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Original Article

Polymethylmethacrylate imbedded with antibiotics cranioplasty: An infection solution for moderate and large defects reconstruction?

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Abstract

Background: In cases where autologous bone graft reconstruction is not possible (such as comminuted fractures, bone graft reabsorption, or infection) and the use of synthetic material is required, polymethylmethacrylate (PMMA) use is a safe and efficient solution. Studies comparing the incidence of postoperative complications between autologous and synthetic cranioplasty are heterogeneous, not allowing a conclusion of which is the best material for skull defects reconstruction. Current medical literature lacks prospective well-delineated studies with long-term follow-up that analyze the impact of antibiotic use in PMMA cranial reconstruction of moderate and large defects.

Methods: A prospective series of patients, who underwent cranioplasty reconstruction with PMMA impregnated with antibiotic, were followed for 2 years. Authors collected data regarding demographic status, clinical conditions, surgical information, and its complications.

Results: A total of 58 patients completed full follow-up with a mean group age of 40 years and a male predominance (77%). Major complications that required surgical management were identified in 5 patients, and 10 patients evolved with minor complications. Postoperative surgical site infection incidence was 3.2%.

Conclusion: The infection rate in patients submitted to PMMA flap cranioplasty impregnated with antibiotic is significantly inferior comparing to the data described

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http://surgicalneurologyint.com/Polymethylmethacrylate-imbedded-with-antibiotics-cranioplasty:-An-infection-solution-for-moderate-and-large-defects-reconstruction/

in medical literature. A lower infection incidence impacts secondary endpoints such as minimizing surgical morbidity, mortality, hospitalization period, and, consequently, costs.

Key Words: Cranioplast, infection, methylmethacrylate, neurosurgical procedures, postoperative complications, skull fractures

INTRODUCTION

Decompressive craniectomy is a surgery commonly performed in patients suffering from severe head injury or massive brain hemorraghe, representing, in most cases, the chance for patient survival.[11] Survivors from the primary trauma event may recover with neurological conditions, becoming candidates for cranial reconstruction, once an individual with craniectomy has higher risks for seizures and headaches and the brain is not protected by a rigid structure, making it a vulnerable tissue even to minor trauma. Therefore, a second surgery is required to correct the cranial bone defect, a technique known as cranioplasty.

Elective cranial reconstruction has a higher infection rate when compared to other elective neurosurgical procedures independent of the material used for cranioplasty. Autologous bone cranioplasty has a lower incidence of postoperative infection when compared to synthetic prothesis, whose infection incidence may be as high as 20%.[1,2,7,9,14-16,23] Even though surgeons apply all the procedures that significantly reduce postoperative infection, risks are applied (such as antiseptic preparation, use of sterilized matherials, adequate hand cleaning, and the use of antibiotic profylaxis during anesthesia induction), and the incidence of infection does not decrease from a certain percentage. No study has evaluated the impact over the infection incidence of antibiotic used in polymethylmethacrylate (PMMA) prothesis after cranioplasty.

MATERIALS AND METHODS

Authors conducted an interventional, clinical, longitudinal, prospective, and noncontrolled study with allocation of 58 patients with cranial failure of multiple causes between March 2012 and May 2015. Patients were selected continuously by spontaneous ambulatory demand in a tertiary hospital of high complexity, specialized in head and spinal trauma in southern Brazil, where the historic rate of infection in skull prostheses reaches 20%. Data regarding patient's clinical and neurological conditions, defect topography, comorbidities, reconstruction size, previous and current imaging examinations, and detailed clinical history of previous hospitalization, including the reason for craniectomy, were collected.

All patients were submitted to the standard cranioplasty surgery with PMMA model. Furthermore, infection prophylaxis was performed with intravenous 2 g Cefazolin injected during anesthesia induction. We used PMMA impregnated with erythromycin 0.5 g and colistin 3.00 million IU. All patients remained for 24–48 hours with an epidural drain. The defect size was calculated on a GE workstation with Advantage Workstation software 4.4, and were classified as small (<75 cm^2), moderate (75–125 cm^2), or large (>125 cm^2), according to previous studies.[12]

The study was approved by the hospital committee of ethics in research, and a completed consent form was collected from all participating patients and/or their parents.

