33%) in the TCP group did not need any blood transfusion. We had one patient from the bone group with local pain at the iliac crest 6 months after surgery. However, pain disappeared without any therapy.

The CT scans to measure the bone mineral density were performed at 11 ± 8 (range 3–33) months after surgery. Seven CT scans were available in the TCP group

Table 4 Complications and management of these complications. TCP β -tricalcium phosphate

Complication	Bone group (n=19)	TCP group (n=9)
Lumbar decompensation, no reoperation required	1	
Cast syndrome, infusion therapy		1
Puncture of a deep haematoma	1	
Late deep infection, hardware removal and anterior fusion (VDS according to Zielke)		1

and 17 in the bone group. The mean value of the bone mineral density was 430 ± 111 (range 273–629) mg/cm^3 in the TCP group and 337 ± 134 (range 130–669) mg/cm^3 in the bone group ($P=0.16$; n.s.). The results of the CT measurements relative to the bone density are summarised in Fig. 6.

No pseudarthrosis was observed. The time until the TCP granules disappeared on the plain X-ray films and were completely substituted by homogeneous bone was 8 ± 2 (range 6–10) months (Fig. 7).

Complications were seen in four patients (14%; Table 4), but these complications were not related to the bone graft or the bone substitute.

Discussion

The efficacy of different ceramics in obtaining spinal arthrodesis has been studied both in animal models and in selective clinical studies [13]. In animal models the fusion has been analysed mainly in sheep [8, 9]. Some authors demonstrated better results with autologous bone, others found similar results, in term of fusion rate, when using a mixture of hydroxyapatite and TCP or coralline hydroxyapatite [13, 18].

Clinical data on the use of ceramics as graft extenders for autologous bone fusion of deformities have been presented by Delecrin et al., Heise et al., Le Huec et al., Passuti et al. and Ransford et al. [6, 10, 12, 15, 17].

Delecrin et al. operated on 58 patients with idiopathic scoliosis using Cotrel Dubousset (CD) instrumentation [6]. Posterior spinal fusion was performed using autologous bone in 30 patients using local bone combined with blocks containing both hydroxyapatite and β -tricalcium phosphate in 28 patients. They observed less blood loss in

the patient group with ceramic blocks. The satisfactory correction of the deformity was maintained to a similar degree in the two groups. They concluded that harvesting iliac bone is no longer necessary for such surgeries.

Le Huec et al. presented a study of 54 patients who underwent dorsal spondylodesis for idiopathic scoliosis [12]. Twenty-four patients underwent grafting with a mixture of autologous cortico-cancellous bone and TCP sticks, while 30 patients received a graft consisting of a mixture of autologous and allogenic bone frozen at -80°C , as in our study. The authors found TCP resorption after 2 years, which is clearly a longer time period than the one we found in our study using TCP granules. Loss of correction was 8% in the autograft/allograft group, but only 2% in the TCP group.

Passuti et al. [15] used calcium phosphate blocks in 12 patients with scoliosis for whom sufficient bone graft was difficult to obtain (neurologic scoliosis and osteogenesis imperfecta). They found normal clinical and radiologic outcome with histologic evaluation, as performed in two patients, demonstrating both the bioactivity and the osteoconduction of this material.

In a prospective randomised study at five hospitals in the UK and France, Ransford et al. investigated 341 patients with idiopathic scoliosis. The patients were grafted with autologous bone ($n=171$) or synthetic porous ceramic ($n=170$) [17]. They also found a loss of correction of 8% in the autograft group versus 3% in ceramic group. Fifteen autograft patients had pain at the donor site at 3 months. They found normal haematological and serum biochemistry results and no adverse events related to the graft material or evidence of allergenicity.

We found comparable results in our study when compared with the literature. However, it was difficult to assess whether a solid fusion had occurred. It is critical to use bone mineral density as a way to assess the bone quality or the rate of spinal arthrodesis. Further research is needed to investigate this problem in more detail.

Conclusion

Based on the results of this small study, we consider β -tricalcium phosphate to be a good bone substitute for dorsal spinal fusion in adolescent idiopathic scoliosis. According to clinical and radiological parameters, together with the bone mineral density results, β -tricalcium phosphate in granular form has similar fusion rates to autologous bone.

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