

A Trial to Improve the Outcome of Patients with Cleft Palate Repair by Using Human Fibrin Glue: A Study in 20 Cases

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ABSTRACT

Introduction: Cleft palates are among the commonest craniofacial abnormalities. Cleft palate repair is not free of complications. The formation of a fistula is the most common complication of palatoplasty.

Aim of Work: To rectify the benefit of using human fibrin glue as a catalyst in primary palatoplasty and its effect on lowering the development of postoperative complications.

Methods: Primary palatoplasty was performed for twenty patients by double flap palatoplasty with human fibrin glue as a catalyst in the reform from January 2019 to June 2019. Fibrin glue was prepared from fresh frozen plasma to obtain thrombin and cryoprecipitate to obtain fibrinogen. Then was injected between the two palatal flaps and at the suture line as well.

Results: Out of twenty patients, 5 cases (25%) showed post-operative complications. Two cases (10%) were complicated by oronasal palatal fistula one of them (5%) were small (2mm) at the intersection of soft and hard palate without any nasal regurgitation and closed spontaneously within two months of post-operative follow-up. The other one (5%) continued for further surgical repair, and it also had early wound infection. Two cases (10%) were complicated by upper airway obstruction, and one patient (5%) was complicated by hemorrhage.

Conclusions: The rate of occurrence of complications was less than in other studies that did the same procedure without the utilization of fibrin glue in the repair. More research with more patients and a more extended period of follow-up are recommended.

Key Words: Cleft palate – Repair – Fibrin – Glue – Palatal fistula.

Disclosure: No conflict of Interest.

Ethical Committee Approval: The study was approved by the ethical committee of the General Surgery Department, Faculty of Medicine; Beni Suef University.

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INTRODUCTION

Cleft palates are among the most typical craniofacial abnormalities. They result from a failure of fusion during the second month of gestation. They have an incidence of about 1 in every 2000 to 2500 births. They are usually but not always associated with a cleft lip. In a small percentage of cases, the cleft palate is one of the multiple congenital anomalies in a major genetic syndrome. The extent of the cleft varies: Some just affect the soft palate, while others extend into the hard palate but do not affect the alveolar ridge. The defect may be unilateral or bilateral [1].

Cleft palate repair is not free of complications. The formation of a fistula is the most common complication of palatoplasty. Other consequences include total wound dehiscence, oropharyngeal infection, airway obstruction, pneumonia, bleeding, feeding difficulties, aspiration, hyperthermia, postoperative airway occlusion, otitis media, and fatality [2].

Fistula formation after palatoplasty is hypothesized to be caused by several causes. They include patient factors such as age at surgery, type and extent of cleft, and associated syndromes, as well as treatment issues such as the operating surgeon's experience, type of repair, tension at the closure site, circulation issues, hemorrhage, infection, postoperative anemia, and lack of post-operative supervision [3].

Cleft palate surgery can result in an oronasal fistula, which can be problematic in various ways. Food and drink leakage, as well as speech impairments, are issues in some cases. However, not all fistulae cause similar problems. Oronasal fistulae can cause various symptoms depending on their size and location. Even if it was a little fistula at

first, it would grow in size when the maxillary arch expands due to orthodontic therapy [4].

Bergel first used fibrin glue in 1909 to establish homeostasis. Preparation of the fibrin glue involves several steps and can be performed in approximately 10min. Fibrin glue mimics the final stage of the coagulation cascade [5].

Fibrin glue is a tissue sealant made up of fibrinogen, factor VIII, fibronectin, and traces of other plasma proteins in high concentration. An antifibrinolytic agent such as aprotinin and thrombin are among the other components. These ingredients enhance hemostasis by clot formation. With calcium, thrombin activates fibrinogen and results in fibrin clot formation, which reduces bleeding and better wound healing with decreased fibrosis and scarring as it is almost absorbed during the healing process. The utilization of Fibrin glue is very beneficial for tissue sealing with less inflammatory response, hemostasis, and a better healing process [6].

