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Evaluation of Bioactive Glass for Mastoid Obliteration: A Guinea Pig Model

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Abstract. *Background: Mastoid obliteration seeks to replace an open mastoid cavity with material that will become viable and free of infection and cholesteatoma. The purpose of this study was to evaluate the efficacy of bioactive glass ceramic particles for mastoid obliteration using a guinea pig animal model. Materials and Methods: Ten male guinea pigs (weighing 250-300 g) with normal eardrums and Preyer reflexes were used. Bulla obliteration using bioactive glass was performed on the left side in all guinea pigs. The implanted bioactive glass ceramic particles were examined clinically and radiologically by computed tomography (CT) and histologically. Results: Clinically, there were no signs of inflammation, infection or implant exposure in all guinea pigs. The CT scans showed hyperintense areas that represented new bone formation. Histological evidence of new bone formation was observed in the implant specimens that included: active osteoblasts, osteocytes, chondrocytes and osteoid tissue. There was a definite bond between the implant and the bone interface at the areas of new bone formation. No inflammatory or foreign body reactions, caused by the bioactive glass ceramic particle implantation, were observed in the surrounding tissue. Conclusion: Our results suggest that bioactive glass ceramic particles are an ideal implant material. Further studies on bioactive glass ceramic particles should include a larger animal trial to lay the groundwork for human studies.*

The primary goal in the surgical management of chronic otitis media with cholesteatoma is the creation of a dry, safe ear through removal of disease and alteration of anatomy to prevent recurrence. Canal wall up techniques (CWU) preserve the anatomy of the posterior canal wall, eliminating the need for periodic bowl cleaning and avoiding the risk of recurrent bowl infections. However, the recurrence rate may be as high as 67% in children after current CWU procedures (1). Canal wall-down (CWD) mastoidectomy is generally more successful in chronic active otitis media with cholesteatoma. This approach can reduce the recurrence rate to as low as 2% (2).

A major disadvantage of the CWD technique is the accumulation of debris in the exteriorized mastoid cavity, which requires periodic cleaning and on occasion avoidance of water contact to prevent bowl infections. Some of the cavity problems have been reduced by obliteration techniques (3-6). Mastoid obliteration seeks to replace the open mastoid cavity with material that becomes viable and free of infection and cholesteatoma. This leads to an epithelized lateral surface that isolates the mucosalized mesotympanic space while ablating the mucosalized and pneumatized mastoid space. The obliteration of mastoid cavities has been performed with cartilage (7), bone chips (3), bone pate (8), adipose tissue (9), hydroxyapatite granules (10), vascularized muscular or musculoperiosteal flaps (11), and temporoparietal fascial flaps (12).

Alloplastic implants are artificial materials that have been used for mastoid obliteration as well as skull base bony defects. The benefits of these materials are their availability, biocompatibility and absence of immunogenic properties. Bioactive glass was originally used as a synthetic bone graft material for filling osseous defects for periodontal, vertebral and orthopedic indications; it has recently been FDA approved for marketing as NovaBone-C/M for orbito-facial uses. Bioactive glass particles come in varying sizes ranging from 90 to 710 μm. Bioactive glass stimulates osteogenic stem cells to produce potent mitogenic growth factors, which are continually absorbed and released from the glass surface to enhance the proliferation of new bone along its interface (13, 14). Few studies have been conducted and report on mastoid obliteration using bioactive glass particles (15, 16). In a study conducted by Oonish *et al.* (16), new

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Key Words: Mastoid obliteration, bioactive glass, new bone formation.

