Bone Cements as Adjuvant Techniques for Ossicular Chain Reconstruction

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Hypothesis: The osseointegrative capacity of medical-grade bone cement can be used to improve fixation and prevent displacement of an ossicular prosthesis in a guinea pig model.

Background: Successful ossiculoplasty requires a firm connection between the vibrating tympanic membrane and the inner ear. In patients requiring revision ossiculoplasty, half of failures are due to prosthesis displacement. Bone cements have been used as prosthetic material in craniofacial surgery, and their adhesive and osseointegrative properties make them ideal for use in ossicular reconstruction.

Methods: Twenty-four adult male guinea pigs underwent a postauricular surgical approach for access to the middle ear. Hydroxyapatite and Dahllite cements were used in an alternating fashion to fix ossicular bone. Four animals were killed immediately to demonstrate mechanical bonding of the ossicles at the time of application. Nineteen animals were killed 8 weeks postoperatively to assess bonding capacity and histologic inflammation.

Results: Both cements mechanically bonded the ossicles at the time of application, but Dahllite cement set faster in the moist environment of the middle ear space. Histologic examination showed bonding of the ossicles with both cements, with little evidence of inflammation or foreign body reaction.

Conclusions: Hydroxyapatite and Dahllite bone cements showed evidence of osseointegration with ossicular bone in the guinea pig model. Further studies are under way to determine the osseointegrative capacity of Dahllite cement between the guinea pig malleus and a partial prosthesis, and any ototoxic effects with use in the middle ear. Key Words: Bone cement—Hydroxyapatite—Dahllite—Ossicular reconstruction.


Successful ossicular reconstruction requires a firm connection between the vibrating tympanic membrane and the inner ear. In patients requiring revision ossiculoplasty, half of failures are due to prosthesis displacement (1). Bone cements have been used as prosthetic material for several years in orthopedic and craniofacial surgery, and have recently received approval by the United States Food and Drug Administration for use in non–weight-bearing regions of the skull and temporal bone. Hydroxyapatite cement (HAC) (BoneSource, Stryker-Leibinger Corp., Kalamazoo, MI, U.S.A.) is a calcium phosphate preparation that sets in vivo to an implant composed of microporous hydroxyapatite. Similarly, Dahllite cement (DC) (Norian Craniofacial Repair System, Synthes Corp., Paoli, PA, U.S.A.) is a calcium phosphate preparation that sets in vivo to an implant with a mineral composition comparable to that of bone. Bone cements have been indicated for augmentation or restoration of bony contour in the craniofacial skeleton, including the fronto-orbital, malar, and mental areas. They are also indicated for use in the repair of neurosurgical burr holes, contiguous craniotomy cuts, and other cranial defects with a surface area of no larger than 25 cm² per defect. However, the suitability of HAC and DC as adjuvants to ossicular reconstruction has not been shown previously.

The specific aims of this study were to determine whether bone cements will mechanically bond to ossicular bone at the time of application and will maintain fixation of ossicular bone postoperatively. In addition, histologic studies will evaluate bone remodeling in the ossicle–bone cement interface and determine the degree of inflammation and foreign body reaction.

MATERIALS AND METHODS

This study was approved by the Institutional Animal Care and Use Review Committee at the Naval Medical Center, Portsmouth, Virginia. Normal male nonalbino guinea pigs, weighing approximately 500 to 800 g, were used in this study because they have been used successfully in models of human middle ear function. The only significant structural difference in the animal model relevant to this experiment included an ossicular chain with a compact, fused malleoincudal bone com-

Supported by unrestricted grants from Stryker-Leibinger Corporation and AO North America.

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plex instead of two distinct bones. The structures of the guinea pig middle ear and temporal bone, along with the surgical approach to the middle ear, have been well described in the literature (2–4). The preoperative and postoperative care of these animals was overseen by the staff veterinarian to ensure proper and humane treatment.

Twenty-five guinea pigs were used for this study and stratified into two groups. Four animals were included in the time zero group, and 21 animals were included in the survival group. The time zero group of animals underwent bilateral ossicular chain reconstruction with HAC or DC used in an alternating fashion to perfect the surgical technique and document binding of the ossicles with bone cement at the time of application. Animals in the time zero group were killed after completion of the procedure. The animals in the survival group underwent surgery on the right ear using standard aseptic technique. The animals were killed 6 to 9 weeks postoperatively, and the temporal bones were removed and submitted for histopathologic examination.