Flaps can be held with fibrin glue instead of sutures or pins. The covalent connections between fibrin and collagen, or fibrin, fibronectin, and collagen, explain the sticky properties of solidified Fibrin Glue. Fibrin Glue can be made from pooled blood or single donor blood. Single donor blood is either autogenous or allogenic. Fibrinogen is a soluble blood component that makes up 0.2% of whole blood volume. It becomes an insoluble fibrin network in the intrinsic and extrinsic blood coagulation cascades [7].

PATIENTS AND METHODS

The study involved twenty patients with primary cleft palate referred from Beni-Suef University's outpatient surgical clinic. From January 2019, extended for two years, they had primary palatoplasty with the utilization of human fibrin glue in the repair.

All the twenty patients fulfilled the following criteria:

Inclusion criteria: Age: 6 months to 4 years old, gender: males & females, patients who are undergoing primary palatoplasty, and informed parental consent.

Exclusion criteria: History of hypersensitivity reaction to fibrin glue ingredients, patients who are not fit for surgery, failure to obtain informed consent, patients with major co-morbidities e.g. cardiac anomalies and syndromic patients.

For all patients, the following was done:

Pregnancy history: Ages of the parents, maternal health, medications taken during the pregnancy, personal habits, such as alcohol or cigarette use during the pregnancy, and the occupations of both parents may also suggest potential teratogens exposure.

All patients were examined for weight, length, and orthodontic consultation. Measure the infant's head circumference to see if they are normal, tiny, or large for gestational age. This is especially essential in newborns who may acquire Weight at a slower rate before surgical correction. I

Routine labs and investigations: Obtain complete blood count and coagulation profile. Other investigations were done to exclude any other anomalies, e.g., Echo.

Informed consent for the study: Palatoplasty with fibrin glue and explaining its benefits and possible complications.

Operative details: Anesthesia: Patients were operated under general anesthesia.

Position: Supine position with head tilting 20 degrees for better vision and securing the endotracheal tube centrally.

Medication: Systemic antibiotic was given to the patient after the sensitivity test half an hour before the surgical interference.

Systemic steroids were given pre-operatively as prophylaxis for any allergy.

Applying Dingman was the first step to be taken at the operating theater after induction of anesthesia with pre-operative photos to be taken.

The palatal index (Fig. 1) was obtained preoperatively. This index is the proportion between the width of the cleft (cleft severity) and the sum of the width of the 2 palatal segments (tissue deficiency) measured at the level of the hard and soft palate junction Based on these measurements, the index classifies 3 degrees of severity for the cleft palate: Mild (palatal index of 0-0.2), Moderate (0.2-0.4), and Severe (>0.4) [8].

A mixture of 1cc of Adrenaline 1mg with 200 ccs of isotonic saline was prepared, and an adequate amount was injected under the flaps to be raised.

This study used two flaps of palatoplasty repair; The procedure began with the soft palate cleft's edges being pared and the hard palate cleft incised

along the junction of the oral and nasal mucoperiosteum. Inside the alveolar ridge, a lateral incision was made from the canine to a point immediately behind the hamulus posteriorly. The anterior end of the lateral incision is connected to the cleft margin by an oblique incision. From the hard palate, the mucoperiosteal flap has been elevated. The larger palatine blood vessels travel from the greater palatine foramen to the flap when the oral mucoperiosteal flap is turned back. On this side, the mucosa has been lifted from the septum (vomer), which is linked to the palate edge.

Two flap palatoplasty can be performed by extending the relaxing incisions along the alveolar borders to the edge of the cleft. This design flaps entirely dependent on the circulation from the greater palatine vessels but is also much more versatile in terms of their placement. The flap is then based anteriorly and laterally because no incisions are done at the gingival/palatal junction.

