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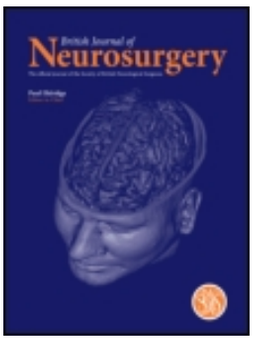

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ORIGINAL ARTICLE

Safety of untreated autologous cranioplasty after extracorporeal storage at − 26 degree celsius

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Abstract

Background. **Given the improved survival of patients requiring decompressive craniectomies, the frequency of subsequent cranioplasties are on the rise. The most feared complication of autologous cranioplasty is infection and one method for reducing the rate of infection, is to store the bone flaps at subnormal temperatures. However, to date there is no defined temperature for flap storage and temperature ranges from − 18 to − 83°C have been described in literature. Considering our limited resources it has been the practice at our center to store bone flaps at − 26°C. In this study, we have retrospectively reviewed our practice and have audited this choice of temperature with respect to the frequency of infections.** ***Methods.*** **A retrospective review was conducted for all cranioplasties performed at our center between January 2001 to March 2011, using autologous bone which was cryopreserved according to institutional protocol. During this period the operative and cryopreservation protocol remained the same. All patient records including charts, notes and laboratory findings were reviewed with a specific focus to identify infections.** ***Results.*** **Of the 88 patients included in the study, only 3 (3.40%) patients were found to show signs of infection. Of these, two patients had superficial surgical site infections which resolved with oral antibiotics (Co-Amoxiclav 1 gm BD for 7 days). However the third patient developed deep surgical site infection requiring re-exploration and washout. All three patients had complete resolution of infection with preservation of autologous bone.** ***Conclusion.*** **Despite our method of keeping the bone flap in freezer at − 26°C we have reported an acceptable rate of infection and raised the notion whether there is a justification for sophisticated and costly equipment for bone flap preservation, especially in resource depleted setups.**

Keywords: autologous bone; cranioplasty; decompressive craniectomy; infection; temperature

Introduction

With emerging evidence supporting decompressive craniectomies for various indications, it is obvious that the frequency of cranioplasties will simultaneously rise.[1] A variety of materials have been tried for cranioplasties although autologous bone flap removed at the time of decompressive craniectomy and preserved for later use; still remains the most widely used due to its availability, low cost, excellent cosmetic results, likelihood of engraftment, remodeling and growth, low risk of infection and virtually no risk of rejection.[2] However, the use of autologous bone has been associated with a risk of complications as well, the most common being infection and resorption.[3] Reported rates of postoperative infections are around 12% which is very high for a clean surgical procedure.[4]

Various methods have been introduced to reduce this rate, most notably the storage of flap at subnormal temperature.[5] This however predisposes the flaps to increased risk of resorption and poor survival of viable osteocytes. Moreover, these temperatures are financially taxing and difficult to maintain. Comparatively higher temperature ranges provide some degree of protection to surviving osteocytes and from possible risk of resorption, although they are associated with a theoretical risk of increased predisposition to infections.[6] To date the optimum temperature which offers a safe and infection free storage environment to the flap while balancing the survival of osteocytes has yet to be determined and temperature ranges from − 18 to − 83°C have been described.[7]

Being one of the busiest neurotrauma centers in a city of over 17 million populations, we receive a large volume of patients requiring emergency decompressive craniectomies and subsequent elective cranioplasties. With limited resources and access to more advanced storage facilities, it has been the practice at our center to store free bone flaps in an operating room based deep freezer at − 26°C. Herein, we have presented our experience with these cases with special emphasis on frequency of infections.

Methods

Study protocol

A retrospective review was carried out of all cranioplasties performed at the Aga Khan University Hospital, Karachi,

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over a ten-year study period (Jan 2001–April 2011). Initially, a list of patients who underwent decompressive craniectomies for medically intractable intracranial hypertension at our institution was compiled from hospital records and cross referenced with theatre records and Neurosurgery database. Of these, only those patients were included who underwent an autologous cranioplasty, and whose bone flaps were preserved using institutional protocols for cryopreservation. Patients, whose bone flaps were removed for reasons other than intractable intracranial hypertension, such as for tumor involvements, infections, or because of extensive damage due to trauma, were excluded. Patients whose bone flaps were stored in anatomical locations such as subcutaneous pockets or contralateral subgaleal space were also excluded, as were those patients whose bone flaps were either autoclaved prior to replacement, or were combined with synthetic material for better coverage. Patients with follow-up less than three months were also excluded, unless they had documented infection within the post-operative period.

