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Use of hydroxyapatite in spine surgery

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Abstract Hydroxyapatite- (HA-)based ceramics have been evaluated for a variety of applications in spinal surgery, utilizing in vivo animal models and human clinical series. In vivo animal studies have shown efficacy for these materials as a bone graft substitute in interbody fusions and as a bone graft extender or bioactive osteoinductive material carrier in posterolateral lumbar fusions. Clinically, HA ceramic has been shown to be effective as a bone graft extender in posterior spinal fusion surgery for childhood scoliosis, and as a structural bone graft substitute in anterior cervical spine fusions. As an osteoconductive material, it appears to function best as a bone graft extender or carrier for an osteoinductive bone growth factor rather than as a stand-alone bone graft substitute in nonstructural clinical applications. Injectable HA ceramics also hold promise as biocompatible and bioresorbable materials for use in spinal screw fixation strength augmentation and in minimally invasive vertebral body strength augmentation either following fracture or prophylactically in osteoporotic vertebrae.

Keywords Hydroxyapatite · Spinal fusion · Bone morphogenetic protein carrier · Vertebroplasty

Introduction

Surgical techniques and instrumentation systems to provide segmental fixation, providing added stability and the ability to correct deformity, have become increasingly refined and available [3, 11]. This has been an important factor in the recent increase in popularity of spinal fusion surgery. For a spinal fusion (arthrodesis) to be successful, even in the presence of spinal instrumentation, living bone tissue must bridge adjacent vertebrae to provide long-term support. Failure of bony fusion (pseudoarthrosis) remains a significant problem in spine surgery. Basic indications for spinal fusion include spinal instability, correction and/or stabilization of spinal deformity, following complete discectomy (as in the anterior cervical spine) for decompression, and in certain cases of pain syndromes thought to be due to painful disc degeneration or focal spinal arthritis.

Bone grafting typically accompanies a spinal fusion. The grafted bone material spans the vertebral elements to be fused, providing a scaffold for ingrowth and replacement by a connected bridge of living host bone. Autologous bone graft from the iliac crest continues to be the gold standard material for use in achieving a successful spinal arthrodesis [9]. Even with the use of autologous bone graft, spinal fusions fail to heal and pseudoarthrosis develops in 5–35% of patients [5]. Mechanical enhancement of spinal fusion with rigid internal fixation has improved fusion rates in general, but it has not completely eliminated the occurrence of nonunion. As a result, osteogenic enhancement of spinal fusion is becoming increasingly sought after.

Problems certainly exist with the use of autologous bone grafting. Procurement of autologous bone adds to overall operative time and blood loss, and disrupts an otherwise normal structure of the body. Donor site complications reported include wound infection, hematoma, pelvic

fracture, and cutaneous nerve neuromas [7, 38]. Significant complications with its use may occur in up to 10% of patients and minor complications may occur in as many as 25–30% of patients [4, 30]. Also, only a limited amount of autologous bone is available for grafting, and clinical scenarios exist where no autologous bone is available following multiple previous bone graft procedures. In addition, unpredictable bony incorporation and even resorption of autologous bone graft material is sometimes observed. These problems of donor site morbidity and pseudoarthrosis have fueled the search for a dependable bone graft substitute that possesses both osteoconductive and osteoinductive properties.

In addition to multiple local and systemic factors that influence bone formation, the selection of graft material will influence the outcome of a spinal fusion [9]. Graft materials placed into the spinal fusion bed participate in the fusion process in several ways, which depend on the properties of those materials. Osteogenic properties allow the grafts to directly produce bone, osteoinductive properties allow the grafts to stimulate osteoprogenitor mesenchymal cells to differentiate into bone producing cells, and osteoconductive properties allow the grafts to support bone growth and serve as a scaffold supporting neovascularization and ingrowth of osteoblasts and bone production. Bone graft substitutes that have a bone-like geometric construct, such as a porous hydroxyapatite ceramic, often have an osteoconductive property derived at least in part from its internal porous structure [3]. Porous ceramics in general are osteoconductive materials with the physical property of a graft material that allows the ingrowth of neovasculature and infiltration of osteogenic precursor cells during the bone growth process, known as creeping substitution. A graft material that is only osteoconductive transfers neither osteogenic cells nor inductive stimuli, but rather acts as a scaffold or trellis that supports the bone growth.

