

ORIGINAL RESEARCH

Hydroxyapatite Cement in Craniofacial Reconstruction

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OBJECTIVES: To evaluate the long-term efficacy of hydroxyapatite cement in craniofacial reconstruction, specifically examining the role (if any) of radiation, implant location, and cement type.

STUDY DESIGN: A retrospective chart review was conducted of all patients presenting to the senior surgeon (Y.D.) for craniofacial reconstruction from September 1997 to April 2004.

METHODS: Data were collected including type of cement used, size of defect, complications, need for removal of cement, reason for defect, and pathologic results of examination of removed cements.

RESULTS: One hundred two patients were identified who underwent craniofacial reconstruction with hydroxyapatite cements, 7 of whom required complete implant removal (6 Norian and 1 Mimix), and 4 (2 Norian and 2 Bone source) of whom required partial implant removal for foreign body reaction. Five of the removals were in patients who underwent postoperative radiation.

CONCLUSIONS: Hydroxyapatite cements are safe in craniofacial reconstruction. The highest risk of implant infection comes from reconstruction in the area of the frontal sinus, immediately beneath coronal incisions, and in patients who receive postoperative radiation treatment. Based on our results, there does appear to be a statistically significant difference in rates of infection and foreign body reaction between the different types of hydroxyapatite cement. We would not recommend implantation of this material in contact with the frontal sinus. Caution should be exercised when it is placed directly beneath an incision or in patients receiving postoperative radiation, particularly if a boost dose is given.

EBM RATING: C

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Deformity of the craniofacial skeleton may arise from various causes, including tumor resection, severe infection, trauma, or congenital deformity. Restoring appropriate contour and support in the cranio-orbital region following loss or removal of bone may be quite challenging. Since the late 1800's when Muller described using calvarial bone grafts for reconstruction, they have remained the gold standard.¹ Autologous bone grafting supplies an abundant amount of native tissue that has a high likelihood of osseous integration with little risk of rejection or infection long-term. However, autologous bone grafts may present difficulties in reconstruction including donor site morbidity, prolonged operating times, limited availability, and difficulty to contour.² Bone grafts may be relatively easily contoured and curved in the pediatric population. However, in adults, it is often difficult to achieve the precise three-dimensional contour normally found in the cranio-orbital region.³ Thus, there has been an ongoing search by reconstructive surgeons to find alternative means of reconstruction with alloplasts. In fact, alloplast reconstruction of the calvarium dates back to the year 2000 BC in ancient Peru when a gold plate was used to camouflage a trephination defect.⁴ Since that time, various alloplasts have been utilized in craniofacial reconstruction. The most commonly utilized material has been methylmethacrylate. It suffers from several drawbacks including lack of osseointegration, secondary infection, plate fracture, necrosis of surrounding tissues during setting as it forms during an exothermic reaction with temperatures reaching 110°C, and difficulty shaping once polymerization occurs.^{5,6} The risk of second-

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ary infection or extrusion may be seen years after initially successful implantation.

In 1986, Brown and Chow described a calcium phosphate cement that self-hardened and formed pure hydroxyapatite.⁷ Since its introduction, hydroxyapatite has been used for a variety of osseous reconstructions and appears to represent an improvement over other alloplasts currently available for craniofacial reconstruction. It is self-curing, is made of natural minerals, osseointegrates, and forms during an isothermic setting reaction.^{7,8} Various authors have suggested that hydroxyapatite cement appears to be safe when utilized for calvarial repair even with direct dural contact, frontal sinus obliteration, and other skull and skull base reconstructions.^{3,6,9-11}

Currently there are 3 commonly utilized hydroxyapatite cements available for use in the United States (Bone Source, Stryker Leibinger, Freiburg, Germany; Mimix, Biomet, Warsaw, IN; and Norian CRS, Synthes-Stratec, Oberdorf, Switzerland). Bone Source consists of tetracalcium phosphate and dicalcium phosphate dehydrate mixed with water in a powder-to-liquid ratio of 4:1. It is mixed and forms a paste, which begins to set in 10 to 15 minutes, with final setting taking 4 hours. It is minimally resorbable and must be kept dry to set. The final product of the chemical reaction is pure hydroxyapatite. The base of Norian is monocalcium phosphate, α -tricalcium phosphate, and calcium carbonate. It is completely resorbable and begins to set in 10 minutes with complete setting in 12 hours. The base products are mixed with sodium phosphate and in an isothermic reaction form dahllite. Dahllite is a carbonate form of apatite that is fully biocompatible and is remodeled through the same mechanisms as normal bone. Unlike Bone Source, Norian can set in the presence of fluid.¹² Mimix is composed of tetracalciumphosphate and α -tricalcium phosphate, which, when mixed with dilute citric acid, forms hydroxyapatite.

To date, no study has reviewed these 3 synthetic materials and compared their efficacy in facial reconstruction. In this article we will review our substantial experience with all 3 of these cements in craniofacial reconstruction.

MATERIALS AND METHODS

A retrospective chart review of patients undergoing craniofacial procedures between September 1997 and April 2004 who had craniofacial reconstruction with hydroxyapatite cements was performed by the senior author (Y.D.). The study included patients presenting at a large county hospital and to the surgeon's private practice. Data regarding type of implant used, patient age, reason for implant, location of implant, average implant size, amount of implant, radiation exposure, and postoperative complications were entered into a Microsoft Access database.