Each guinea pig was premedicated with intramuscular ketamine for sedation, and general anesthesia was conducted with inhalation isoflurane via a nose cone adapter. A superior approach as described by Asarch et al. (2) was used to expose the epitympanic bulla and the middle ear space. The epitympanic space was entered by incising the periosteum over the lateral wall of the temporal squama and removing the underlying bone, using a series of rotating cutting and diamond burrs under continuous irrigation. The malleo-incudal complex was separated from the stapes and removed by detaching it from the tympanic membrane. The complex was then divided at the score between the malleus and incus with a scalpel. The separated ossicles were reaproximated with bone cement, HAC and DC being used alternately in successive animals. A thin bed of bone cement was applied to the medial surface of the epitympanic bulla, and the reaproximated malleo-incudal complex was carefully placed on the bed of cement. The rationale for this technique was to increase the surface area of contact between the ossicle and bone cement and therefore to potentially increase the likelihood that any given histologic section would show the desired interface. The cement was allowed to harden, and Gelfoam was packed loosely around the malleo-incudal complex in its native position and the surrounding bone. Vi-}

RESULTS

Intraoperatively, both bone cements were easily molded and shaped when prepared according to package instructions with sodium phosphate. Both cements mechanically bonded the ossicles at the time of application, but DC set faster in the moist environment of the middle ear. DC began to harden within 6 to 8 minutes, whereas HAC began to harden in 15 to 20 minutes.

Two animals in the time zero group received HAC, and two received DC. A single animal from the HAC time zero group died at the end of the surgical procedure. The temporal bone was removed, and subsequent necropsy did not provide any explanation for the early death. Ten animals in the survival group received HAC, and 9 received DC. One animal stratified to the DC survival group was excluded from the study because it had multiple anatomic anomalies, including bilateral auricular deformities and cataracts. This animal could not be replaced before the conclusion of the study. All the animals in the survival group recovered from anesthesia without difficulty and resumed a normal diet within the first several days. All these animals survived until they were killed 6 to 9 weeks after surgery.

To develop the surgical technique and determine the best means of conducting an ossicle-to-ossicle reposition with bone cement, the surgical procedure varied between animals in the time zero group. Bone cement was placed at various locations between the malleo-incudal complex in its native position and the surrounding bone in each animal. Histologic examination of the specimens showed apposition of bone cement to the native bone.

The temporal bones of the survival group animals were inspected grossly at the time they were removed. All specimens had evidence of either partial or complete osteoneogenesis at the drilled surgical site, prohibiting inspection of the ossicles in the epitympanic bulla. Visual confirmation of fixation of the ossicles with the bone cements could, therefore, not be undertaken without potentially disturbing the connection.

Ossicles were identified in 18 of 19 (94.7%) histologic specimens. Histologic examination of these specimens showed bonding of the ossicular bone with both cements. Figure 1 demonstrates an ossicle-to-ossicle interface re-paired with HAC. All specimens demonstrated a significant amount of new bone growth around the ossicles where the bone cement was placed, and the degree of osteoneogenesis was similar among all specimens. This study did not attempt to grade the degree of osteoneogenesis present. There was evidence of osteoclastic bone resorption of the cement and replacement with new bone growth at the ossicle-bone cement interface. New bone growth was signaled by the presence of osteoblasts,
FIG. 1. Photomicrograph of undecalcified specimen demonstrating ossicle-to-ossicle interface repaired with hydroxyapatite cement, 7 weeks after application of cement. There is evidence of osteoclastic resorption of the cement and replacement with new bone formation (osteoblasts) at the interface (hematoxylin and eosin, ×200).

closely spaced lacunae, and disorganized cement lines when compared with native and mature bone.

There was little evidence of inflammation or foreign body reaction in the survival group specimens, with 19 of 20 (95%) survival specimens demonstrating no inflammatory change (Grade I) in the middle ear or epi tympanic region. Of the 19 Grade I specimens, a few inflammatory cells were noted in the external auditory canal in two specimens and within small blood vessels in one specimen. Only one temporal bone specimen demonstrated a moderate amount of inflammatory change and was graded III/IV. There was evidence of an acute inflammatory cell infiltrate composed of polymorphonuclear leukocytes predominantly, a few lymphocytes and plasma cells, and rare multinucleated giant cells. This presentation was consistent with an acute infectious process.

