Nonporous Hydroxylapatite Granules as an Extracranial and Extranasal Augmenting Material in Dogs: Technique and Initial Findings

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The purpose of this study was to evaluate the use of nonporous hydroxylapatite (HA) granules as an extracranial and extranasal augmentation material in dogs. Clinical evaluation revealed that the HA granules became stable within 6 weeks and lost some of the augmented height. Histologic evaluation revealed no evidence of inflammation, bone resorption, or bone formation; also the granules were separated from other granules and the cranial surface by a layer of collagen fibers. This study concluded that nonporous HA granules are a practical extracranial and extranasal augmentation material, but its final augmentation contour is difficult to predict and control because of the consistency of the material. Either researchers need to develop a better method to stabilize HA granules in extracranial and extranasal applications or they need access to an HA block material that maintains better augmented contour.

Human craniofacial deformities may have numerous etiologies, but they can be readily divided into four basic subgroups: congenital, traumatic, neoplastic, and iatrogenic. Many syndromes such as Crouzon’s, Pfeiffer’s, and Apert’s are associated with craniofacial disorders. The public often interprets a substantial craniofacial defect as a sign of mental disturbance or retardation; consequently, many patients with such a problem may be inhibited from living a normal psychosocial life.

The major indications for cranioplasty are disfigurement and mechanical vulnerability. Treatment of large, complicated craniofacial deformities can usually be accomplished with craniofacial osteotomies, with or without an augmentation procedure. (Tessier, 1967, 1971). The treatment for an isolated forehead or facial bone deformity can be accomplished either with osteotomies alone or by an augmenting procedure. Osteotomies are extensive procedures, which may cause many complications, whereas an augmentation procedure with bone or alloplastic material is usually much safer.

Augmentation of the cranium and the forehead area with various autogenous grafting materials has been utilized in the past, using one of the following techniques: transposing a pedicle flap consisting of skin, periosteum, and the outer table of the skull (Konig, 1890; Muller, 1890); grafting autogenous tibial bone (Berndt, 1898; Delangeniere and Lewin, 1920); sliding an osteoperiosteal graft from the outer calvarial table (Von Hacker, 1903; Lexer, 1924); using bone chips derived from drill holes in the outer table of the skull (Keen, 1905; Shehadi, 1970); taking iliac crest corticocancellous grafts (Mauclaire, 1914; Mowlem, 1944; Carmody, 1946; and Kiehn and Grino 1953); making a split rib onlay graft (Levin, 1924; Longacre and De Stafano, 1957; Millard and Tates, 1964; and Korlof, 1973); grafting rib cartilage (Peer, 1955); and taking autogenous calvarial segments (Tessier, 1982). Banked or processed bone grafts have also been advocated in craniofacial reconstruction utilizing one of the following techniques: frozen, preserved cranial plate (Elliot and...
tutions (including the University of Minnesota) have also been conducted (Rothstein et al, 1984; Kent et al, 1983). HA granules improved the height and contour of patients' ridges and the granules were stable at 6 weeks postimplantation. There was subjective evidence that the material settled and some clinical evidence that the augmented contour was, to some extent, diminished.

Materials and Methods

Eight adult dogs ranging in weight from 20 to 25 kg were studied. The dogs were prepared for surgery utilizing sterile technique and general anesthesia. Each dog had its cranial and nasal areas shaved and prepped with Betadine scrub and solution. Subsequently, a 2.5-cm horizontal incision was made in the cranial scalp area (Fig. 1). Surgical dissection extended through the skin, subcutaneous tissue, and pericranial fascia to the cranial bone. Utilizing a periosteal elevator, the cranial and nasal bones were exposed. (Fig. 2). Alveograf * HA material (supplied in sterilized packages, each containing a syringe which has 0.75 g granules and is covered by a permeable cap) was mixed with normal saline (Figs. 3 and 4). The syringe was then placed into the created cranionasal pocket (Fig. 5). Twenty grams of material were then delivered to augment the nose and cranium. Following placement of HA granules, the area was closed with 000 chromic suture. Figure 6 shows a schematic drawing of the dog profile for the augmented nose and cranium. The animals were placed on 300,000 units of penicillin, injected 1 hour preoperatively and then daily for 5 days. The dogs were followed clinically and radio graphically. Four dogs were sacrificed at 3 weeks and four at 3 months postoperatively. The tissues were then placed in a formalin solution and processed for decalcified histologic preparation.