The lateral side of the palatal flap has excellent mobility, and the medial side of the palatal flap

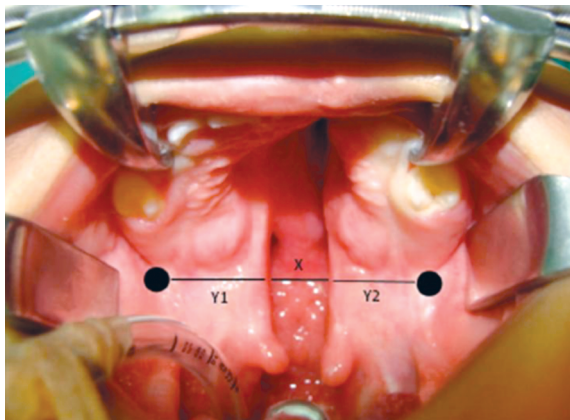


Fig. (1): Palatal index $X/(Y1+Y2)$ [8].

has been dissected to gain width by losing the height of the palatal arch in this case.

The closure of the oral layer follows this, and the lateral release incisions will make repair tension-free, as shown in Fig. (2).

Fibrin glue: Fibrin glue was prepared from fresh frozen plasma to obtain thrombin from it by adding calcium chloride to the plasma and using a centrifuge at 3200 cycles per minute for 20 minutes at 4-6°C in a cooling centrifuge and can be stored in a refrigerator for 3 hours, and from cryoprecipitate to obtain fibrinogen. We obtained fresh frozen plasma and cryoprecipitate from the Beni-Suef University Hospital blood bank. A dual-syringe provided was used to apply fibrin glue, with one side containing one-centimeter fibrinogen and the other side containing one-centimeter thrombin after being prepared, Fig. (3).

Fibrin glue will be applied by the dual syringe between the oral and nasal layers of palatal repair and at the suture line also Fig. (4).



Fig. (2): Closure of oral layer.



Fig. (3): The dual-syringe with thrombin in one side and fibrinogen in the other side.

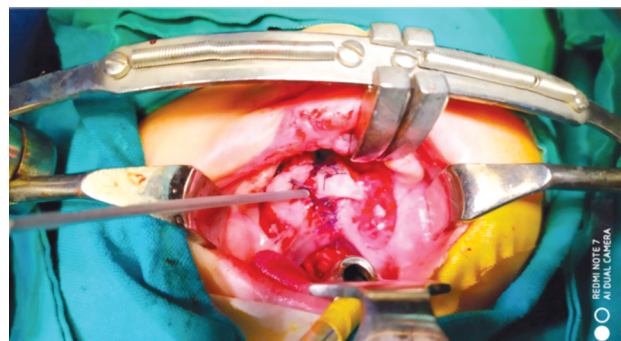


Fig. (4): Injection of fibrin glue between nasal and oral layers by dual-syringe.

After the fibrin glue injection, we waited about 5 minutes before the patient recovered from anesthesia for adequate clotting of the glue and to be fixed at the areas infiltrated in it.

Post-operative details: All patients were admitted to the in-patient section for close monitoring and detection of the early postoperative complications such as bleeding, breathing problems & de-

hiscence of the wound. Close observation for respiratory distress, face edema and puffiness of the eyes, heart rate, and urine output to detect any early signs of fibrin glue allergy.

Post-operative feeding instructions are as follows: Drinking clear fluids was encouraged to avoid oral fungal infection. For the first five days, only water and clear fluids were allowed post-operatively. In the following five days, milk was added to the previous regimen. And the following five days soft diet was introduced by using a syringe. Breastfeeding & bottle-feeding were all prohibited for two weeks after the operation.

Post-operative pictures were taken for documentation of follow-up data.

Follow-up: All patients were followed-up post-operatively for at least six months to detect any complications. The patients were followed-up two times per week in the first two weeks, weekly for two months, and monthly for the later four months.

Statistical analysis: SPSS 17 (Statistical Package for Scientific Studies) for Windows was used to analyze the data. The following is a list of variables and their descriptions: The mean, standard deviation (S.D.), minimum, maximum, and range were used to describe quantitative quantities. Numbers (No.) and percentages were used to describe qualitative factors (percent). The Kolmogorov-Smirnov test of normality was used to examine the data for normalcy. The Chi-Square test was used to compare the qualitative variables (X^2). When one or more predicted cells were less than 5, the Fisher exact test was employed instead of the Chi-square test. Pearson correlation test was used to determine binary correlation. The correlation coefficient (r) and p -values expressed the findings. The significance level for all statistical tests was set at 5%. (p 0.05).