Ceramics

A number of osteoconductive ceramic bone graft substitutes have received attention as alternatives to autogenous bone. Calcium phosphate ($CaPO_4$) ceramics, which include hydroxyapatite (HA) and tricalcium phosphate (TCP), have been the most widely investigated and used in orthopedic surgery. Both are structured with pores that range from 100 to 200 μm in diameter. Their porosity enables mesenchymal cell migration, adhesion, proliferation and differentiation into osteoblasts within their pores. This unique structure constitutes their osteoconductive characteristics [3].

HA and TCP ceramics are both brittle materials with low fracture resistance. They can be varied in chemical and structural composition. Different preparative methods lead to either a compact or porous material with interconnective macropores that are the spatial and structural equivalent of cancellous bone. In a biologic system, more crystallization and higher material density result in greater mechanical strength and resistance to dissolution, and promote long-lasting stability. In contrast, an amorphous ultra-structure and greater porosity enhance interface activity and bone ingrowth, as well as early biodegradation of the material. Commercially available HA is resorbed very slowly, if at all, under normal physiologic conditions, whereas TCP generally is resorbed within 6 weeks after implantation. When used as a mixture, biodegradable HA/TCP graft material has the ability to dissolve, break down and allow new bone formation and remodeling required to attain optimal mechanical strength without interference. A fully non-resorbable graft material may hinder remodeling, prolong the strength deficiency of new bone and leave permanent stress risers in the fusion mass [4].

An alternative to synthetic calcium phosphate derivatives is natural coral, which has been used clinically to augment bone graft and in combination with platelet-derived growth factors. Composed of 97% calcium carbonate in the form of aragonite, coral is structurally similar to cancellous bone. It is extremely biocompatible and has yielded promising clinical results. The unique structural geometry of coral promotes rapid resorption and reossification without the risk of immunologic reaction or infectious disease transmission. An alternative formulation is coralline HA, which converts much of the calcium carbonate to HA [32].

Animal experimentation

The ability of calcium phosphate ceramics to act as bone graft substitutes for spinal fusion has been studied in many animal spinal fusion models with conflicting results [13, 21]. Part of the confusion may be due to the many different animal models utilized. The biology of healing of a spinal fusion differs depending on the anatomic structures surrounding the fusion region and the forces acting on the fusion bed. Also, the healing potential and amount of available bone surface area in the different anatomic fusion sites is variable. Interbody fusion models assess spinal fusion occurring within the disc space between two vertebral bodies. The structural grafts used in this type of fusion model are acted on by compressive mechanical loads and are within a bed of flat plates of vertebral endplate bone. Posterior and posterolateral fusion models assess spinal fusion of the adjacent posterior bony elements of the spine, including the lamina, facet joints, and transverse processes. Graft materials used in this location are generally not solid and structural, and heal under distraction or tension loads. The mass of morselized graft material is covered around the majority of its surface by muscle and other soft tissues, not bone. The concomitant use of spinal instrumentation with any fusion model affects

the mechanical loading of the graft bed, generally limiting the amounts of load seen by the graft material. Instrumentation can also affect the type of load applied, such as allowing a facet joint fusion to occur under compression rather than tension. Differences in species used may also play a role. Taken together, these factors make direct comparisons of different studies impossible to interpret properly.