RESULTS

A total of 58 patients were included in the study, with a higher proportion of males (75.58%) and a global mean age of 40 ± 14 years. Brain injury secondary to head trauma was the main indication for craniectomy, especially traffic accidents (car and motorcycle accidents represented 24% of our population) followed by falls (13.79%) [Table 1].

Data regarding medical condition before cranioplasty is shown in Table 2. The incidence of seizure was 29%; ventricular peritoneal shunt was performed during the primary hospital stay in 5 patients once they presented symptoms of hydrocephalus.

Table 1: Descriptive statistics

Feature	N	%	Mean	SD	Variation
Gender					
Female	14	24,14%			
Male	44	75,86%			
Age			40	14	14-76
Female			42	12	14-57
Male			40	14	17-76
Craniectomy Etiology					
Motorcycle Accident	9	15,52%			
Falls	8	13,79%			
FRI	7	12,07%			
Crush	6	10,34%			
TBI	6	10,34%			
Car Accident	5	8,62%			
Tumor	2	3,45%			
Others	15	25,86%			

FRI: Firearm-relatedinjury

Most cranioplasties were right hemicraniectomy reconstruction (48.28%), followed by left and frontal reconstruction. Only 5 patients had bone failure size smaller than 75 cm^2, and 91% harbored a moderate or large cranial bone defect [Table 3].

Cranioplasty complications are described in Table 4. The incidence of infection was 3.2% (only 2 cases); 1 patient submitted to bifrontal reconstruction and another to hemicranial reconstruction. Three other cases also evolved with major complications, 2 with extradural haematoma and 1 with skin necrosis, totalling 5 cases of major surgical complications.

Analyzing the 2 patients who had epidural hematoma, authors identified that 1 case occurred in late after thesurgery (40 days postoperative) secondary to a *de novo* traumatic brain injury. The second patient was due to inadvertently anticoagulant reintroduction in the immediate postoperative period.

Table 2: Clinical characteristics previous to cranioplasty

Medical comorbities	N	%
Seizure	18	(31,%)
Hydrocephalus	9	(15,5%)
Ventricular shunt	5	(8,6%)

Table 3: Cranioplasty characteristics of the 58 procedures performed

	N	%
Defect side		
Bifrontal	1	1,72%
Right	28	48,28%
Left	22	37,93%
Frontal	6	10,34%
Vertex	1	1,72%
Cranial bone defect size (cm)		
<75	5	8,62%
75-125	15	25,86%
>125	38	65,52%
Reconstruction type		
PMMA	58	100,00%

Table 4: Post-Cranioplasty Complications

Post CP Complications	n	%
Extradural hematoma	2	(3,4%)
Wound dehiscence	2	(3,4%)
Infection	2	(3,4%)
Phlebitis	1	(1,7%)
Skin necrosis	1	(1,7%)
Post CP seizure	7	(12%)

Two patients were operated because of infected epidural collection. One patient was previously submitted to a bifrontal reconstruction with exposition of the frontal sinus, and developed a *Staphlycoccus aureus* infection (bacteria identified in the epidural liquid culture). It is noteworthy to mention that the patient constantly explored the wound with the nails. In this case, drainage of the collection was performed without removal of the PMMA. The other patient had a ventricular peritoneal deviation (VPD) previous to cranioplasty, and developed epidural collection postoperative. In order to accelerate collection absortion, authors changed shunt valve to a high pressure system. After the exchange, the patient suffered a minor traumatic brain injury with increase in epidural collection. At this moment, authors decided to close the shunting, howevern hydrocephalus and subcutaneous collection increased, developing surgical site infection. The patient required reoperation to drain the collection, staying with high-pressure shunt, which resolved the infection and hydrocephalus.

Central scalp necrosis was a complication presented by one patient with previously damaged skin secondary to trauma mechanism. Skin necrosis with exposed CP plate required a plastic surgery to rebuild surgical site with skin flap rotation, without removing PMMA prosthesis. Out of the 5 patients reapproached, only 1 had the CP plate removed.