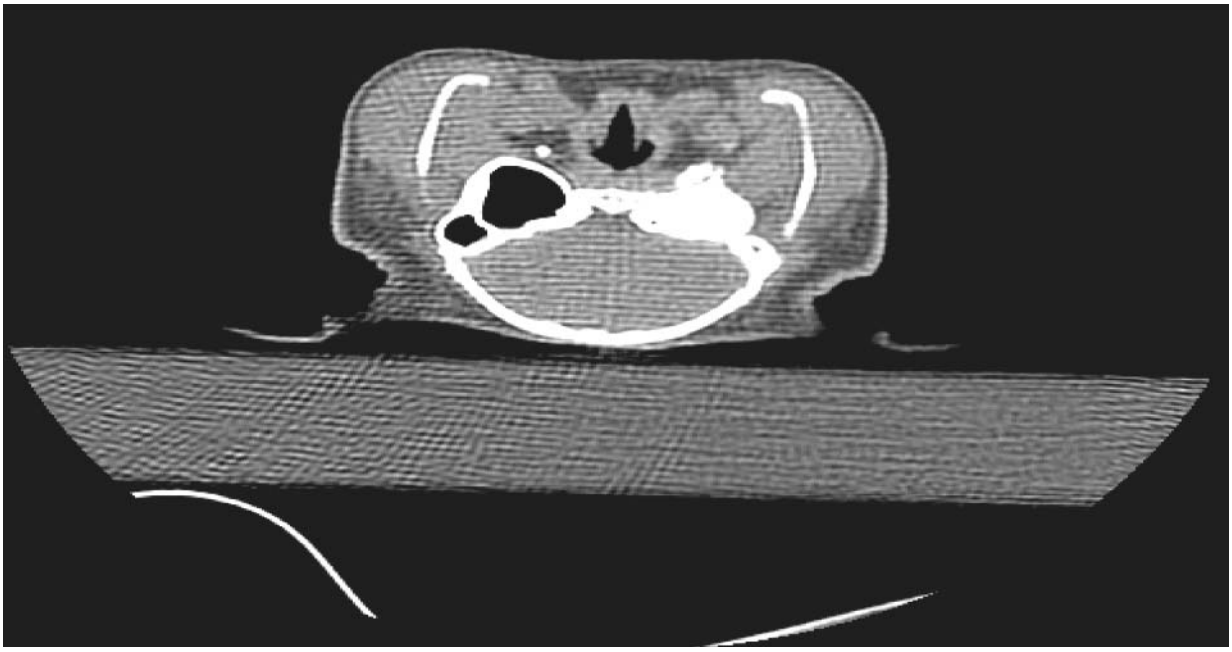

Figure 1. *The hyperintense occlusion of bulla with bioactive glass seen on axial CT scan at five months after obliteration.*

bone formation occurred much faster and more completely in bony defects filled with bioactive glass implants than in those filled with hydroxyapatite.

The purpose of this study was to evaluate the efficacy of bioactive glass ceramic particles in mastoid obliteration, using a guinea pig model.

Materials and Methods

Ten male guinea pigs (weighing 250-300 g) with normal eardrums and Preyer reflexes were used and housed separately in sterile cages. The guinea pigs were anesthetized with an intramuscular injection of ketamine and xylazine. Lidocaine 1% with 1/100,000 epinephrine was injected into the soft tissue over the tympanic bulla and a submandibular incision was made. The tympanic bulla was exposed and a hole drilled in the temporal bullae. After removing the mucoperiosteum of the bulla using a microelevator with alligator forceps, bulla obliteration using bioactive glass was performed on the left side in all guinea pigs. The bioactive glass ceramic particles used in this study were NovaBone-C/M (Porex Surgical, Inc., Newnan, CA., USA). The bioactive glass particle size was 120 μm. The soft tissues were closed over the bullae with absorbable sutures to hold the material in place.

The implanted bioactive glass ceramic particles were examined clinically and radiologically by computed tomography (CT) and histologically. The guinea pigs underwent axial CT scans of the bullae five months after implantation. The shape of the implanted material and presence of new bone formation were compared with the right side of each animal. After euthanasia, all guinea pigs were decapitated, and the bullae were removed immediately and fixed in formalin for two weeks. The specimens were then decalcified in ethylene-diamine-tetraacetic acid for four weeks, dehydrated in an ethanol series and embedded in paraffin. Sections of 5 μm thickness were taken through the center of the bulla parallel with the long axis of the bullae. Hematoxylin and eosin staining of the histological sections was performed.

Results

Clinically, there were no signs of inflammation, infection or implant exposure in any of the guinea pigs. The CT scans showed hyperintense areas that represented new bone formation (Figure 1). Histological evidence of new bone formation was observed in the implant specimens and included: active osteoblasts, osteocytes, chondrocytes and osteoid tissue. Islands of trabecular bone surrounded the bioactive glass ceramic particles and active osteoblastic activity was present on the surface of new bone (Figure 2). A fibrovascularization was noted in the implanted area. There was a definite bond between the implant and bone interface at the areas of new bone formation (Figure 3). No inflammatory or foreign body reactions were caused by the bioactive glass ceramic particle implantation in the surrounding tissue.