Emery et al. compared fusion rates of different osteoconductive commercially available ceramic materials in a canine thoracic anterior interbody fusion model [11]. They compared fusion rates of autogenous tricortical iliac crest graft to HA corraline, HA ceramic, HA/TCP (60/40%) ceramic composite, and a calcium carbonate ceramic. All fusions were performed using anterior spinal instrumentation. They found superior fusion rates for the autogenous iliac bone group as compared to all of the ceramic groups, both in histologic evaluation and biomechanical testing. Toth et al. assessed the effect of porosity of the ceramic composite in a goat anterior cervical spine fusion model [34]. Autograft was compared to 30%, 50%, and 70% porosity implants of 50/50 HA/TCP. The more porous implants were hypothesized to trade off some overall strength for improved bone ingrowth and union rate. Biomechanical and histologic evaluation of the fusion mass was done at 3 and 6 months after surgery. All of the tested ceramic implants performed equal to or better than autograft iliac crest bone. The more porous implants had a higher union rate early on, but also had a higher incidence of graft fracture. Overall fusion rates were 67% for the ceramic implants and 50% for autograft. The relatively low fusion rates in all groups were likely due to excessive neck motion in the goat; however, these low fusion rates put into question the ability of this model to be validly extrapolated to human anterior cervical fusions.

Delecrin et al. showed the influence of the fusion site micro environment on incorporation of ceramic and new bone formation in a canine posterior lumbar fusion model [9]. They evaluated bone growth into a macroporous ceramic implant in both an interlaminar fusion site and a posterolateral intertransverse fusion site, using block HA/TCP (60/40%) composite as a graft. The percentage of newly formed fusion bone was significantly higher at the laminar fusion site compared to the intertransverse site, where decorticated bone in the fusion bed was scarce. These results demonstrate a clear deficiency of osteoinduction properties of the graft, and a consequent reliance on bone growth induction, with the decorticated bleeding bone in the fusion bed serving as a source of stem cells and osteogenic factors.

Bozic et al. evaluated the effect of added direct-current electrical stimulation on the fusion rate of an osteoconductive coralline HA ceramic/bone marrow composite bone graft substitute in a rabbit intertransverse process (posterolateral) lumbar spinal fusion model [6]. The HA/bone marrow aspirate composite alone or combined with 40 mA or 100 mA direct-current electrical stimulation were compared to autograft bone. Fusion success was equivalent in the lower-current group and autograft group (50% vs 57%), but was significantly higher in the high-current test group (87%), demonstrating a dose-dependent effect of the direct-current stimulation. The fusion masses in the high-current group were also significantly stronger and stiffer biomechanically and showed a significantly larger fusion mass histologically. The ceramic/marrow aspirate alone test group had significantly fewer successful fusions (25%) than the autograft or current stimulation groups.

Zdeblick et al. analyzed the efficacy of porous HA graft as a substitute for autogenous or allogenic bone graft following anterior cervical discectomy in a goat cervical spine fusion model [39]. Results of single-level ACDF were satisfactory regardless of the graft material used. In multilevel fusions, the fusion rates drop dramatically and complications such as postoperative kyphosis and neural compression increase. Plate stabilization of the HA material led to graft incorporation rates comparable to the autogenous bone group and superior to the allograft bone results. Mechanically, however, while the HA and allograft groups were comparable, they were significantly inferior to the autogenous graft group, leading to early collapse of the fusion mass. Histological assessment revealed incomplete creeping substitution and failure of graft substitution in all three groups. Interestingly, following graft collapse in vivo, fusion rates were similar to unfractured grafts, but with residual severe postoperative kyphosis rendering its use impractical.

The efficacy of interconnected porous HA granules in achieving posterolateral lumbar fusion in sheep was examined by Baramki et al., who evaluated lumbar spinal fusion radiologically and mechanically in a sheep spine fusion model [2]. Bisegmental posterolateral intertransverse lumbar fusion with instrumentation was performed using either no graft material, autologous bone, HA alone, or a HA/autograft composite graft in a 1:1 ratio. The autologous bone group achieved a 100% fusion rate, compared with 72% fusion for the bone/HA composite group, 50% fusion for the HA alone group, and only 15% fusion for the sham operation without any graft material. Spinal arthrodesis using HA alone or mixed with bone as graft material promoted segmental fusions, but not reliably.