Results

Clinical evaluation revealed that all incision lines healed. There was early evidence of hemato ma formation in the extracranial, extranasal area. The hematoma was evacuated by aspiration. None of the implants were lost or exposed. The HA granules were mobile at 3 weeks, but were stable at 6 weeks postimplantation. There was subjective evidence that the material settled and some clinical evidence that the augmented contour was, to some extent, diminished.

*Alveograf: trademark for hydroxyapatite material. Manufactured by Sterling Winthrop Research Institute, Renseller, NY, and distributed by Cook-Waitte, Inc.
FIGURE 1 Schematic drawing showing the horizontal incision that was made in the cranial area.

FIGURE 2 Schematic drawing showing subpericranial dissection utilizing a periosteal elevator.

FIGURE 3 Photograph showing sterilized packages of Alveograf material, each containing a syringe filled with 0.75 g granules and covered by a permeable cap.
FIGURE 4  Photographs showing Alveograf material being mixed with normal saline. Upper left corner shows sterilized Alveolograf material and a normal saline bottle. Upper right, lower left, and right corners show the contents of the syringe being mixed with normal saline via the permeable cap.

FIGURE 5  Schematic drawing showing placement of the hydroxylapatite granules by syringe to augment the nasal bone.
Radiographic evaluation verified the extranasal (Fig. 7) and extracranial (Fig. 8) positions of the material in all cases. There was no radiographic evidence that the HA material resorbed or migrated. It was difficult to document radiographic changes in augmented height because of the lack of a standardized radiographic technique; furthermore, bone resorption under the HA material was difficult to assess because of the material’s radiopacity.

Histological evaluation revealed that in the 3-week study group the HA granules were separated by a fine layer of connective tissue (Fig. 9). HA granules in the 3-month group were separated by a more mature layer of collagen fibers (Fig. 10). There was no evidence of inflammation. The bone-HA interface was separated by a layer of collagen fibers, and there was no evidence that the HA material bonded to bone or to itself (Fig. 11). Also, there was no evidence of bone formation or resorption.

**Discussion**

Autogenous bone has been used to reconstruct various craniofacial deformities. Its disadvantages are: limited quantity to restore a large...
FIGURE 9 Photograph of a decalcified histologic section showing hydroxyapatite cranial augmentation in the 3-week group. (Notice the separation of the granular spaces by a thin layer of collagen fibers.)

FIGURE 10 A and B photographs of histologic sections showing hydroxyapatite granules (arrows) separated by layers of collagen fibers.
defect; limited moldability; increased patient morbidity due to a second surgical procedure; increased operative and possible hospitalization time; and unpredictable postoperative resorption. (Beumer and Tipold, 1972; Schultz, 1981). Autogenous bone resorption has been reported in up to 50 percent of those cases involving craniofacial reconstruction. (Gunther, 1967; Korflof et al, 1973; Bauer et al, 1974). Some authors advocate “overcorrection” when utilizing autogenous bone in craniofacial augmentation to overcome resorption problems (Bauer et al, 1974). Overcorrection is not generally accepted as precise enough, however; thus, sometimes a further operation is necessary to obtain an acceptable result (Machtens et al, 1979).

Reimplantation of autoclaved bone results in a high incidence of infection (Cooper et al, 1977). Reimplantation of cryogenically preserved cranial plate bone has yielded good results, but partial resorption of the transplant itself is observed when there has been excessive delay between craniotomy and reimplantation (Hardt and Steinhausen, 1979).