Discussion

Bioactive glass is composed of silicon dioxide, sodium oxide, calcium oxide and phosphorus pentoxide (13). The composition of these compounds including low silica content (45% by weight) is critical for the bioactive glass to bond to bone (16).

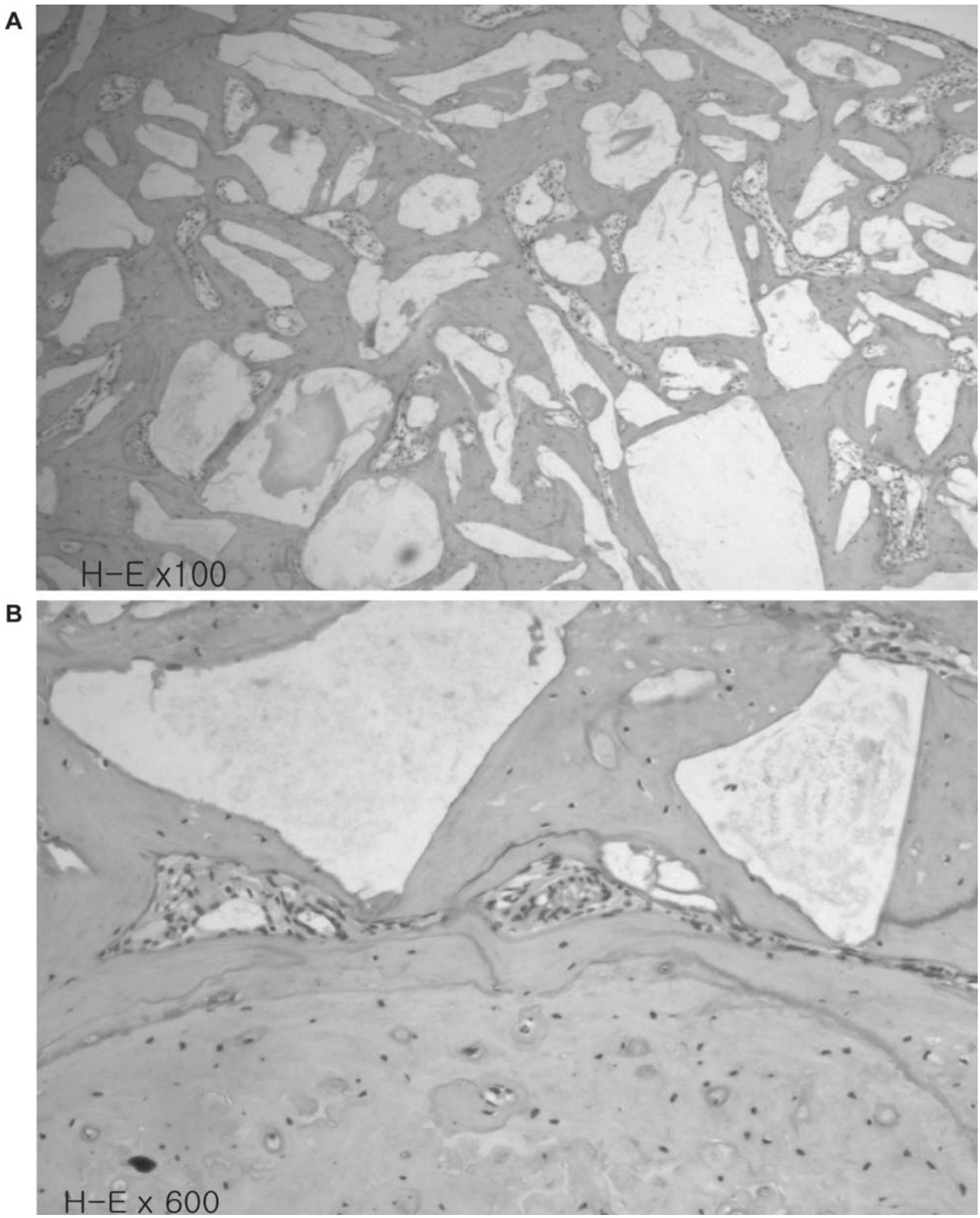

Figure 2. *Temporal bulla completely obliterated by bioactive glass ceramic particles (staining voids) and bone tissue (A) (hematoxylin and eosin, magnification x100). Islands of trabecular bone surrounded bioactive glass ceramic particles and active osteoblastic activity was present on the surface of new bone (B) hematoxylin and eosin, magnification x600).*

