The effect of Acellular Dermal Matrix on the success of primary palatoplasty with intravelar veloplasty

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Abstract

Background

Acellular Dermal Matrix graft is usually used to repair fistulas following a cleft palate and has had positive results. But its use for primary palatoplasty has been less studied. Our aim was to compare the usefulness of using Acellular Dermal Matrix transplantation for primary palatoplasty with intravelar veloplasty in contrast to its lack of use.

Materials and methods

A total of 72 children with cleft palate were included in the study. A prospective case-control observation was conducted. A case group underwent primary palatoplasty with intravelar veloplasty using Acellular Dermal Matrix and the control group had the same surgery without using Acellular Dermal Matrix. Patients were monitored for stula formation, post-operative infection, and ulcers.

Results

Postoperative stula was one of the observed complications in patients with a cleft size greater than 15 mm, in the case group, in 3 out of 24 patients (12.5%) and the control group, in 6 out of 11 patients (54.5%), stula occurred after surgery. Postoperative infection and wound dehiscence was not observed in any group.

Conclusions

The nature of the cleft palate and the lack of muscles and structures necessary to repair the palate make stula formation more likely in patients with a larger cleft palate. Based on the results of this study, the use of an Acellular Dermal Matrix in patients with a cleft greater than 15 mm is significantly effective in reducing fistula formation.

Background

The surgical procedure used to correct or repair a palate in a person with a cleft palate is called palatoplasty (1). The primary goal is to close the cavities between the mouth and nose so that patients could have natural speaking (2), ingestion, respiration, and development of structures in their mouth (2, 3). Palatoplasty could be used for any degree of cleft palate. This surgical procedure is usually operated on infants with the ages between 6 to 12 months as the most suitable ones (4). Following the closure of the palate layers, an intravelar veloplasty is performed to correct and change the position of the palatal muscles (5). Because of the improvements in palate performance, the patient's complaint about the complications decreases (6, 7). If palate reconstruction is successful, the velopharyngeal area closes completely and the patient obtains the proper speech capability (6). Although it has not yet been fully scientifically proven, it seems that palatoplasty may reduce the chance of patients with cleft palate having middle ear inflammation and developing deafness (2). Various techniques including local...
mucoperiosteal ap, V-Y two-layer repair, superior lip mucosal or myomucosal flap, buccal myomucosal flap, superiorly based facial artery myomucosal flap, tongue flap, free flap, free cartilage graft. Distraction Osteogenesis, Acellular Dermal Matrix have been reported for the cleft palate (8-10).

Fistula, infection and bleeding are the complications reported after cleft palate repair (11). Factors leading to the occurrence of fistula include the width of the cleft, the technique used in the surgery, the inappropriate repair of the cleft, the inappropriate selection of the suture region and thus the pressure on the area, age and gender of the patient during surgery (12). After primary palatoplasty, the primary palatal fistula formation with a probability of 0 to 67% and recurrence of about 25% to 100% were reported. If the cleft palate is closed with the epidermal mucus flaps, the probability of recurrence of forming a fistula is higher (13).

Medical researchers have proposed various methods to reduce fistula formation including the use of buccal flaps (13), bone grafting (14), buccal myomucosal flap (15) Buccal fat pad flap (16), buccal mucosal flap (17), and high growth factor (PRGF) plasma (18).

Acellular Dermal Matrix (ADM) is widely used in multiple plastic surgeries (19). Acellular matrices have different usages including their potential role in the regeneration of organs or tissues. The ability to mimic the physiological conditions in the microscopic environment of the recipient tissue is one of the advantages of using these matrices (20). Once ADM is used in transplantation, it acts as a scaffold for the implantation of the recipient’s cells and a facilitator of subsequent adhesions and angiogenesis. These natural scaffolds are used in the manufacture of artificial limbs and tissue repair and could be considered a solution to one of the biggest medical challenges from organ failure to plastic surgeries (21).