Ten patients had minor complications (16.1%); 2 cases of surgical wound dehiscence, 1e case of phlebitis in the right upper limb, and 7 patients (11%) had seizures.

Even though the authors did not consider a postoperative complication, the presence of epidural collection underneath PMMA plaque in the immediate postoperative cranial CT scan was found in 56.4% of patients. Spontaneous absorption occurred in most cases during follow up, and only 9 patients still had epidural collection in the 12 month postoperative CT scan [Figure 1]. All cases of epidural collection were treated conservatively once they were asymptomatic [Figure 2].

DISCUSSION

The elevated incidence of infection after cranioplasty is a subject that instigates neurosurgeons, especially because it is an elective, controlled, aseptic procedure. Therefore, incidence of up to 20% described in medical literature should not be common.[1,2,7,9,14-18,23] Moreover, once a cranioplasty flap is infected, usually flap removal is needed, which implicates a new surgery with bleeding and anesthetic risks, antibiotic treatment for at least 4 weeks, extending aesthetical disfiguring period and

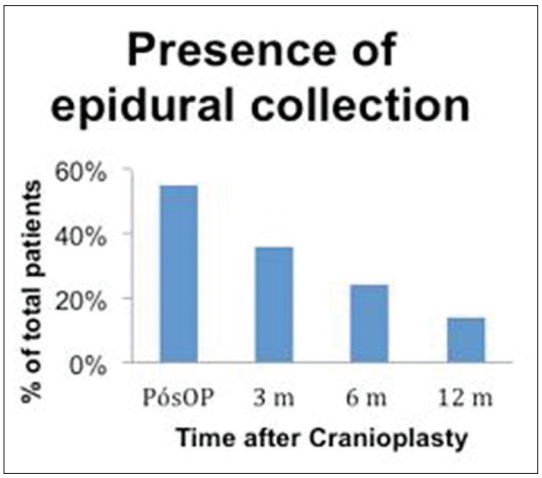

Figure 1: Evolution of epidural collection postoperative to 12 months of follow-up

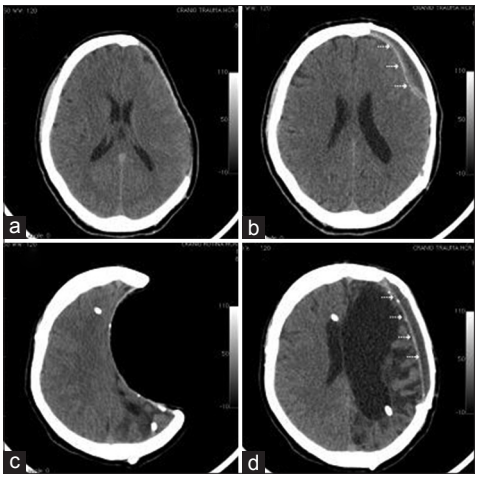

Figure 2: Aspect of the skull before cranioplasty (a, c) and after the surgical procedure (b, d). Presence of collections (arrows) after cranioplasty. Brain re-expansion may also be seen with visualization of the cortical sulci at the injured side, undetected in preoperative image

still requiring a new surgery to correct cranial defect and resulting in patient's morbidity and hospital treatment costs increment.

In the scenario described here, it is important to find out new techniques to optimize the procedures previously described to diminish the number of postcranioplasty infection rate. The use of prostheses with antibiotics is an established procedure in many orthopedic surgeries. Authors chose the antibiotics erythromycin and colistin based on the bacterial spectrum of coverage offered by these antibiotics in association (erythromycin has a coverage for Gram-positive organisms such as *Staphylococcus spp* and *Streptococcus spp*, whereas colistin has a Gram-negative coverage over *Escherichia coli*, *Enterobacter, Klebsiela Pseudomonas)*.

Analyzing possible risk factors to explain the higher incidence of infection after cranioplasty, the items usually associated with higher risks are timing of surgery (early versus late), cranial defect location, surgical site conditions (skin and subcutaneous state), and the presence of other catheters (VPD).