All patient records including charts, notes and laboratory and radiology data were reviewed for each patient and the data was extracted into a predesigned questionnaire. While reviewing the records specific focus was kept on post-operative infections and its management.

Protocol for bone flap storage

Our institute follows a standardized protocol for decompressive craniectomies in trauma, whereby a flap of approximately 12×12 cm is raised. At the time of decompressive craniectomy, the bone flaps were preserved as soon as the decision to leave the bone flap out was made by the operating surgeon, thus minimizing exposure time. For non-penetrating injuries, no efforts were made to clean the bone prior to storage. The bone flaps were wrapped in two layers of sterile waterproof paper, followed by placement in a close fitting sterile air tight plastic bag. This package was in turn placed in a bigger sterile plastic bag, and sealed in an air tight manner. The flaps were then labeled, logged and subsequently placed in an operating room based freezer maintaining a constant temperature of -26°C. Most domestic freezers range between -4 and -30 degrees Celsius, with a median of -18 degrees Celsius, thereby offering an easily available method for storage.

Cranioplasty technique

All cranioplasties at our institution are done by senior neurosurgery residents or fellows, supervised by attending neurosurgeons. There were no selection criteria for patients undergoing cranioplasty. All patients who underwent a decompressive craniectomy and survived were offered and underwent a cranioplasty. A single dose of antibiotics is administered to the patient at the time of induction. Anti-epileptics are only administered if the patient is already on anti-epileptics and pre-operative drug levels are below therapeutic range.

A 2 centimeters strip shave is usually done to expose previous scar. The skin is prepared with povidine iodone scrub, solution and 2% chlorhexidine solution for 4 min each. After standard water proof (non disposable) draping, the skin is incised and hemostatic clips are applied. The galeal flap is raised to create a plane between the galea and underlying material which according to individual case maybe artificial dura, fascial flap (harvested from pericranium) or Surgicel. The craniectomy edges are then defined either using monopolar coagulation diathermy on top of the bone, or periosteal elevator which is slid between the bone and underlying dura. The bone is retrieved and thawed within its packing, at operating room temperature. Flaps are removed from their packing only after the galeal flap had been raised and craniectomy edges are properly defined to minimize exposure time. On removing the bone from its packing, it is cleaned of all bone dust, attached soft tissue and loose fragments and immersed in povidine iodine solution for 10 min, followed by brief irrigation with a diluted solution of hydrogen peroxide (1:1 dilution with normal saline). It is then thoroughly rinsed with antibiotic mixed normal saline solution, the entire procedure requiring between 12 and 15 min. The effect of povidine iodine and hydrogen peroxide could potentially reduce the number of viable osteocytes, however, studies have indicated that skull flaps cryopreserved at 300C for more than 6 months are non-viable. Further culture of such skull flaps yielded no viable osteoblasts at 3 weeks.[8]

The bone flaps are fixed using either titanium plates or silk sutures depending on the patient's financial capabilities. In case of bilateral flaps, two surgeons operate simultaneously to reduce operating time.

Subgaleal drains are not routinely placed prior to closure, but if placed, are removed within 48 post-operative hours. Skin is closed with continuous interlocking nylon sutures or stainless steel staples based on the attending surgeon's preference. Prophylactic antibiotics are continued for 24 h only.

Infections were classified as described by Narotam et al into superficial and deep. Infections were considered as superficial if only the scalp was involved, and included cases of wound erythema, and considered deep when it occurred beneath the galea, and included subgaleal pus, osteitis, abscess/empyema or ventriculomeningitis.[9]

Results

Over the study period, 180 patients underwent elective cranioplasties. On charts review, 92 patients were excluded as their bone flaps were either stored in subcutaneous pockets, autoclaved prior to replacement, refashioned with synthetic material such as poly methyl meth acrylate (PMMA), or follow-up period was shorter than 3 months. Eighty eight was the final number of patients included in the study. These patients were then analyzed for risk of infection.