RESULTS

In this study, the age of patients at the time of operation is classified into early (less than 14 months), ten patients 50%, and late (more than 14 months), ten patients 50%. According to the palatal index in this study, 12 cases (60%) in a moderate group of a palatal index (palatal index 0.2-0.4), and 8 cases (40%) in a severe group of a palatal index (palatal index more than 0.4). According to the post-operative hospital stay, 17 patients (85%) stayed one day in the hospital post-operatively, 3 patients (15%) stayed 2 days to be followed up as one of them had a complication of reactionary

hemorrhage, and 2 patients had nasal obstruction post-injection of fibrin glue. According to the type of complication, we had 6 complications (30%) in our study. Two cases (10%) were complicated by Upper airway obstruction post-injection of fibrin glue, and One case (5%) had reactionary hemorrhage at recovery from anesthesia. According to the presence of fistula after the operation, Two patients (10%) presented with oronasal fistula after surgery, One of them (5%) had a fistula located at the junction between soft and hard palate (type III Pittsburgh classification), It was small fistula (2mm) without any nasal regurgitation. It was followed-up and spontaneously closed after 2 months. The other patient (5%) had a fistula in the hard palate (type IV Pittsburgh classification); its size was 3 mm with nasal regurgitation and continued beyond our follow-up time for further surgical intervention. Two patients with postoperative palatal fistula had a wide cleft palate with a severe palatal index (more than 0.4). One with a hard palate also had a wound infection in the first post-operative week. Table (1).

Table (1): Distribution of the studied cases according to different parameters.

	Number	Percent
<i>Cleft palate and cleft lip:</i>		
Cleft palate with cleft lip	4	20
Cleft palate without cleft lip	16	80
<i>Frequency and percentage of timing of operation:</i>		
Early (less than 14 months)	10	50
Late (more than 14 months)	10	50
Total	20	100
<i>Palatal index:</i>		
Moderate	12	60
Severe	8	40
Total	20	100
<i>Post-operative hospital stay:</i>		
One Day	17	85
Two Days	3	15
<i>Type of complication:</i>		
Fistula	2	10
Upper airway obstruction	2	10
Hemorrhage	1	5
Wound infection	1	5
Total	6	30
<i>Presence of fistula:</i>		
Fistula	2	10
No fistula	18	90
Total	20	100

There is no significant difference between the presence of fistula and the timing of the operation, p -value=0.305, and the correlation coefficient was 0.229. Table (2).

Table (2): Correlation between presence of palatal fistula and age of the patient at the operation.

	Fistula	No fistula
Age at operation:		
<i>Early (less than 14 months):</i>		
Number	0	10
% within this age at operation	0.0%	100%
% within presence of fistula	0.0%	55.5%
<i>Late (more than 14 months):</i>		
Number	2	8
% within this age at operation	20%	80%
% within presence of fistula	100%	44.5%
Total:		
Number	2	18
% within age at operation	10%	90%
% within presence of fistula	100%	100%

There is no significant difference between the presence of fistula and palatal index, p -value=0.209, and the correlation coefficient was 0.281. Table (3).

Table (3): Correlation between presence of palatal fistula and palatal index.

	Fistula	No fistula
Palatal index:		
<i>Moderate (N=12):</i>		
Number	0	12
% within Palatal index	0.0%	100%
% within occurrence of fistula	0.0%	66.7%
<i>Severe (N=8):</i>		
Number	2	6
% within Palatal index	25%	75%
% within occurrence of fistula	100%	33.3%
Total (N=20):		
Number	2	18
% within Palatal index	10%	90%
% within occurrence of fistula	100%	100%

Case (1): Female patient 9 months old with primary cleft palate with moderate palatal index (0.3); Figs. (5-12).



Fig. (5): Primary cleft palate pre-operative.