DISCUSSION

Three main categories of ossicular defects prevent the transmission of sound pressure across the middle ear: loss of ossicular continuity, fixation of the ossicles, and a combination of the two. The goal of functional ossicular reconstruction is to obtain permanent restoration of hearing while minimizing residual conductive loss and avoiding sensorineural hearing loss. Fundamental to successful ossicular reconstruction is the restoration of the connection between the cochlear fluids and the tympanic membrane. The ossicular prosthesis should connect the stapes or oval window with a broad, flat surface beneath the overlying drum. It should accommodate placement under some tension without extrusion, erosion of surrounding tissues (5), or loss of sound conduction advantage caused by displacement.

Successful tympanoplasty with ossicular reconstruc-
tion requires elimination of middle ear and mastoid disease, an intact tympanic membrane, a middle ear space that contains air and is lined with mucous membrane, and a secure connection between a mobile tympanic membrane and the inner ear (6). In one review of 945 cases of alloplastic middle ear prostheses inserted over a period of 4.5 years (1), the take rate was 94%. In patients requiring revision ossiculoplasty, 50% of the failures were due to prosthesis dislocation. Stabilizing the prosthesis on the stapes may also be a potential problem. Prosthesis extrusion, the cause of failure in approximately 5% to 7% of partial and total ossicular replacement prostheses (7), is usually the result of a mucous membrane or eustachian tube ventilation problem. Atelectasis around a partial ossicular replacement prosthesis invariably leads to extrusion or displacement within the middle ear (8). Even after precise placement of the prosthesis, and packing of the middle ear with absorbable material, the stability of the prosthesis cannot be ensured postoperatively. Several factors in the postoperative period may influence prosthesis position, including negative middle ear pressure and the tendency toward atelectasis, the biocompatible/integrative properties of the prosthesis to the undersurface of the tympanic membrane, recurrent or persistent middle ear disease and fibrosis, and the healing properties of the tympanic membrane itself.

Many natural and semisynthetic materials are available for reconstruction of the ossicular chain. Choices include autografts (from the same organism), homografts (from the same species), heterografts (from a different species), and alloplasts (synthetic biomaterial). The use of human tissue is potentially limited by accessibility, particularly in revision surgery; a limited storage life; and the potential for transmission of disease (9). Alloplastic middle ear implants are attractive for middle ear reconstruction for several reasons, including ready availability, sterility, ease of insertion, and suitability for bridging the ossicular gap when the incus or the stapes suprastructure is missing. The success or failure of any alloplast hinges on many factors, including its chemical composition, biostability, physical form, mechanical properties, and site of implantation (10).

Although any synthetic biomaterial may be considered for use in the middle ear, theoretically, the most successful and best-tolerated alloplastic implants would be composed of chemical materials that are naturally found in the body. The majority of the human skeleton is composed of calcium, whereas the soft tissues are primarily composed of carbon and water (10). Carbon-based polymers such as polymethylmethacrylate have been used extensively as primary adhesive cement for the fixation of orthopedic joint prostheses and in cranioplasty and craniofacial reconstruction. However, an exothermic polymerization phase, a tendency toward the development of a fibrous capsule around the implant, lack of tissue ingrowth, and a chronic inflammatory response (10) preclude its use in the middle ear. Third-generation cyanoacrylates have been approved by the United States Food and Drug Administration for topical use tissue ad-
hesives and have recently been used in ossicular reconstruction in an animal model (11,12). Further studies are required to assess the long-term toxicity and efficacy of this substance in ossicular chain reconstruction. Bone cements may well be the most promising substances recently in use for reconstructing the ossicular chain. A preliminary study demonstrated the effectiveness of Oto-Cem (Oto-Tech, Raleigh, NC) in reconstructing a fore-shortened incus, with substantial improvement in hearing in the overwhelming majority of patients (13).

Hydroxyapatite is the primary mineral component of teeth and bone (14) and constitutes 60% to 70% of the calcified skeleton (10). All forms of HA are biocompatible; HA does not cause a foreign body giant cell reaction, a sustained inflammatory reaction, toxic reactions, or an increase in serum calcium or phosphate levels (14). Hydroxyapatite cement (HAC) is a calcium phosphate preparation that can be shaped intraoperatively and sets in vivo to an implant composed of microporous hydroxyapatite (14). Hydroxyapatite cement is delivered as a powder and is mixed with sterile water to form a moist cement in vivo. Although HA is not osteogenic, it is osteoconductive in that it can serve as a scaffold on which bone can grow (14). Under in vitro conditions at 37 °C, pure HAC sets in approximately 15 minutes and the chemical reaction is completed within 4 hours, at which time the only reaction product is HA with no byproducts. As an alternative to mixing HAC with sterile water, sodium phosphate solution may be used to accelerate setting time. However, it is the authors’ experience that HAC begins to harden in 15 to 20 minutes when mixed with sodium phosphate solution according to package instructions. The primary conversion of HAC to HA, approximately 4 hours postoperatively, is unaffected by the use of sodium phosphate solution.