ADM is derived from the dermis, which is soft tissue. During the process of decellularization, the skin’s extracellular matrix structure is retained. This skin graft does not lead to immune response stimulation due to its lack of cells; therefore, patients do not require to receive high doses of immune system suppressors. As a result, they are used in the initial closure of wide openings in soft and hard tissues such as cleft palate and lip (22).

In recent years, ADM has been used to repair the cleft palate fistula (23); however, the use of this graft and particular surgical technique for primary palatoplasty has been less studied (24). The present study was designed to investigate the usage and effect of ADM in the early stages of palatoplasty. The result help in improving the quality of life of patients with Cleft pallet.

Materials And Methods

This research is a case-control, prospective observational study. The participants were the patients who were referred to the Cleft palate clinic of Isfahan University of Medical Sciences. After being examined by the experts (The Cleft palate treatment team consisting of a maxillofacial surgeon, plastic surgeon, orthodontist, pediatrician and speech therapist), they were registered for primary palatoplasty. Inclusion
criteria were having ages between 6 months to 6 years old and cleft palate Veau classes II to IV. Exclusion criteria were parents’ unwillingness to give consent, diagnosis of a craniofacial syndrome, a disorder such as Ehlers Danlosus Syndrome and Pseudoxanthoma elasticum which are characterized by wound healing defect, and the Veau class I cleft palate. All children referred to Alzahra University Hospital in Isfahan in 2017 who had inclusion criteria were divided into two groups (72 patients): primary palatoplasty with ADM and other primary palatoplasty procedures. Patients were 32 girls and 40 boys (16 girls and 20 boys in each group) 6 months to 6 years old. None of the patients were excluded from the study. Patients were monitored for 6 months following the primary palatoplasty.

**Palatoplasty method**

In all patients, palatoplasty was performed by a single plastic surgeon. For the patients who were in the case group, ADM (2 × 4 cm ultra-thin sheet, 0.3–0.4 mm thickness, REGEN ALLOGRAFT) was transferred to a sterile field, soaked in a suitable physiological serum or recipient's blood for about 15-20 minutes. (mandatory). The piece used is prepared in a square shape and the corners were drilled so that there would be no sharp points.

General anesthesia through the general tracheal tube with a topical injection of lidocaine 1% with 1:100,000 epinephrine as well as the dose of first-generation cephalosporin for prophylaxis, was induced. (cefalotin 50 / kg in children and 1 g / IV in adults). Then, the location of the cleft palate in the oral mucosa on the bone surface of the palate was separated from the nasal part by the surgeon. In the next step, the palate mucoperiostoneal flap covered the cleft flap and about 2 to 3 mm of it, and was prepared as a pocket for ADM (Figure 1). The ADM was placed around the cleft palate and below the surface of the mucoperiosteum flap was sutured with vicryl or monocryal 4.0. For 36 patients in the study group ADM, and 36 patients in the control group the same method without ADM was used. Patients were followed up 6 months after their recharge from the hospital. The width of the cleft palate was defined using the Veau classification.

Recommended care after primary palatoplasty were oral antibiotic therapy, using chlorhexidine mouthwash for one week and a diet containing drinks and soft foods for three weeks after the palatoplasty.

**Statistical Analysis**

The demographic characteristics between the two groups were statistically compared using T-test and Chi-square test or Fisher exact test. and a P-value <0.05 was considered statistically significant.

**Results**
Table 1 represents patient characteristics briefly, including demographics, cleft, and hospitalization stay time of patients in the case and control groups. There were no statistically significant differences in patient demographics including age at operation, sex, or hospital stay and distribution of cleft widths. Cleft characteristics based on the Veau classification had statistically significant differences in two groups.

There were no statistically significant differences in postoperative fistula formation in the study and control groups. In patients treated with ADM, in three cases (8.3%) six controls (16%) the fistula formation was observed. But fistula rate in the subgroup >15mm Cleft width was statistically significantly lower in the study group (12.5%) versus the control group (54.5%, $P = 0.04$). The other complications including infection and bleeding were similar between the groups. Complications are resumed in Table 2.

### Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Study Group (n = 36)</th>
<th>Control Group (n = 36)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at operation (mo), mean (SD)</td>
<td>27.3 (17.6)</td>
<td>25.0 (9.4)</td>
<td>0.49</td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>20 (56)</td>
<td>20 (56)</td>
<td>1</td>
</tr>
<tr>
<td>Female</td>
<td>16 (44)</td>
<td>16 (44)</td>
<td>1</td>
</tr>
<tr>
<td>Hospital Stay (H), mean (SD)</td>
<td>54 (14.7)</td>
<td>48 (13.8)</td>
<td>0.54</td>
</tr>
<tr>
<td>Cleft characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Veau classification, n (%)</td>
<td></td>
<td></td>
<td>0.03*</td>
</tr>
<tr>
<td>Soft+ secondary hard palate</td>
<td>14 (39)</td>
<td>24 (67)</td>
<td></td>
</tr>
<tr>
<td>Soft+ secondary hard palate+ primary hard palate</td>
<td>22 (61)</td>
<td>12 (33)</td>
<td></td>
</tr>
<tr>
<td>Cleft width (mm), mean (SD)</td>
<td>15.1 (5.1)</td>
<td>14.7 (6.1)</td>
<td>0.77</td>
</tr>
<tr>
<td>&lt; 5 mm</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>5-15 mm</td>
<td>11</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>&gt;15mm</td>
<td>24</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>ADM use, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>36 (100)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>NO</td>
<td>0 (0)</td>
<td>36 (100)</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Complications
### Complications

<table>
<thead>
<tr>
<th>Complications</th>
<th>Study Group (n = 36)</th>
<th>Control Group (n = 36)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fistula, n (%)</td>
<td>3 (8.8)</td>
<td>6 (16.6)</td>
<td>0.285</td>
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<tr>
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<td></td>
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<tr>
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<td>0</td>
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</tr>
<tr>
<td>5-15 mm</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>&gt;15 mm</td>
<td>3</td>
<td>6</td>
<td>0.004*</td>
</tr>
<tr>
<td>No</td>
<td>33 (91.2)</td>
<td>30 (83.4)</td>
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</tr>
<tr>
<td>Bleeding, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>0(0)</td>
<td>0(0)</td>
<td>0.0</td>
</tr>
<tr>
<td>No</td>
<td>36 (100)</td>
<td>36 (100)</td>
<td></td>
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<tr>
<td>Infection, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>0(0)</td>
<td>0(0)</td>
<td>0.0</td>
</tr>
<tr>
<td>No</td>
<td>36 (100)</td>
<td>36 (100)</td>
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</table>

* Shows P value <0.05, statistically significant differences

### Discussion

The cleft palate is one of the most common craniofacial anomalies which requires a multidisciplinary treatment approach. Physiotherapy, nutrition, orthodontic management, and speech therapy can improve the quality of life of patients with cleft palate. Primary palatoplasty is usually recommended at early ages which ultimately leads to the return of the natural speech production mechanism. In palatoplasty, tension-free two-layer closure of oral cavities without penetration of water and fluids reduces the risk of the oronasal fistula. The repair will be effective when less tension is exerted on the oral layers (23). The success criteria of primary palatoplasty are the rate of oronasal fistula, Velopharyngeal insufficiency (VPI), and achievement of natural speech (25). Repairing soft palate, hard palate and the vomer resulted from a cleft is a challenge for the surgeon. Application of Autogenous mucosal grafts causes injury to the donor site and leads to an increase in postoperative complications, Therefore, as an alternative, the use of ADM (which is a freeze-dried acellular dermal matrix that consists of a preserved basement membrane and an extracellular matrix and collagen bundles plus elastic fibers is the main component of it) had benefits (26). The advantage of ADM compared to the previous allografts includes the lack of any cells that potentially can transmit viruses and the absence of class I and II histocompatibility complex associated with transplant rejection (27).