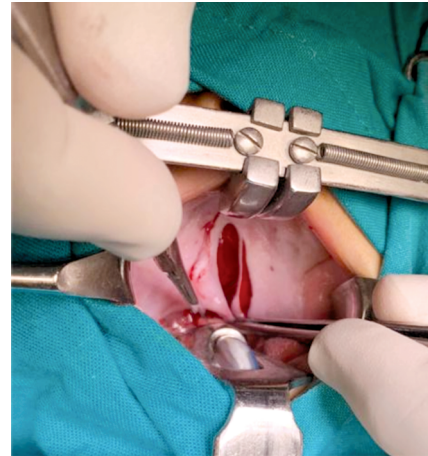


Fig. (6): Incisions at cleft edge.



Fig. (7): Closure of the nasal layer.

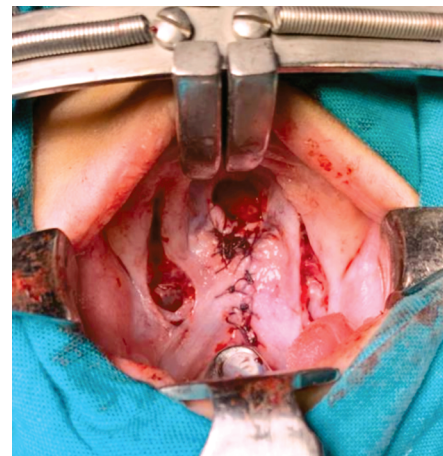


Fig. (8): Lateral release incisions and closure of oral layer.

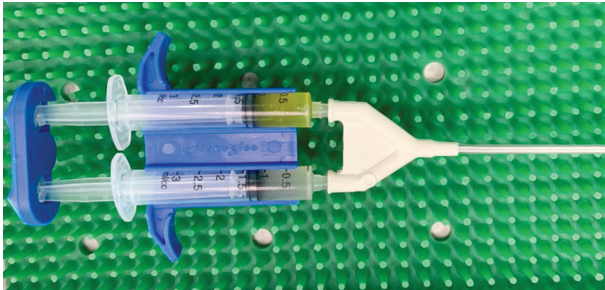


Fig. (9): Dual syringe with fibrin glue.

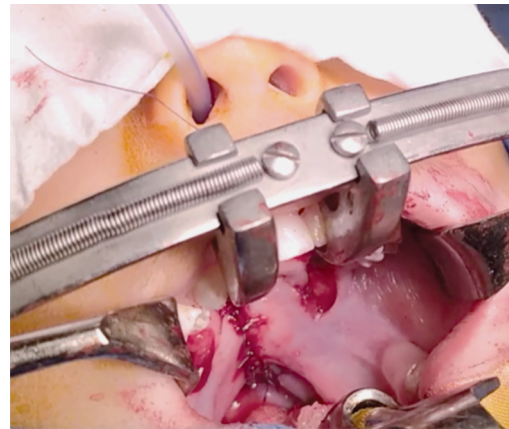


Fig. (10): Insertion of Nelaton catheter from the nostril to the pharynx before injection of fibrin glue. N.B: The catheter inserted bilaterally.



Fig. (11): Injection of fibrin glue between nasal and oral layer and at suture line.

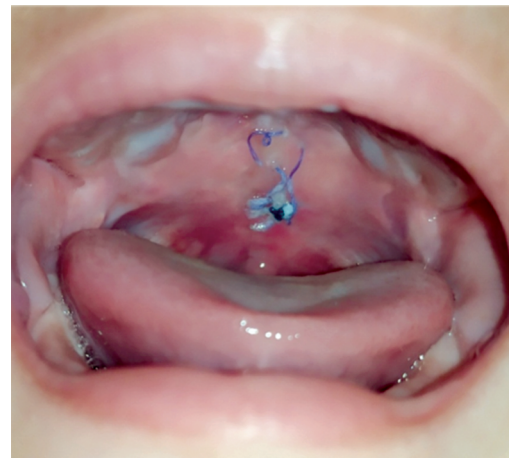


Fig. (12): Two months post-operative.

Case (2): Male patient 12 months old with primary cleft palate with moderate palatal index (0.3). Figs. (13-20).