HA/TCP use as composite or as carrier systems in animal models

Ceramic composites, which consist of the osteoconductive ceramic combined with an osteoinductive agent such as demineralized bone matrix (DBM), bone marrow, extracted bone matrix proteins, or osteogenic growth factors such as recombinant bone morphogenetic protein (BMP), have been investigated extensively [12, 16, 19]. Walsh et al. sought to determine the effectiveness of HA/TCP/col-

lagen composite composed of type I bovine dermal collagen, 65% HA, and 35% TCP ceramic as a bone graft substitute or expander for autologous bone graft in a posterolateral spine fusion model in sheep [36]. Dual-energy X-ray absorptiometry between the transverse processes revealed that the mineral densities formed by the collagen/HA/TCP composite was significantly higher than the autogenous bone graft group. Histologic analysis confirmed that the composite was highly compatible and was well incorporated into the fusion mass, and induced the formation of thick trabeculae and a mixture of lamellar and plexiform bone. The autogenous bone graft group had a smaller fusion complex, composed primarily of lamellar bone with thinner and fewer trabeculae. Both groups had similar mechanical properties. Another study, using a rabbit interbody fusion model, showed enhanced incorporation of porous HA blocks by the addition of DBM [27]. The animals implanted with the HA/DBM composite showed significant earlier fusion consolidation than the animals implanted with DBM alone, HA alone, or autograft. By 6 months, however, the results were comparable to those attained using autograft bone.

The efficacy of collagen/ceramic/autograft composite was also compared with that of autograft alone in a dog posterior spinal fusion model [40]. At 12 months, histologic quantification of bone ingrowth, as well as results from biomechanical testing, was similar in both groups. Muschler et al. compared posterior fusions in a dog segmental posterior spinal fusion model using autograft, collagen/ceramic composite, collagen/ceramic/autograft composite, and no graft material [22]. Autograft bone alone was the most effective graft material tested, and had a statistically superior union score. Results using the ceramic composites alone were no better than those without any graft materials. The addition of demineralized bone protein extract to the composite, however, significantly improved the union score, which was comparable to that obtained using composite plus autograft bone. Later, Muschler et al. evaluated the efficacy of collagen/ceramic (60% HA, 40% TCP) composite in inducing bone formation in comparison to autogenous iliac bone graft in a dog segmental posterior spinal fusion model. They found that such a composite was inferior to autogenous bone graft in inducing bone formation and fusion [23]. In addition, combining the collagen/ceramic composite with autogenous cancellous bone graft hindered bone formation, and reduced the rate of successful fusion. These results suggest that an autogenous cancellous bone graft carries both osteoconductive and osteoinductive potential, as compared to the lack of osteoinduction potential of the collagen/ceramic composite component of a mixed graft.

Growth factors are relatively short peptides that exert their mitogenic and differentiative effects on cells by binding to cell surface receptors and provoking a signal transduction cascade that results in cellular response. Takahashi et al. examined the efficacy of recombinant human bone morphogenetic protein-2 (rhBMP-2) in enhancing anterior cervical spine interbody fusion when added to a block HA graft in a goat cervical spine model with three-level anterior fusions [31]. Porous HA grafts that contained 0, 5, and 50 mg of rhBMP-2 were placed concurrently with anterior cervical spine fixation plates to achieve interbody fusion. The fusion rate, radiological findings, biomechanical stiffness, and histological appearance were evaluated at 1, 4 and 12 weeks postoperatively. At 12 weeks, manual testing showed a 100% fusion rate in the spines with HA grafts containing high-dose rhBMP-2; however, only a 50% fusion rate was shown in spines with grafts that contained no or low-dose rhBMP-2. On radiographic and histological studies, the biological process of fusion was seen to be more advanced with the larger concentration of rhBMP-2. Biomechanical testing demonstrated significantly higher stiffness values for grafts that contained high-dose rhBMP-2 than those without rhBMP-2 in flexion, extension, and lateral bending tests at 12 weeks. Histological analysis demonstrated that the rhBMP-2 increased the amount of bone apposition on the surface of the HA grafts and promoted bone formation in the porous structure without increasing the penetration distance.

