Closure of Recurrent Cleft Palate Fistulas With Plasma Rich in Growth Factors

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Received 15 September 2010; accepted 15 June 2011

KEYWORDS
Cleft palate; Fistula; Platelet-rich plasma; Growth factors

Abstract
Introduction and objective: Fistulas represent a significant challenge in the treatment of cleft palate. The best outcome of a palatoplasty is obtained with a competent velopharyngeal sphincter and a palate without fistulas. The recurrence of primary cleft palate fistula is reported as high as up to 76%, and to nearly 100% in recurrent fistulas.

Plasma rich in growth factors (PRGF) is an autologous blood product with biologically active substances that enhance tissue repair mechanisms such as chemotaxis, cell proliferation, angiogenesis, osteogenesis and remodeling. Its use in cleft palate fistulas has not been reported.

Our objective was to evaluate closure of recurrent cleft palate fistulas using PRGF mixed with autologous bone graft.

Methods: An experimental, prospective, longitudinal study was carried out from April 2008 to July 2010 on 11 recurrent cleft palate fistulas that were closed with local mucoperiosteal flaps and placement of autologous bone graft mixed with PRGF.

Results: Complete closure of palate fistulas was achieved in 90.9% (follow-up of 6–24 months), decreasing the reported incidence for the recurrence by other authors with other techniques.

Conclusions: The use of PRGF mixed with autologous bone graft seems to be an effective, safe and low-cost technique for the closure of recurrent cleft palate fistulas. However, we consider its study must be extended.

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Introduction

Palatal fistulas are a major problem in the treatment of patients with cleft palate. The formation of fistulas after primary palatoplasty has been variably described, since the classification systems for fistulas differ. Cohen et al. described a 23% incidence of palatalt fistula formation after primary palatoplasty. Emory et al. carried out a literature review, which found the presence of up to 36% of palatal fistulas. Smith et al. described an incidence between 0% and 76% of palatal fistula after primary palatoplasty. Recurrence after repair of a palatal fistula is even higher, with reports that range from 25% to 33% to nearly 100%. The most common sites of fistulization are the hard palate and the junction of the hard and soft palates, although it can also occur in the soft palate.

Cohen et al. classified fistulas by their size into small (1–2 mm), medium (3–5 mm) and large (more than 5 mm). By their location, the Pittsburgh classification divides them into: (1) uvular, (2) soft palate, (3) junction between hard and soft palate, (4) hard palate, (5) junction between primary and secondary palate, (6) lingual alveolar and (7) labial alveolar. Cohen et al. has suggested that the variables that increase the risk of palate fistula are the type of primary defect (Veau classification), the type of primary repair surgery (significantly more frequent in Wardill–Klinier type closures) and the experience of the surgeon.

Palatal fistulas have traditionally been closed using local mucoperiosteal flaps. However, they recur in 1 out of every 3–4 patients. The risk of recurrent fistula increases once the closure of the primary defect has failed. The fibrosis and decreased vascularization that occur with each surgery could explain this increase in risk. Several authors have described different surgical techniques for recurrent palatal fistulas closure to decrease this recurrence, such as using lingual flaps,6,7 buccal flaps,8 bone grafts,9–14 buccal mucosal osseoplastic flaps,15 buccal fat flaps,16 conchal cartilage,17 acellular dermal matrix18 and turbinal flaps19.

Plasma rich in growth factors (PRGF) is an autologous blood product with a high platelet concentration. It is used to manage and maximise both surgical and nonsurgical wound repair. The main components of PRGF are the following types of growth factors: platelet-derived, vascular endothelial, beta-type transforming, epidermal, fibroblast and insulin-like I. These factors promote the synthesis of the extracellular matrix, stimulate the synthesis of type I collagen, fibronectin and osteonectin, deposition of extracellular matrix and chemotaxis. They also decrease the synthesis of metalloproteins and plasminogen activating factor, thereby reducing the destruction of the extracellular matrix. They inhibit osteoclast formation as well, but promote bone resorption by the mechanism of prostaglandins.20 Cell repair and regeneration are also promoted by stimulation of mitosis and cell migration, and the synthesis of proteins such as fibronectin is also promoted. They also contain chemotactic agents for endothelial vascular cells, thereby promoting wound neovascularization. A pro-angiogenic action has been observed by chemotactic action on endothelial cells.

The main uses of PRGF to date are in dental and maxillofacial surgery, to repair defects caused by dental extraction22 or tumour resection,23 as well as for alveoloplasty.24 Other specialties have studied its effect in surgical procedures such as acromioplasty,25 arthroscopy,26 rhytidectomy with fat grafts,27 skin wounds28 and infiltration...
due to ankle ligament injury.\textsuperscript{29} Accelerated healing, decreased risk of infection, less postoperative discomfort and faster recovery were reported in these publications.

There have been no studies on the closure of palatal fistulas using PRGF with autologous bone grafts in patients with cleft palate sequelae. The aim of this study was to evaluate the effectiveness of PRGF in the surgical closure of palatal fistulas.

**Methods**

**Study Design**

We carried out a prospective, longitudinal, cohort study that included all patients with a history of cleft palate, with or without cleft lip, presenting at least one recurrent palatal fistula, who attended the Otorhinolaryngology Service at Dr. Valentin Gomez Farias Regional Hospital (ISSSTE) during the period between April 2008 and July 2010. The study was approved by the research and bioethics committee of the hospital and all patients gave their informed consent.

We recorded the variables studied, including: gender, age, type of primary defect according to the Veau classification, size of fistula according to Cohen and location of fistula according to Pittsburgh, as well as the number of prior closure attempts. We documented the study with photographs of the patient and a computed tomography study performed one day before surgery. All patients were referred for assessment and management by the psychology service.