Analysis of the data revealed a mean age of 33 ± 14.8 years, 77.3% ($n = 68$) of our patients were males, 22.7% ($n = 20$) were females. Of the sample, 76% ($n = 67$) had no known comorbids, the rest had one or two comorbids, and seven patients had multiple (> 2) comorbidities. The leading primary pathology was blunt traumatic brain injuries in 45% ($n = 45$), followed by cerebrovascular accidents in 23% ($n = 22$), penetrating traumatic brain injuries in 13% ($n = 12$), and tumors in 40.5% ($n = 4$) of cases. Nearly all (96%, $n = 85$)

index surgeries were performed at our center and the rest were performed elsewhere and referred to us for further management. The three patients who underwent index surgeries at outside centers were shifted to our center for further management within 24 h with their bone flaps. The bone flaps were transferred to our center within standard packing, similar to ours, in cold environments. These flaps were than preserved at our storage facility.

The various flaps used included standard trauma (71%, n = 63), frontal (12.5%, n = 11), parietal (9%, n = 8), and temporal (6.8%, n = 6) flaps. Of these, 69.5% (n = 61) were unilateral and the rest (30%, n = 27) were bilateral. All craniotomy bone flaps were preserved using cryopreservation at − 26°C. Cranioplasties were performed after a mean delay of 78.05 ± 66.7 days.

The detail of cranioplasty technique has been described above. The flaps were secured using silk sutures (40%, n = 36), vicryl sutures (22.7%, n = 20), titanium plates (25%, n = 22), or wires (11.4%, n = 10). Galeal closures were done using absorbable vicryl in all patients and skin was closed using either sutures (69.3%, n = 61) or staples (30.7%, n = 27) depending upon the surgeons' preference. Subgaleal drains were placed prior to closure in 36.4% (n = 30) of the patients and no patient underwent placement of an epidural or subdural drain. The mean duration of surgery was 185.2 ± 67.3 min, resulting in an average blood loss of 365 ± 263 ml. Fourteen patients (15.9%) required intraoperative blood transfusions and mean duration of hospital stay was 12 ± 17 days. Patients were advised to follow-up in clinic at 2 weeks and 4 weeks post-operatively for complications of the procedure. Follow-ups beyond 4 weeks were conducted if the patient came to clinic for an unrelated visit or voluntarily felt the need for a follow-up visit. Since most patients had other issues warranting follow-up visits, the average duration of follow-up was 9.31 ± 14.01 months. Patients were considered lost to follow-up if they missed their 4 week follow-up. Of the 88 patients 12 were lost to follow-up in our series i.e. did not show for the 4 week follow-up visit. However all 88 patients had a 2 week follow-up visit.

Of the 88 patients only 3 (%) patients were found to show signs of infection at follow-up. Two patients had superficial wound site infection, and one patient had deep wound site infection involving subgaleal space. All of these patients were young with no prior history of medical conditions predisposing to infections. All three patients underwent decompressive craniectomies for blunt traumatic brain injury (TBI) and in none were any external lacerations noted prior to surgery. Standard trauma flaps were raised in all three cases and once patients' intracranial hypertension was controlled, elective cranioplasties were carried out after a mean duration of eight weeks of initial surgery. Silk sutures were used to anchor the bone flaps in all the cases. Both patients with superficial surgical site infections settled on oral antibiotics (Co-Amoxiclav 1 gm twice daily for 7 days) and no formal cultures were sent. The patient with deep wound infection required wound re-exploration and wash out. As the underlying bone appeared unaffected at the time of exploration, it was not removed. The tissue culture grew Staphylococcus aureus, which was pan sensitive, and patient responded well to three weeks of antibiotics (one week intravenous and two weeks oral) with unremarkable follow-ups till two years (Table I).

Apart from these three cases, the other complications included extradural hematoma in one patient requiring evacuation, and hydrocephalus in two patients, both requiring temporary CSF diversion only.