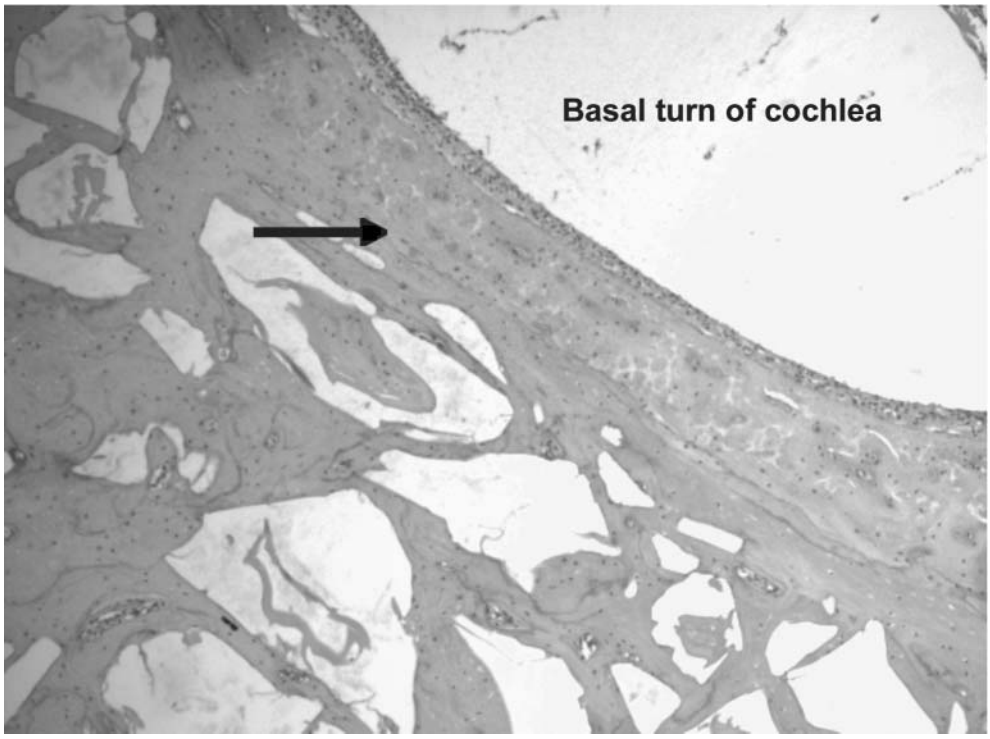

Figure 3. *Definite bony integration at the interface (arrow) between new bone and the native bone of the otic capsule (hematoxylin and eosin, magnification x500).*

Animal studies using bioactive glass have demonstrated trabecular bone formation as early as two to four weeks faster than bone formation using hydroxyapatite, tricalcium phosphate and other alloplastic materials (17). Within minutes of exposure to blood or saline, an ion exchange is initiated at the surface, releasing sodium and hydrogen ions (18). Hydroxy groups within the surrounding solution break the silicon-oxygen bonds within the glass particles, releasing silicic acid. The accumulating silicic acid condenses, forming a negatively charged gel at the surface of the glass that is rich in silica and calcium. This rapidly forming surface gel allows the particles to form a cohesive mass that is easily spread and packed in a bony defect. Within a few hours, calcium phosphate is produced within the silica-rich surface gel, forming a separate layer over its surface that then crystallizes in hydroxycarbonate-apatite (HCA) (19). The growing layer of HCA crystals mediates further osteogenesis through a controlled release of silicon from the glass surface that stimulates local osteoprogenitor cells to produce transforming growth-beta (TGF-β). The TGF-β stimulates differentiation and growth of osteoblastic stem cells, leading to a rapid proliferation of bone in contact with the glass particles (20). Particles are initially incorporated as part of the framework in the growing bone. The spaces between the condensed particles form a porous-like structure that enables fibrovascular and bony ingrowth. Osteoclasts eventually break down the particles, and all of the constituents of the Bioglass degrade over time, leading to the formation of trabecular bone (19). In this study, all guinea pigs were euthanized at five months. Excellent biocompatibility and bone adaptability were observed.

In conclusion, our results suggest that bioactive glass ceramic particles are an ideal implant material. Further studying with a larger animal trial is necessary to lay the groundwork for human studies.

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