When the use of ADM was first proposed for cleft palate surgery, successful results were observed in a small group of patients. A few years later, Kirschner in an empirical study in 2006 presented the results of using ADM to repair cleft palate fistulas. Four other studies assessed the applicability and utility of using ADM to prevent the occurrence of fistula in primary palatoplasty (28). In recent years, various studies regarding the use of ADM in reconstructive surgeries such as cleft palate repair were performed, which have had promising results (29-31).
The largest collection of information about the use of ADM in primary palatoplasty was published by Losee et al. in 2008. In order to close the cleft in these patient's implantation of ADM and an algorithmic approach that would provide proper stable repair and also close the nasal cavity was used. The size of the cleft was not mentioned in this study; however, the closure of the cleft was achieved in 92.2% of the patients. The use of ADM in tenuous repair and the closure of the cleft and nasal defect resulted in satisfactory results (32). Our study also got the same results as the aforementioned study in our work. It should be noted that there are different techniques for palatoplasty, which, are chosen based on not just the advantages or disadvantages, but also according to the surgeon's skill and mastery (33). The method we use was Extended muscle release Intravelar Veloplasty. Based on the Veau classification, types of cleft palate are classified according to the degree of cracking and fissure site. The greater the cleft, the less filler tissue to perform the repair.

Most of the cleft palates are repaired with a local flap but rarely, there are large clefts of the palate that requires intra/extra oral or a free flap. Due to the contracture effect in the repair process, perhaps the fistula gets enlarged by the scar. The severity of the scar could disrupt the development of the palate (34).

A prospective study that conducted on 130 patients undergoing primary palatoplasty (II and III Veau classification) demonstrated that the incidence of fistula in the study group using ADM was 1.5% versus 12.3% in the control group. The results of this study showed strong evidence of the positive effect of using ADM in the prevention of fistula following primary palatoplasty (35)

A Systematic Review published in 2014 stated that there is correlation between Veau classes III and IV and the incidence of fistula (36). In our study at first glance, it seems that taking advantage of ADM does not make a significant difference in the reduction of fistula formation but when we assess the formation of fistula according to the cleft classification, it is obvious that the cleft size is a significant factor in the probability of fistula formation (Veau class III)

The results of the study demonstrated that using ADM in patients with fissures larger than 15 mm can significantly prevent the occurrence of a fistula. Accordingly, to solve this issue, using ADM as a scaffold and coverage tissue that helps tissue growth and angiogenesis at the desired site could be helpful.

If we study the subgroups according to the size and width of the incision, a significant difference can be observed in the subgroup with a size greater than 15 mm. It seems that taking advantage of ADM can be effective in reducing the formation of postoperative fistula, so it is suggested that in order to reduce the health care costs due to the fistula repair reoperation, which is imposed on the patient and the health care system, more studies are needed in this field.

If a similar type of surgical technique to previous studies is selected, the confounding factors of the study will be less and a better explanation for the results can be provided.
The small sample size was one of the limitations of this study

Declarations

Acknowledgment

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Authors' Contributions

H.A. conceived the main idea. M.H, Z.M. and A.G. contributed in data gathering and analysis. SH. F, F.D F.M and A.G drafted the manuscript H.A. Z.M, A.G and SH. F revised the manuscript and acted as the guarantor of the manuscript. All authors read and approved the final manuscript.

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Availability of Data and Materials

SPSS data of the participant can be requested from the authors. Please write to the corresponding author if you are interested in such data.

Ethics Approval and Consent to Participate

Written informed consent was obtained from all study participant’s parents and/or legal guardian(s). in our study. The purpose of this research was completely explained to the patients, and they were assured that their information would be kept confidential by the researcher. The study was approved by the ethical committee of Isfahan University of Medical Sciences.

All methods were carried out according to the relevant guideline and regulations

Consent for publication
Informed consent was obtained from study participant's parents and/or their legal guardians to publish the information/image(s) in an online open-access publication

**Competing Interests**

The authors declare that they have no competing interests.

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Figures
Figure 1

Using Acellular Dermal Matrix (ADM) in palatal repair