Dahllite cement is also a calcium phosphate preparation that can be shaped intraoperatively and sets in vivo to an implant with a mineral composition comparable to that of bone. The structural similarity to bone enables the body to remodel and replace the calcium phosphate implant with new bone growth. Dahllite cement is delivered as a sterile powder to the operating room and is mixed with prepackaged solution to form an injectable, moldable cement. Under in vitro conditions at 37 °C, DC begins to harden after 2 minutes and sets in approximately 10 minutes. It will maintain its shape and volume until it is replaced by host bone. Dahllite cement undergoes a process of cell-mediated resorption followed by new bone formation. The process of remodeling depends not only on the metabolic rate but also on the degree of loading forces applied to the implant, and the vascularity of the host site. The most distinguishing feature of DC is that it sets in a wet environment. A wet environment ensures that the solution will not evaporate and that DC can fully convert from its base constituents to carbonated apatite. The crystalline structures form within the first few minutes of the hardening phase, and form a latticework that can withstand fluids. By contrast, HA cements require a longer time for crystallization to occur, and the granules tend to break apart in a wet environment.

There are inherent difficulties in processing specimens with bone cement. In this study, the malleoincudal complex was sectioned, reapproximated with bone cement, and repositioned in the tympanic bulla to facilitate processing and histologic examination of the specimens. Standard decalcified processing techniques must be avoided to preserve the interface between the ossicle and calcium phosphate cement. In exchange for visualization of that interface, the precision of a thinly sliced specimen with multiple fine cuts is lost. The undecalcified methylvacrylate-embedded specimens must be sectioned with a tungsten carbide blade that, by convention, results in the loss of approximately 1.4 mm of tissue from each section during processing. This occurs because each histologic specimen measures 30 to 50 μm in width, and approximately 50 μm of tissue is lost on either side of the specimen.

This study demonstrates several important points. First, the bone cements mechanically bond the ossicle at the time of the procedure, and this fixation is maintained postoperatively at 6 to 9 weeks. Dahllite cement has several characteristics that favor its use in the middle ear, including its faster setting time and its ability to set in a moist environment without crumbling. Second, there is little evidence of an inflammatory cell response or foreign body reaction at the site of bone cement application, consistent with previous studies demonstrating the biocompatibility of hydroxyapatite (14). Last, there is evidence of replacement of the bone cement with new bone growth where the bone cement was applied. This is consistent with previous animal studies that describe the ingrowth and replacement of existing HAC by host bone (15). The cause of the exuberant bone growth in the surgical site is unclear. Additional studies in a larger animal model are necessary to more clearly define the etiopathology of the osteoneogenesis and its potential clinical implications.

There are limitations to this preliminary study, however. First, because of the overgrowth of bone at the surgical site in the survival animal group, visual confirmation of fixation could not be performed. The site was not opened because this could have resulted in disruption of a stable bond. The fixation had to be verified histologically. Second, the strength of the bond was not assessed. The long-term results of use of the bone cements in the middle ear are not known. Preliminary results suggest that controlled application of the cements is necessary to ensure that bone remodeling takes place in the desired location. Last, the potential toxicity with use of the bone cements in the middle ear has not yet been evaluated. Studies currently under way will analyze the osseointegrative capacity of bone cement between an ossicle and a HA prosthesis, and evaluate possible ototoxic effects with use of the cement in the middle ear, including the impact on auditory brainstem responses in the guinea pig.

In conclusion, medical-grade calcium phosphate ce-
ments have many desirable properties that may make them useful as adjuncts to ossicular chain reconstruction. Potential applications for this bone cement include not only anchoring a native ossicle or prosthesis, but also repairing a fractured ossicle or reconstructing a foreshortened ossicle. The ability to firmly bond ossicular bone and allow new bone growth at the site of application with little or no inflammatory reaction makes Dahl-lite cement an attractive candidate for continued study.

REFERENCES