**Surgical Technique**

Minutes before the surgery, we extracted 10–20 ml of venous blood from each patient, depending on the size of the defect. This was centrifuged to obtain PRGF by the technique described by Anitua\textsuperscript{30} and reserved until 15 min before its use. Under general anaesthesia, we evaluated the nasal floor by endoscopic approach in search of the fistula (Fig. 1). We infiltrated the region around the fistula via the palate with lidocaine at 2\% with epinephrine 1:100 000. We designed local mucoperiosteal flaps by separating the oral mucosa from the palatal mucosa. Then we took the bone graft, crushed it to mix with the activated PRGF gel (Fig. 2) and placed it between two sheets of solid collagen. The nasal mucosa was closed to introduce the mixture between the palatal and nasal mucosa, filling the bone defect (Fig. 3). The palatal mucosa was closed with Vicryl 5-0. All patients were operated on by the same surgeon.

**Follow-up**

A photographic record of the palate was prepared by photographs during surgery, at 2 and 4 weeks, and later at 2, 4, 6, and 12 months (Fig. 4). The preoperative and postoperative CT scans were also recorded (Fig. 5). Assessment
of fistula closure was performed subjectively, using the evaluation by each patient (passage of solid or liquid food into the nostrils), and objectively, using a test with dyed mouthwashes, as well as through intraoral and endoscopic nasal inspection.

**Statistical Analysis**

No statistical analysis was performed due to the sample size.

**Results**

None of the patients were excluded or eliminated because all continued their evaluations for at least 6 months. We performed 11 surgical closures of palatal fistulas in 6 patients, 50% (n = 3) female and 50% (n = 3) male. The ages of patients at the time of surgery were between 10 and 33 years. Two patients presented double palatal fistula and one presented triple fistula. We studied the closure of 11 palatal fistulas in all. The type of cleft palate according to Veau was incomplete unilateral in 67% (n = 4) and unilateral complete cleft palate in 33% (n = 2). According to the Cohen1 classification for the size of the fistulas, we found 3 small (27%), 4 medium (36%) and 4 large (36%) fistulas. All patients had previously undergone surgical closure of the fistula, without success in 3 of 5 times. According to their location, 45% (n = 5) were found between hard and soft palate, 27% (n = 3) in the hard palate, 18% (n = 2) in the junction between the primary and secondary palate and 9% (n = 1) were labial alveolar. Fistulas were found in the left side in 81.8% (n = 9) of cases and in the right in 18.2% (n = 2).

With respect to autologous bone grafts, we obtained 4 from the perpendicular plate of the ethmoid, 2 from the middle turbinate (concha bullosa), 1 from the mastoid and 1 from the iliac crest. All patients presented an abundant production of fibrin during the first week, which decreased until its disappearance within 2 weeks. Palate pain was almost nil in all patients. There were no cases of infection in any of the patients.

Closure was demonstrated in 90.9% (n = 10) of the palatal fistulas.

**Discussion**

Patients with cleft palates are subjected to an average of 4 surgical procedures, including primary palatoplasty,

![Figure 4](image1.png)  
**Figure 4** (A) Preoperative photograph. (B) Postoperative photograph after 4 months.

![Figure 5](image2.png)  
**Figure 5** (A) Preoperative CT scan showing the nasopalatine fistula. (B) Postoperative CT scan after 8 weeks, showing the bone graft (circle) and absence of nasopalatine fistula.
pharyngeal flap, pharyngoplasty, recurrent fistula closure and placement of ventilation tubes, among others. This is an exhausting process for patients and also represents a significant expense to healthcare systems. A patient with palatal fistula suffers passage of solids and liquids into the nasal cavity, increased frequency of upper respiratory tract infections and changes in voice resonance; all this in turn leads to low self-esteem. Having noted the benefits that PRGF offered in other surgical procedures, we decided to study whether its application during palatal fistula closure decreased recurrence.

The results in our study were satisfactory, as it was possible to reduce the recurrence rate compared to others described in the literature, ranging from 40% to nearly 100% in recurrent palatal fistulas. These authors agree that the rate of fistula recurrence increases in accordance to the number of closure attempts. In our study, all fistulas had a minimum of 3 prior surgical failures.

In this study, we decided to obtain the graft from a previous pathological area in each patient. We obtained improvement in nasal function, while the palatal fistula was closed. It is important to point out that patients must follow postoperative care, which is sometimes difficult due to their age. In the case of our patient who presented recurrence of the fistula, there had been good evolution during the first 3 weeks, until she injured her hard palate with solid food. In addition, this patient presented a triple fistula, which may have led to increased risk of flap ischemia due to increased tension. This patient was reoperated one year later using PRGF, achieving successful closure.

In Mexico, there is a significant surgical delay in the comprehensive treatment of patients with cleft lip and palate due to population marginalisation issues and to the high cost for patients, who must often relocate to receive healthcare. This is why we consider it essential to reduce the recurrence of fistulas, so as to reduce the number of surgical procedures, as well as the expenses involved.

Conclusions

The use of PRGF mixed with autologous bone graft for the closure of palatal fistulas by local mucoperiosteal flaps is an innovative alternative that can offer significant benefits for patients with a history of cleft palate. Being completely autologous, it is a safe option because infectious or rejection risks are not added. It seems to be an effective technique, demonstrating success in over 90% of patients in our study. However, we believe it is important to extend this study to obtain significant results.

Conflict of Interests

The authors have no conflicts of interest to declare.

References


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