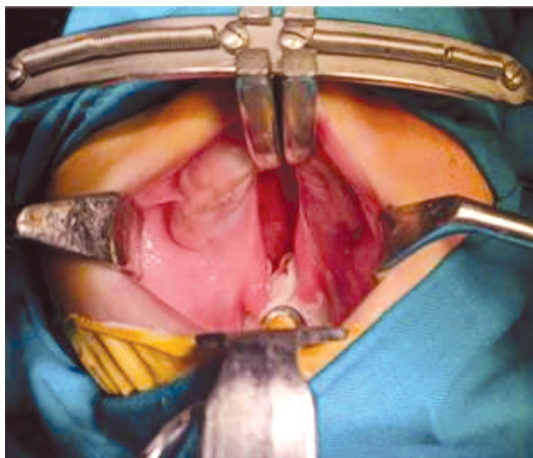


Fig. (13): Primary cleft palate pre-operative.

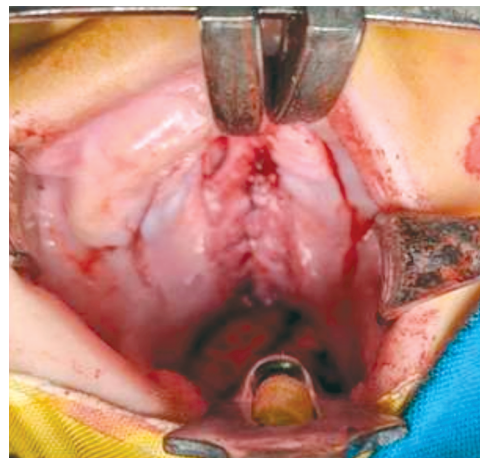


Fig. (14): Closure of nasal layer by interrupted sutures.



Fig. (15): Release incisions and raising of mucoperiosteal flap.

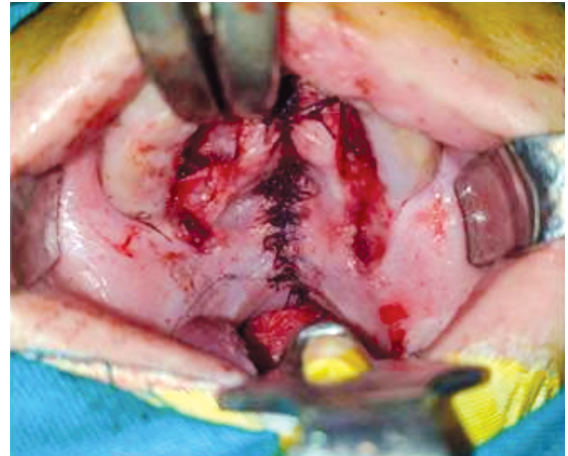


Fig. (16): Mobilization of the flaps medially and closure of oral layer.

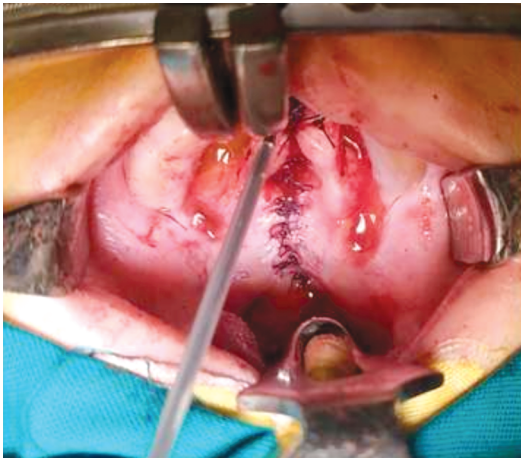


Fig. (17): Fibrin glue injected between oral and nasal layers and at the suture line.



Fig. (18): Two weeks post-operative.



Fig. (19): One month post-operative.



Fig. (20): Three months post-operative.

DISCUSSION

Palatal surgery aims to close the passage between the oral and nasal cavities and create a functional velum that allows good speech production. Many approaches have evolved to fulfill the

fundamental aims of palate repair and primary healing with a single operation.