Synthetic materials are now commonplace as a deformity-correcting augmenting material. The ideal bone-replacement material should be chemically inert, noncarcinogenic, noninflammatory, nonallergenic, dimensionally stable, somewhat soft, and easily fabricated (Blocksma and Braley, 1965). It should also be easily shapable and contourable to fit individual needs, should not cause any underlying bone resorption, should be structured neither to dispose to infection nor evoke a healing response that would alter its characteristics during healing, should possess a low thermal conductivity, and should not distort during routine sterilization procedures. This ideal bone-replacement material has not yet been developed.

Metals are no longer used in craniofacial augmentation because of numerous complications that have developed, including: infection, corrosion, extreme heat- and cold-caused pain in the augmented area (due to metal’s high thermal conductivity), erosion through the pedicle flaps and into the orbit, and foreign body reaction to the implant (Burke, 1940; Kiehn and Grino, 1953). Other associated problems are that metals are heavier than nonmetallic alloplastic materials; they produce various artifacts on CT scanners; their electric conductivity precludes accurate interpretation of electroencephalograms; and they are radiopaque, which may prevent accurate interpretation of routine radiographic studies (Millard and Tates, 1964; Beumer et al, 1979).

Methylmethacrylate and silastic silicone implants are generally preferred as alloplastic implants in cranial reconstruction (Unger and Sollmann, 1964). Silastic silicone implants have been reportedly removed in 50 percent of cases because of infection (Steinhauser and Hardt, 1977; Foustanos et al, 1983). Although the silastic material is nonresorbable, it sometimes causes resorption in the underlying bone (Steinhauser and Hardt, 1977; Peled et al, 1986). Previously, the use of heat-cured acrylic made a two-stage procedure necessary in order to obtain a properly fitting plate in craniofacial reconstruction. Currently, the use of cold-cured methylmethacrylate has simplified the technique to one stage. A specific disadvantage of cold-cured methylmethacrylate is its exothermic reaction. In 1977, Asimacopoulous et al, reported an animal experiment in which polymerization of methylmethacrylate in direct contact with cranial defects raised the temperature of the epidural space from an initial level of 36°C to 64°C, despite constant, copious irrigation with chilled saline. The temperature remained elevated for

FIGURE 11 Photograph of histologic section showing the hydroxylapatite-bone interface. (Notice the separation of hydroxylapatite and bone by a thick layer of collagen fibers.)
The use of HA materials for alveolar ridge augmentation has proven successful in more than 100 cases performed over the past 5 years at the University of Minnesota. This material has been successfully used to augment the alveolar ridge and can withstand mastication forces for up to 7 years when a denture is placed over it. Our clinical observations revealed that most of the “settling” occurred initially and during the first 3 months following alveolar ridge augmentation. Once the material consolidated completely, minimal loss of augmented height was observed over a 7-year follow-up period. Also, radiographic evaluation of our cases showed no evidence that the HA material caused underlying bone resorption (Waite et al, 1984). This observation was supported by Kent et al (1983) who reported that, following alveolar ridge augmentation procedure with the HA granular material, 10 percent of the augmented height was lost. They also observed a 20 percent loss of augmented height when HA granules were combined with autogenous cancellous bone. Accordingly, it appears that utilization of HA granules as a synthetic, bone-substitute material in alveolar ridge augmentation more successfully maintains augmentation height than does autogenous bone alone, which resorbs up to 40 to 60 percent within the first year (Wang et al, 1976). Extracranial and extrafacial augmentation with HA granules does not subject the material to continuous pressure, as is the case in alveolar ridge augmentation. For this reason, less settling of the material can be expected once the material consolidates. The question of what happens to HA material if the augmented area is subject to impact needs further investigation.