There is no consensus in medical literature to define early cranioplasty, however, most articles describe that cranial bone reconstruction performed up to 3 months of craniectomy as early surgeries. Late cranioplasty has lower incidence of infection when compared to early procedures. A possible explanation for this finding is a bacterial overgrowth after the first surgical procedure when the aseptic conditions may reduce the proportion of bacteria from the skin microbiota which increases the proportion of pathogenic germs, increasing the risks of infection in a second skin incision.[21]

Skull location of cranioplasty influences the infection risks, as described by Gooch *et al.*[8] who found a 67% complication incidence among bifrontal cranioplasty compared with 27% incidence of total complications of hemicranioplasty. A multicenter English study conducted by Coulter *et al.*[5] found a statistically significant difference of infection when comparing bicoronal (36% of infection rate) with cranioplasty in other skull sites (infection incidence 16.4%). An explanation for higher risks of infection among patients submitted to bifrontal cranioplasty is the comunication to the facial sinus, which predisposes surgical site to contamination even after surgery once there is comunication between the cranial flap to the environment.[13]

Seven patients (11%) in this series were victims of frontal defect, 2 with large bifrontal skull defect. During surgery, frontal sinus was exposed in 5 of the patients (8% of total), however, none of them developed postoperative infection. One patient with large bifrontal defect, without sinus communication, developed post-surgical infection, which corroborates the high incidence of infection among these patients.

Hostile surgical local for cranioplasty is described as tissues previously submitted to radiation therapy, with active infection or cerebrospinal fluid leaks, the presence of skin lesions or scars secondary to the head trauma. Eight patients (13%) who presented at least one of the conditions described above were submitted to cranioplasty in our study; 3 patients had previous head radiation therapy, 2 had previous osteomyelitis, 2 had subdural empyema, and 1 patient had failure of previous cranioplasty. None of these 8 patients developed any kind of postoperative complications.

The presence of ventricular peritoneal shunt is believed to be a risk factor for postoperative infection in the shunting system as well as in the cranioplasty, either by direct surgical contamination or hematogenous bacteria spread.[19] Among our patients, 5 patients had PVD previous to cranioplasty. The shunt system was closed in 3 patients, who evolved without symptoms with no

need of reopening. This result is consistent with those described by Tsang *et al.*,[22] where 5 patients with VPD who were removed during cranioplasty evolved without hydrocephalus symptoms during follow up.

The most common complication in our population was the presence of liquid collection underneath PMMA plaque. This finding occurred in 35 (56.4%) patients, even though all cases had aspiration drain located in the epidural space during a mean duration of 36 hours and the dura mater was anchored in the PMMA plaque. According to medical literature, epidural liquid formation may be a normal body reaction to the presence of a synthetic material in contact to the dura mater and subcutaneous tissues. Therefore, many authors do not classify this finding as a surgical complication because the liquid is not infected and do not cause any symptoms.

A retrospective study conducted by Chang *et al.*,[3] who did not describe the size of cranial defect reconstruction, detected a 8.6% incidence of postoperative epidural collection in patients without drain, and 2.4% incidence among patients with epidural drain. A prospective study performed by Kim *et al.*[12] described an incidence of 40% of post-cranioplasty epidural collection, with spontaneous absorption in 62.5%, however, surgical intervention was required in 35.4% of cases. The two main risks factors for epidural fluid collection are the size of cranial bone defect (consequently the cranioplasty size) and the presence of air underneath PMMA flap. In our study, the incidence of fluid collection was higher when compared to other articles. Authors believe that the higher incidence described in our series are due to the study method, which was a prospective study, and because a CT scan was performed in the first 24 hours after surgery, data that is missed in retrospective studies.

The association of epidural collection with the size of cranial defect reconstruction had already been described.[18] Analyzing our patients, the incidence of postoperative epidural collection was 53% in moderate size defects, and 64% in large cranial defects ($P \leq 0.018$) [Figure 3]. All cases had a benign resolution, most evolving with spontaneous drainage and no patient required surgical reoperation. However, in the 12 months follow-up 14.5% of patients with epidural fluid collection still had the fluid, asymptomatically. Authors found a higher incidence of fluid collection in patients with inadvertent dural perfuration during cranioplasty (89%), although the resolution of epidural fluid followed the same patterns shown by patients with collection without durotomy.