Palatal cleft care aims to improve quality of life by assisting speech and maxillofacial development. There are four primary elements to consider

when evaluating the quality and timeliness of cleft palate repair: The occurrence of oronasal fistulas, the requirement for subsequent surgery to treat velopharyngeal insufficiency, the need for maxillary osteotomy surgery, and the occurrence of alveolar bone grafting revision surgery are all factors to be considered [9].

Cleft palate repair is not free of complications. The most common side effect of palatoplasty is the formation of an oronasal fistula (ONF). Complete wound dehiscence, oropharyngeal infection, airway obstruction, upper respiratory tract infection, pneumonia, bleeding, feeding difficulties, aspiration, fever, postoperative airway obstruction, otitis media, and mortality are some of the other consequences recorded [10].

Cohen SR et al., [11] for the Von Langenbeck, Furlow Double Opposing Z Plasty, and VeauWardill Kilner Pushback Procedures, 43%, 10%, and 22%, respectively, had fistula rates.

Double flap palatoplasty shows a lower rate of postoperative oronasal fistula; the rate of the fistula is (5%) and has a better velopharyngeal function. The postoperative oronasal fistula rate is (5%) with double flap palatoplasty. The velopharyngeal function is also better [12].

According to their research, Singh V et al., [10] mentioned that Some authors argued that nothing could be done about the sutures being separated immediately following surgery. The inflammation from the oral wound occurs rapidly, making it impossible to keep the sutures in place. Given the evidence, it is practically hard to do a secondary suture. He recommends leaving the wound alone for six months before attempting surgery.

The reasons for palatal mucoperiosteal flap separation are dead space, hematoma, infection, trauma, and inadequate sutures. The hematoma in the hard palate region prevents healing between the two layers. The edges are inflamed by the fifth postoperative day, and the sutures have cut through, resulting in wound dehiscence. Other factors that can lead to palatal fistula formation include suture tension, necrosis of the anterior section of mucoperiosteal flaps, and poor wound healing [13].

Good hemostasis, proper approximation of the mucoperiosteal flap with the sutured nasal mucosa, and drainage holes in the nasal lining can help prevent this problem [8].

Oronasal fistulas are linked to complications, including hypernasality, audible nasal escape, regurgitation, and recurrent infections that may necessitate further surgery [14].

Many doctors and surgeons looked for ways to provide patients with better outcomes and fewer problems. Despite this, it's estimated that more than half of patients who require a surgical correction for fistulas were treated for them, and two-thirds of secondary repair patients needed further surgery to close the wound successfully. Fistulas are a crucial part of treating the cleft palate [15].

Fibrin Glue has the advantages of being safe, practical, and effective. Many authors have looked at the use of Fibrin Glue to fix skin transplants. Haemostasis, graft adherence and acceptance, and antibacterial action are three areas where potential advantages can be found. Fibrin Glue helps wounds heal faster by acting as a template for cellular migration and proliferation. It's also an excellent vehicle for delivering cultured cells, growth hormones, and antibiotics. Aside from the high cost, the downsides of using Fibrin Glue are small. As with any blood product, there is a risk of infection, hypersensitivity, or transfer of serum-related disorders. The rewards of potential benefits must be evaluated against the dangers of potential risks [15].

This study aims to see how effective fibrin glue is as a cleft palate repair supplement. We anticipate adopting a fibrin sealant that is well tolerated and causes few post-operative problems.

In our study technique used for repair of the cleft was double flap palatoplasty in all cases; all cases were operated upon by one-stage repair.

Uncomplicated cases stayed one day postoperatively, while early post-operative complications such as nasal obstruction and hemorrhage stayed 2 days post-operatively in the hospital for follow-up cases.

As regard to Nguyen et al., 2014, made a study on a total of 14,153 patients who had cleft repair with a mean length of stay (LOS) of 2 days (SD, 0.04) [16].

According to complications in our study, There were no deaths or major life-threatening complications. Complications were classified into two groups. The first group with early complications; refers to the complications that occurred within 2 weeks after surgery. And group two with Long-term complications; refers to the complications that occurred beyond 2 weeks after surgery.