Jarcho et al, (1977) implanted HA granules and plugs into femoral bony defects in beagle dogs and concluded that there was no evidence of inflammation or foreign body reaction. New bone formed around the HA material and adhered strongly to it, which might mean that chemical bonding occurred between the HA material and bone. The HA granules were surrounded by collagen fibers, but there was no evidence of bone formation between the HA granules or at the HA-bone interface. The absence of bone formation in our study can be attributed to the difference between implanting HA within a bony defect (as in the case of the Jarcho et al experiments) and implanting it subperiosteally as in our research. When a small bony defect is created in the bone, healing (blood clot formation and organization, and bone formation) usually occurs within the bony defect. If HA granules are implanted within the bony defect, healing occurs, and blood clots will organize around them. There is more potential for bone formation within the granules because the HA material is surrounded by bone on all but one surface (superiorly). However, when HA granules are implanted subperiosteally there is a greater chance that collagen fiber healing will occur rather than bone formation healing because the material contacts bone on only one surface (inferiorly). It is our opinion that when the HA granules are placed subperiosteally over the bone they act as a space-filler, and thus bone will not grow between the granules.

In 1984, Drobeck and associates, placed HA granules in soft tissue for 6 years. Their results showed that the HA particles were encapsulated with a thicker layer of collagen fibers. There was no evidence of bone formation, indicating that the material does not have osteoinductive capabilities. Also, several biopsies were performed on some of our patients who had a subperiosteal placement of HA granules, and the results showed no evidence of bone formation.

One of the major complications associated with HA granular material in mandibular ridge augmentation is displacement. We have experienced difficulty maintaining HA granules within the augmented area until the material consolidates. It usually takes 3 to 4 weeks to reach the stage of initial stability. For this reason, various methods have been developed to maintain the material within the augmented alveolar ridge (El Deeb, 1985). We expect a similar problem in using HA granular material for various facial or cranial augmentations. Procedures currently under development to ensure stability include mixing the granular material with either a resorbable plaster of Paris or various forms of collagen. Adding plaster of Paris and collagen to HA granules helps the material set faster. Subsequently this should decrease the incidence of material displacement and maintain the augmented contour. In 1986, Waite and Matukas, used a hydroxyapatite and collagen mixture as a zygomatic augmenting material. They found that the combined mixture overcomes the tendency for the particles to migrate if the periosteum is not intact or overdissection occurs. Also, various forms or devices to stabilize the material can be utilized.
to maintain it within the augmented craniofacial area. Currently, various porous and nonporous HA blocks are being marketed. They are utilized for various facial augmentations and may maintain augmented facial contour better than the granules.

A comparison of the properties of nonporous HA with the properties attributed to the ideal implant material reveals that HA fulfills most of the requirements of the ideal material. HA is readily available, noninflammatory, noncarcinogenic, nonallergenic, resistant to distortion from routine sterilization procedures (autoclave, gas, or radiation), nonresorbable, noncausal of underlying bone resorption, and adaptable to individual needs. HA also seems to possess some resistance to infection. In none of the cases studied at the University of Minnesota was the augmenting material removed because of infection. Similarly, no cases of infection associated with the use of the nonporous HA have been reported in the literature. Calcium phosphate’s high alkalinity might explain the low incidence of infection; a fact that is usually the opposite is true in an acidic medium. There are, however, at least two disadvantages associated with HA extracraniacal augmentation material. First, it is radiopaque, which might interfere with the interpretation of routine radiographic studies. Second, since the material lacks some of bone’s properties such as remodelling and growth, it is not suggested for use in young or growing children.

**CONCLUSIONS**

On the basis of the present study it is concluded that: (1) nonporous HA material is a practical extracraniacal and extranasal augmentation material; (2) the final contours of HA granules, if utilized alone, are difficult to predict and control; (3) researchers need to develop a method to stabilize augmenting extranasal and extracranial HA material; (4) researchers need to conduct a long-term follow-up study designed to determine tissue reaction, bone formation (if any), and residual stability; and (5) development of HA granular mixed forms or block materials might further improve the maintenance of tissue contour.

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