RESULTS

One hundred and two patients (31 females, 71 males) were identified who underwent craniofacial reconstruction using hydroxyapatite cements. Follow-up ranged from 6 months to 6.5 years (mean 3.5 years). Twenty-four of the reconstructions were related to trauma and 78 arose secondary to neoplasm. Overall, 37 patients had reconstruction with Bone Source, 41 with Norian, and 24 with Mimix. None of the Bone Source implants required removal, while 1 of the Mimix and 6 of the Norian implants required complete removal. Removals were related to delayed secondary exposure or secondary infection, which occurred an average of 7 months postoperatively. Of note, 2 of the Norian implants were removed for foreign body reactions while the remainder of the implants were removed for secondary infectious reasons. Partial implant removal for foreign body reaction occurred in a further 4 patients (Norian 2, Bone Source 2). Of the 11 implant removals, 6 were related to placement within the frontal sinus or in contact with the frontal sinus. The remaining 5 were from other parts of the craniofacial skeleton. Average defect size was 28 cm² and an average of 28 grams (range of 5-130 grams) of cement was used for each patient. Twenty-five patients underwent radiation therapy, 4 of these preoperatively. Five patients undergoing postoperative radiation required implant removal for postoperative infection. Only 9 of the patients in the study underwent secondary reconstruction with hydroxyapatite cement; the remainder were primary reconstructions. In addition, we specifically examined frontal sinus obliterations with hydroxyapatite cement. A total of 6 frontal sinuses were obliterated completely with only bone cement following nasofrontal duct plugging, and complete frontal sinus mucosa exenteration. In addition, a total of 8 frontal sinuses were obliterated at our institution by another service during this study period. In aggregate, 9 of the 14 obliterated frontal sinuses developed infection or implant exposure at an average of 25 months postoperatively.

DISCUSSION

Previous studies with hydroxyapatite cements have shown them to be safe for various craniofacial reconstructions.^{5,6,8-11,13} It is a calcium phosphate compound in a hexagonal structure which forms by an isothermic reaction. In one animal study, it was shown to be 90% resorbed and replaced by new bone 40 weeks postoperatively.⁸ No previous reports have been made comparing the currently available hydroxyapatite cements and looking at postoperative complications in a variety of applications in craniofacial reconstructions.

In our study, a total of 89.2% of implants went on to heal with excellent aesthetic and functional outcome without exposure, implant infection, or need for removal. If the frontal sinus infections are not taken into consideration, the overall infection/extrusion rate drops to 4.9%. All of these

remaining infections occurred in the subset of patients who underwent implant placement immediately beneath a temporal or bicoronal incision. We have thus modified our incisions to avoid placing them directly over areas of planned hydroxyapatite placement whenever possible. Since doing so, we have encountered no further evidence of infection in these areas (14 months).

Despite early reports of the utility of hydroxyapatite cement in frontal sinus obliteration, in our institution's experience, this approach has been utilized with an unacceptably high rate of implant exposure/infection necessitating major secondary reconstructive surgery with autografts in each case.^{6,13} Our infection/foreign body reaction rate of 64.2% has led us to abandon this method of frontal sinus obliteration in favor of other means of reconstruction, including fat graft and pedicled pericranial flaps.¹⁴

Radiation therapy, whether given preoperatively or postoperatively, does not appear to be associated with a significant increase in rates of infection and is in keeping with the overall rate of infection/foreign body reaction encountered (12%). Interestingly, the skin overlying the implant material seems to thin dramatically in some patients and leads to delayed exposure of the implant, especially if a boost dose of radiation is given focally to the area. This has led to delayed exposure (as late as 3 years following initial good healing), necessitating implant removal in 2 cases. It is unknown whether this is related to the implant material itself or the ability of surgically altered scalp skin (bicoronal flap with harvested pericranial flap) to tolerate the doses of radiation administered (70 Gy).

In our series, Bone Source did not become infected and did not have to be completely removed. When compared to Norian, this was statistically significant ($P = 0.004$) and when compared to Mimix approached the 95% confidence interval with $P = 0.056$. The significance of this finding is not known but may be related to the difference in biochemical structure.

A total of 14 patients underwent biopsy of the implant material during their follow-up period. These biopsies were performed during secondary reconstructive procedures or for recurrent neoplasms. All biopsy specimens (Bone Source 7, Norian 5, and Mimix 2) showed evidence of osseous in-growth into the hydroxyapatite cement matrix. None of the implants had been completely replaced by bone in any of the samples examined by pathology, with the longest follow-up being 6 years following initial placement. This has been suggested by previous reports.¹⁵ This would suggest that when this material is utilized in clinically relevant amounts, one may expect osseous in-growth into the periphery of the implant without significant in-growth centrally. This in-

growth should, in theory, make the implant more stable and less prone to infection long-term.

CONCLUSIONS

Hydroxyapatite cements are an excellent choice for craniofacial reconstruction. In our study, frontal sinus reconstruction, placement of implant directly beneath a bicoronal incision, and postoperative radiation treatment were associated with increased risk of infection and implant removal. Preoperative radiation exposure and timing of reconstruction did not play a role in postoperative complications. In addition, osseous in-growth into the hydroxyapatite cement can be expected, though long-term results do not show complete osseous replacement.

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