According to this classification, 4 complications (20%) occurred within two weeks post-operative and 2 complications (10%) as of late complications

We had 6 complications (30%) in our study. 2 were Upper airway obstruction (10%), and we prevented that obstruction in the following cases by using a Nelaton catheter of appropriate size introduced from the nostril till the pharynx during the application of fibrin glue, and we removed it after confirmation of fibrin glue complete coagulation.

One of them was hemorrhage (5%), and we closely observed the patient in the operating room and gave him Tranexamic acid (kapron) with a dose of 5mg per kg body weight. The bleeding stopped spontaneously without the need for surgical intervention or blood transfusion, one was wound infection (5%), and 2 were oronasal fistulae (10%) one of them (5%) was small (2mm) at the junction between soft and hard palate without any nasal regurgitation that closed spontaneously within 2 months of post-operative follow-up and the other one (5%) was the same case that had wound infection in the early post-operative period and continued beyond our follow-up period for further surgical intervention.

In comparative studies, there seems to be no difference between less and older than 12 months concerning the occurrence of fistula [17]. Our data support this view, even if they have to be interpreted with care. According to the age of patients at the age of operation, we classified into early (less than 14 months) ten patients 50% and late (more than 14 months) ten patients 50%. The correlation between the presence of fistula and age at operation was nonsignificant p -value=0.305, and the correlation coefficient was 0.229.

The "pro" of early intervention is that speech development may be improved if surgery is performed sooner. According to preliminary comparison research, the earlier single-step strategy appears to have a positive impact on speech development [18]. However, it should be noted that early palatoplasty might lead to problems with facial growth and the need for future orthodontics and corrective surgery [19].

The frequency of oronasal fistula after primary cleft palate repair without the use of fibrin glue varied in the included studies from 0% [20] to 60.9% [21].

Deshpande et al., [22] were made up of 709 consecutive non-syndromic patients with cleft palate who had a retrospective review. The immediate post-op interval following bleeding control saw a 2.4% take-back rate (17/709). The patient did not receive any blood transfusions. Of the 512

people studied, 20 experienced complications and developed fistulas, resulting in a complication rate of 3.9 percent. They claim that 3.9% of patients will experience early problems after primary cleft palate repair.

Tache et al., [9] the percentage of instances with fistula among all study participants were calculated as 9.94 percent (95 percent confidence level). The average follow-up length was 53.8 months, ranging from 6 months to 16 years (95 percent confidence level).

Tache et al., [9] in one stage of palatoplasty, the mean percentage of fistulas was 9.1%. The Student t -test for group means was not statistically significant ($p=0.184$). There was no statistical difference in fistula frequencies between syndromic and non-syndromic instances or between male and female patients.

Basha et al., [15] twenty participants were involved in a randomized prospective case-control study. 10 patients underwent palatoplasty without Fibrin Glue in Group 1, and 10 patients underwent palatoplasty with Fibrin Glue in Group 2. The participants ranged in age from 18 months to 25 years. During this time, these individuals were monitored for the development of an oronasal fistula. The incidence of fistula formation was zero (no oronasal fistula) in cases where fibrin glue was used. Still, oronasal fistula formation was noted clinically in 30% of patients in the control group.

Parwaz et al., [14] said that researchers discovered that the breadth and extent of the cleft increase the incidence of oronasal fistula development, with a width of 15mm being related to a statistically significant risk of fistula development. These results matched our results that two patients (10%) with postoperative palatal fistula had a wide cleft palate with a severe palatal index (more than 0.4). one with a hard palate also had a wound infection in the first postoperative week.

Conclusion:

Palatal surgery is a complex surgery that needs a devoted surgeon oriented about various surgical techniques with their modifications. One of the adjuvants that are evolute in various surgical procedures and palatal surgery is the fibrin glue with its known effect in improving tissue healing and hemostatic effect in the sake of decreasing the incidence of early complications of bleeding and later on oronasal fistula (ORF).

We are aware of the limitations, including the small number of patients and the lack of a direct

control group (palatoplasty without fibrin glue injection). The variation in complication rates between locations could be due to patient and surgeon aspects. Although the first findings are encouraging, larger studies with a wide range of patients, surgeons, and procedures are needed.

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