Discussion

There is definite reemergence of decompressive craniectomies after favorable results are being reported in prospective trials carried out in trauma and stroke.[10] This has led to more and more salvageable patients who will be potential candidates for delayed cranioplasty. Several methods are available for cranial reconstruction. Among these, re-using cryopreserved autologous bone is considered fairly convenient, safe and cost effective. The advantages are exact reconstruction of skull defects and possible chances of engraftment, remodeling and growth, with obvious per patient cost benefits.[11] In addition there is no need of synthetic materials which can be ill fitting and may be associated with lesser cosmetic satisfaction, foreign body reactions and possibly an increased risk of infection.[12]

The first cases of cranioplasty using extracorporeal cryopreserved autologous bone flaps were reported in the 1950s.[13] This was followed by multiple histological studies showing appearance of osteocytes in frozen bone flaps and preservation of intact Haversian systems and structural proteins necessary for revitalization of theses flaps.[14] As a result this method of preservation gained popularity among different centers. However, there are still no standard guidelines for preservation of bone flaps in term of exact temperature settings, duration of storage, treatment of flap with different disinfectant solutions like povidine iodine, hydrogen peroxide and antibiotic containing saline solutions. This has resulted in different practices at different centers and there is wide variation in temperature settings reported in literature ranging from − 18ºC to − 83ºC, with varied outcomes.[15]

Table I. Details of patient with wound site infection.

Patient details	Indication	Infection diagnosed	Type of Infection	Culture	Antibiotic duration	Other procedure	Follow up
36/M	Blunt TBI	5th POD	SWSI	–	2 weeks	None	3 months
30/M	Blunt TBI	7th POD	SWSI	–	2 weeks	None	5 months
28/M	Blunt TBI	14th POD	DWSI	Staphylococcus aureus	3 weeks	Wound exploration, wash out	2 years

SWSI, Superficial wound site infection; DWSI, Deep wound site infection; TBI, Traumatic brain injury; POD, Post- operative wound site infections.

Infection of the flap is the most feared complication of delayed cranioplasty using cryopreserved bone flaps. To avoid infection, Osawa et al. suggested that bone flaps should be routinely autoclaved before cranioplasty procedure.[16] However, we suggest that autologous bone flaps be autoclaved only if the flap is either suspected to be infected or infiltrated by tumor cells.

Several authors have also reported their results re-using cryopreserved autologous bone. Grossman et al. discussed their nine years' experience of deep freeze bone flap preservation at Soroka University. Cranioplasty was done in 12 patients using these cryopreserved bone flaps with no case of infection.[11] Inamasu et al. compared cranioplasty infection rates between 39 bone flaps stored in a subcutaneous abdominal pocket and 31 bone flaps stored in a freezer at -70^{o}C. Superficial site infection occurred in seven patients, two (5.1%) of which had bone stored subcutaneously, and five (16.1%) had the bone cryopreserved. The difference was not statistically significant ($p = 0.23$).[17] Zingale et al. conducted a meta-analysis of seven studies to compare rates of infection between abdominal pocketing and freezing at temperatures ranging from -16 to -40°C. There were three infections in 82 cranioplasties performed with subcutaneously preserved bone flaps and 22 infections in 337 cranioplasties performed with frozen bone flaps, although this difference was also statically insignificant.[18]

In light of our results we suggest that in developing countries where there is an increased trauma burden complicated by limited resources, craniectomy bone flaps can be saved in ordinary deep freezers without fear of an increased risk of infection. This is important alternative as the financial and industrial requirements of titanium-derived mesh used commonly in more developed countries are not feasible for developing countries.

We realize that results concluded from our study cannot be generalized. These recommendations are not applicable for certain developed countries where tissue storage policies would not allow such a simple solution to the problem.

Conclusion

Extracorporeal storage of untreated autologous cranial bone flaps is safe with significantly low risk of infection at -26 degree celsius. Our practice can be followed in resource challenged neurosurgery centers around the world. Further prospective studies are warranted to validate our protocol.

Declaration of interest: The authors report no declarations of interest. The authors alone are responsible for the content and writing of the paper.

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