Boden et al. used a non-human primate lumbar intertransverse process arthrodesis model to evaluate rhBMP-2 in a HA/TCP carrier as a complete bone graft substitute [4]. Twenty-one adult rhesus monkeys underwent a laminectomy and fusion with either autogenous iliac crest bone or 60/40 HA/TCP blocks saturated with a solution containing 0, 6, 9, or 12 mg of rhBMP-2. Fusion was not achieved in any of the monkeys treated with autogenous iliac crest bone graft. The monkeys treated with the HA/TCP blocks with rhBMP-2 achieved complete fusion. Histologic analysis showed some ingrowth of bone into the ends, but not through the ceramic block in the absence of rhBMP-2. When the ceramic blocks were loaded with rhBMP-2, there was a dose-dependent increase in the amount and quality of bone throughout the ceramic carrier based on qualitative assessment. The HA-TCP composite proved to be a suitable carrier for rhBMP-2 in this posterolateral spine fusion model in rhesus monkeys. Even in the presence of a laminectomy defect, there was no evidence of bone induction outside the confines of the ceramic carrier.

Osteogenin (BMP-3), an osteoinductive protein, was tested together with TCP acting as carrier by Breitbart and co-workers in a rabbit frontal bone model [7]. TCP alone was used as the control. At 1 month, there was minimal bone ingrowth and TCP resorption. At 3 months, both groups showed a modest amount of bone ingrowth. At 6 months, however, the osteogenin-treated group showed a significant increase in bone ingrowth and faster resorption of the TCP compared to the TCP treated group. They found that the addition of the bone inducer (osteogenin) to bone conductor (TCP) increased bone growth, and the

bone was found to have differentiated more fully into lamellar bone in the presence of the bone growth and differentiation-inducing factor, as compared to woven bone on the TCP-only treated group.

Boden et al. compared efficacy of fusion using coralline HA with bone marrow, autogenous bone graft, or osteoinductive bone protein extract for single-level posterolateral lumbar spine fusions in a New Zealand White rabbit fusion model [5]. The animals received a coralline HA implant, either alone or in combination with bone marrow, autogenous iliac crest bone, or 500 ng bovine-derived osteoinductive bone protein extract. Coralline HA alone or with bone marrow produced no solid fusions. When combined with an equal amount of autogenous iliac crest bone, fusion appeared in 50%. When combined with the osteoinductive growth factor extract, the coralline HA resulted in solid fusion in 100%. The fusion masses in the growth factor group were significantly stronger and stiffer. This data indicated that coralline HA with bone marrow was not an acceptable bone graft substitute for posterolateral spine fusion in this model. When combined with autogenous iliac crest bone graft, coralline HA served as a graft extender, yielding results comparable to those obtained with autograft alone. Coralline HA served as an excellent carrier for the bovine osteoinductive bone protein extract, yielding superior results to those obtained with autograft or bone marrow.

One of the important characteristics of a delivery system based on HA/TCP composites is the pore size and overall implant porosity. Works by Itokazu et al. and Radin et al. concentrated on the applicability of HA/TCA to serve as chemotherapeutic, antibiotic and growth factors delivery systems [15, 26]. Urist and co-workers were the first to study the BMP delivery capabilities of TCP, and found that bone and cartilage formation were enhanced 12 fold by combining BMPs and TCP as a carrier [35]. It is not well understood to date, however, whether HA/TCP acts as a slow-release delivery system by directly or indirectly potentiating BMP activity, by protecting BMP from breakdown and digestion, or by serving to distribute BMP in a favorable three-dimensional pattern.

Human clinical studies

The clinical efficacy of ceramics as a graft material for spinal fusion has not been clearly established in animal studies. Better results in general were found with the ceramic composites and ceramic-as-a-carrier system studies. Human clinical series using ceramic alone or as a composite represent one step further in elucidating the safety and efficacy of these materials as an alternative to autologous bone graft [18].