A total of 15 patients in our series developed some type of post-surgical complication, 5 cases had major and 10 minor complications. Among the 5 patients with major complications requiring surgical reintervention, only 1 case had the cranioplasty plaque removed. The patient who evolved with skin necrosis and PMMA plaque exposition was submitted to a plastic skin rotation with satisfactory result, with no need of prostheses removal. Among 10 patients with minor complications 7 had seizures, 2 had surgical wound dehiscence, and 1 had phlebitis.

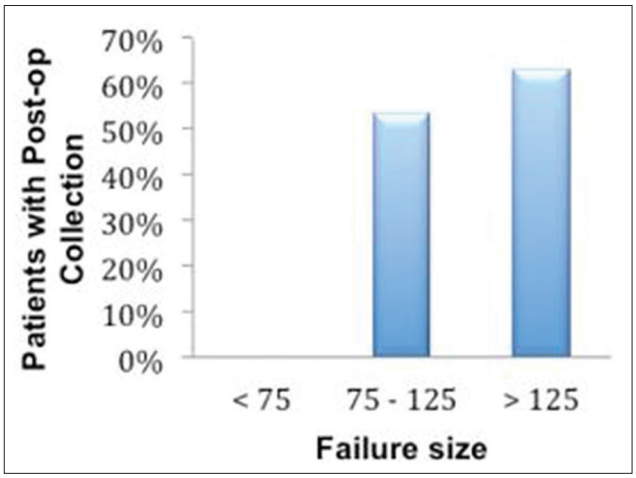

Figure 3: Collection percentage according to skull defect size

Global postoperative surgical site infection rate in this study was 3.2%, a very low rate when compared to other articles, where incidences reached 20% or more.[4,8,10,18,19,22,24] It is imporant to note that our infection rate is almost 10 times lower than the other series, even performing cranioplasty in patients with complex bone reconstruction and with hostile surgical sites.

Authors believed that the predominance of large skull defects requiring long surgical time and the elevated proportion of postoperatory epidural fluid collection could increase the incidence and risks of infection. The constrasting and surprising low incidence of infection in this scenario may be secondary to the use of PMMA plaques imbibed with antibiotics.

Stula[6] argues that his own rate of post-cranioplasty infection was 14%, among 51 patients submitted to cranial reconstruction with PMMA. This incidence decreased to 8.5% when he started adding antibiotics to his cranial PMMA reconstructions. Therefore, this author incorporated the use of antibiotics as a standard procedure in cranioplasty with PMMA. Maybe it is the solution to decrease the incidence of infection in neurosurgical centers with elevated infection rates.

Even though the autologous bone graft is still the preferred method for cranial defect reconstruction, the infection risks, bone absorption, the limitation of donator area, and bone tissue loss in comminous fractures are situations that require defect reconstruction with synthetic materials. Among the many possible materials for skull reconstruction, PMMA is one of the

most frequently used because its possibility of molding the defect, material resistance, and satisfactory aesthetic results.[20] The possibility of PMMA use with antibiotics makes it a viable, low cost, and low infection risk alternative for cranioplasty, which may have an even higher impact in developing countries where there is not enough financial support, for example, to support the use of customized sterile prostheses.

Study limitations

One of the study limitation is the nonexistence of a control group; moreover, the authors did not dose antibiotic blood concentration after the surgery, which would demonstrate a systemic or just local impact of antibiotic use. Another limitation is that all surgeries were performed months after prior craniectomy (late cranioplasty) when the risks of complications and infection are possibly lower when compared to early cranioplasty, although recent systematic reviews did not support this information.[25,26]

CONCLUSION

The use of antibiotic-impregnated PMMA for correction of moderate and large skull defects had a low incidence of infectious postoperative complications. This association may be useful to reduce the morbidity and mortality as well as hospital costs, especially in medical centers where a higher complication rate is expected.

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Conflicts of interest

There are no conflicts of interest.

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