A number of clinical series have been published reporting the benefit of ceramics in spinal fusions for patients with scoliosis. In a study of 12 patients with severe scoliosis by Passuti et al., internal fixation and blocks of HA/TCP (3/2) alone or mixed with autogenous cancellous bone were used to stabilize the spine and fuse the facet joints [24]. Clinical and radiographic assessments of the fusions were performed, and in two cases biopsies of the graft material were obtained. At an average follow-up of 15 months, all patients exhibited complete radiographic fusions. Histologic examination of the biopsy specimens revealed the formation of new bone, which was directly bounded to the ceramic implant surface and inside the macropores. Another study, done with natural coral acting as autograft substitute in 49 patients with idiopathic scoliosis, has shown that natural coral can be used successfully as a graft substitute [25].

In applying their results of animal studies to clinical practice, Delecrin et al., in a prospective randomized study, assessed the clinical and radiologic performances of a synthetic ceramic as a bone graft substitute in scoliosis surgery [10]. Fifty-eight patients with idiopathic scoliosis underwent posterior correction and arthrodesis by posterior spinal fusion using autogenous iliac bone grafts alone or in combination with porous biphasic calcium phosphate ceramic blocks comprised of HA/TCP. The mean postoperative observation time was 48 months. Patients in the ceramic group had a lower average blood loss than those in the iliac graft group and significantly less pain. Radiography demonstrated that successful incorporation of the ceramic blocks occurred within 12 months. Ransford et al. evaluated the use of synthetic porous ceramic as a substitute for autogenous bone graft in posterior spinal fusion for scoliosis in 341 patients undergoing surgery [28]. The 170 patients treated with 60/40% HA/TCP alone had the clear benefit of no donor site pain and morbidity. Overall fusion site morbidity and complication rate were comparable, regardless of the bone graft material used. These results justify the use of calcium phosphate ceramics as bone graft additives for instrumented posterior spinal fusion in some cases, such as when only a limited amount of autogenous bone graft exists.

The most human clinical experience with ceramic materials in spinal fusion exists for anterior interbody fusion of the cervical spine. Thalgott et al., in a nonrandomized, retrospective study of patients requiring anterior cervical discectomy and fusion, evaluated the pattern of incorporation, presence or absence of disc space collapse, maintenance of correction, and clinical outcomes in order to determine the efficacy of coralline HA as a bone replacement in anterior interbody fusions of the cervical spine used in conjunction with rigid plate fixation [32]. The incorporation rate of the HA block into vertebral bone was 100%, and the complication rate due to the graft material was extremely low.

Kim et al. have developed implants made of porous HA, used in more than 90 patients to achieve cervical interbody fusion [17]. Results were reported in 70 patients,

whose surgical indications included cervical spondylosis, disc extrusion, ossification or hypertrophy of the posterior longitudinal ligament, and trauma. Flexion-extension radiographs and tomograms, obtained 6 and 12 months after surgery and every year thereafter, were obtained. Dislocation of the implant occurred in three patients. At 6–12 months after surgery, encasement of the implant and formation of union were observed in all patients. Normal lordosis, if present prior to surgery, was maintained post surgery. The authors found no neurological deterioration related to the site of fusion during the period of observation, and concluded that satisfactory interbody fusion can be achieved by using the HA implants. Similar good clinical results were reported by Hirabayashi and Kumano using HA ceramic spacers to maintain the laminar spread in open door cervical laminoplasty [14].

Other potential uses of HA ceramics in the spine

Injectable HA materials have been studied for use as "cements" to improve the strength of transpedicular vertebral screw fixation. Spivak and co-authors examined the improvement in posterior vertebral screw fixation strength in an unloaded in vivo canine model [29]. A crystalline-HA material was seen to significantly improve screw pull-out strength both initially and after 6 weeks in vivo in an over-drilled model, simulating a loose screw with poor initial fixation strength. Yerby et al. studied the use of an injectable ceramic in augmentation of revision pedicular instrumentation [37]. They examined the immediate effect of using an HA cement to augment revision pedicle screw insertion after failure of the primary pedicle screw fixation in human cadaveric spines by mechanical testing. The pull-out strength of the HA cement-augmented screws was 325% greater than control screws reinserted without HA augmentation. The major potential clinical advantages of an injectable HA "cement" for this application would be a more biocompatible alternative to the polymethylmethacrylate (PMMA) currently used, and the elimination of potential thermal injury due to the exothermic curing reaction of PMMA. These results suggest that HA cements may be a mechanically viable alternative to PMMA for augmenting the strength of primary and revision pedicular instrumentation, and should be considered for future experimental, animal, and clinical testing [33].

Injectable HA materials have also been studied experimentally for use in augmenting the strength of fractured vertebral bodies. Mermelstein et al. conducted a biomechanical study on the stabilization of human cadaveric thoracolumbar burst fractures in order to demonstrate that the addition of a calcium phosphate cement into the fractured vertebral body through a transpedicular approach is a feasible technique [20]. Transpedicular vertebral body reconstruction with HA cement reduced pedicle screw-bending moments by 59% in flexion and 38% in extension and mean initial stiffness in the flexion-extension plane was increased by 40%.

Cunin et al. used osteoporotic human cadaveric thoracic vertebral bodies and in situ vertebral bodies from living mature sheep as model systems to assess coral resorption and new bone formation after injection of coral granules [8]. The distribution of coral granules injected into human cadaveric thoracic vertebral bodies was homogeneous as assayed radiographically. In order to evaluate the use of natural coral as an osteoconductive material, cavities were drilled into vertebral bodies of ten mature ewes and were either left empty or filled with coral. Quantitative evaluation of coral resorption and new bone formation was made 2 months and 4 months after implantation. Osteogenesis was increased in cavities filled with coral in comparison with cavities left empty at both 2 months and 4 months. These results demonstrate the osteoconductivity of coral in granular form for vertebral filling. Interestingly, interconnectivity between adjacent bone trabeculae and newly formed bone was restored.

Bai et al. conducted a biomechanical study comparing two materials for augmentation of osteoporotic vertebral bodies and vertebral bodies after compression fracture in order to compare an injected, biodegradable calcium phosphate bone substitute with injected PMMA bone cement for strengthening osteoporotic vertebral bodies and improving the integrity of vertebral compression fractures in 40 fresh osteoporotic thoracolumbar vertebrae [1]. Osteoporotic vertebrae were injected either with calcium phosphate or PMMA and there was a non-injected control group. Each specimen was then loaded in anterior compression until failure. The second part of the study involved injection of calcium phosphate or PMMA into postfractured vertebrae. The fracture strength and stiffness in the calcium phosphate bone substitute group and those in the PMMA group were similar and significantly higher than those in the intact control group. Anterior vertebral height was increased significantly compared to initial postfracture vertebral body height, with no difference between calcium phosphate and PMMA injections. This study demonstrated that the injection of a biodegradable calcium phosphate bone substitute to strengthen osteoporotic vertebral bodies or improve vertebral compression fractures may provide an alternative to the use of PMMA.

Summary

HA ceramics seem to hold promise for use as an extender of autologous iliac crest bone grafting in spinal fusions. Used alone, they have not been proven to be as efficacious as autograft. In many animal models, the usage of HA/TCP resulted in less than desired fusion results. However, the reported results of spinal fusion using ceramic materials are conflicting both in animal and human clinical studies. These discrepancies are in part due to inherent differ-

ences in the healing process and healing potential of the various types of spinal fusions performed clinically and in animal experimentation. Data from a number of animal studies suggest a potential use for ceramic composites as a bone graft replacement or augmentation material for interbody spinal fusion surgery. The HA/TCP ceramic composite, either with or without added collagen, can serve as a scaffold onto which mesenchymal cells grow and differentiate into bone-producing osteoblasts, form creeping cones of bone in the scaffold, replace and finally degrade the scaffold, forming a solid fusion mass. Combining an osteoconductive ceramic material such as an HA composite with an osteoinductive agent such as rhBMP-2, OP-1, DBM, extracted bone matrix proteins, AGF, osteogenin, or others seems to be the most promising combination for achieving a reliably successful spinal fusion without the use of autogenous bone graft. The use of HA ceramics in augmentation of spinal fixation strength and in augmentation of vertebral body strength holds much promise for future clinical applications.

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