

Original Study

Labial Adhesion: New Classification and Treatment ProtocolMirzaman Huseynov MD^{1,*}, Ali Ekber Hakalmaz MD²¹ Department of Pediatric Surgery, Private Safa Hospital, Istanbul, Turkey² Department of Pediatric Surgery, Gaziosmanpasa Public Hospital, Istanbul, Turkey

A B S T R A C T

Study Objective: To determine the subtypes of labial adhesion (LA) and arrange treatment options accordingly.

Design and Setting: Patients who presented to our clinic with LA between July 2016 and February 2018 were divided into 4 groups. Location of the adhesion area, thickness of the adhesive tissue, and response to topical steroid (betamethasone valerate 0.1% ointment) therapy were identified as common features.

Participants: Seventy-five prepubertal girls.

Interventions and Main Outcome Measures: To determine the subtypes of the LA and evaluate the treatment response of patients in each subtype group.

Results: LA was divided into 4 subtypes according to their common characteristics. For patients with type I, 2 weeks of topical steroid treatment resulted in complete recovery (100%). For those with type II, 12 (80%) patients had complete response to topical steroid treatment for an average of 3 weeks. Type III and IV patients were completely unresponsive to topical steroid treatment.

Conclusion: Classification of LA patients into subtypes and determination of treatment on the basis of this classification make a major contribution in planning the treatment of patients, not by trial-and-error, but using a predetermined strategy.

Key Words: Labial adhesions, Labial agglutination, Labial adhesion management, Prepubertal

Introduction

Labial adhesion (LA) can be defined as fusion of the labia minora in the midline. The disorder is stated by different titles in the literature such as labial fusion, labial agglutination, or labial synechia. LA is not present at birth, and it is thought to develop during re-epithelization of micro-traumatized hypoestrogenized labial skin.¹ LA is one of the most common causes of presentations to pediatric surgery clinics among prepubertal girls.² LAs are usually asymptomatic and are detected incidentally by a meticulous pediatrician. Because they are usually asymptomatic, follow-up is sufficient. However, sometimes blockage of urine flow might predispose to different symptoms such as postvoid dribbling, strain, and irritation during urination, vaginal pain or discharge, and recurrent urinary tract infection. Treatment of such symptomatic cases is indicated.

Several medical (such as topical steroids, estrogen ointments, or combinations) and interventional (such as manual separation, or surgical separation) treatment options are described. However, the individualized choice of treatment method for each patient is still unclear and there is no consensus in the literature. This divergence can essentially result from the fact that LA is considered as a homogenous disease. In our practice, we observed that LA can in fact be divided into many subtypes. Therefore, we offer that the treatment of LA should be planned according

to the characteristics of subtype. In this study we aimed to identify the subtypes of LA and plan treatment options accordingly.

Materials and Methods*Study Population*

After obtaining approval from the institutional board (decision number 24/22.02.2020), the files of 75 patients who presented to our clinic with LA between July 2016 and July 2019 and had an indication for treatment, and treated by the same pediatric surgeon were retrospectively examined. Patients with coexisting perianal, perineal, or vulvar diseases and patients who developed recurrence after the treatment in our clinic were not included in the study. The cases were evaluated in terms of the age at the time of presentation, referral indications, symptoms, presence of diaper usage, treatment modality, compliance with the treatment, and recurrence. Additionally, the patients were divided into 4 groups according to their common features. Location of the adhesion area, thickness of the adhesive tissue, and response of the adhesion to topical steroid therapy were identified as common features.

Indications and Management of Treatment

The indications for treatment of LA in our clinic are identified as: (1) symptoms (recurrent urinary tract infection with no other cause, strain during urination, post-void dribbling); and (2) parents who were concerned about the

The authors indicate no conflicts of interest. Funding: None.

* Address correspondence to: Mirzaman Huseynov, MD, Yildiztepe Mah, Bagcilar Cad No 108, 34203 Bagcilar, Istanbul, Turkey; Phone: +905070250707

E-mail address: mirzamanhuseynov@gmail.com (M. Huseynov).

“abnormal” appearance of the external genitalia of their child with a strong desire to proceed with urgent surgery.

In our clinical practice, if an indication for treatment is present, administration of 0.1% betamethasone valerate ointment (Betnovate, GlaxoSmithKline), 2 times a day is the first-line therapy. Patients are taught to apply the ointment with their finger along the line of adhesions with very gentle pressure. If topical treatment is continued, patients are called back for a control visit at the end of the third and sixth weeks of treatment. If the ointment therapy fails, interventional treatment is performed. We always prefer surgical separation to manual separation as the interventional treatment method.³ After the surgical separation, petroleum jelly is applied to the wound edges for 10 days, twice daily. We consider that this prevents the wound from readhesion until completion of epithelialization of the wound edges.

Follow-up

Patients were called back for control examinations at the third week, sixth week, and third month of recovery and followed-up once a year afterward for a total of 2 years. Meanwhile, mothers of the patients are taught to examine their children monthly in the beginning and encouraged to continue even after discontinuation of patient follow-up.

Definitions

Complete LA was defined as the *complete* adherence of the labia minora (there is generally a tiny or pinpoint opening on the adhesion, just below the clitoris that allows urine outflow).

Incomplete LA was defined as the partial adherence of the labia minora.

Complete response to topical steroid treatment was defined as the complete resolution of adhesion and normalization of the anatomical appearance.

Incomplete response to topical steroid treatment was defined as the absence of any change in adhesion or incomplete resolution of adhesion, with failure to achieve normal anatomic appearance.

Statistical Analyses

Statistical analyses were performed using MedCalc for Windows, version 19.1 (MedCalc Software). A normal distribution of the data was verified using the Kolmogorov-Smirnov test. The homogeneity of variance was determined using the Levene test. Statistical significance between frequencies was calculated using the χ^2 test with Fisher exact test correction. A correlation analysis was performed using Spearman methods. The level of statistical significance was set at *P* less than .05.

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. This was an observational, retrospective study so

it was not necessary to request informed consent. Data were anonymized.

Results

A total of 75 patients were included. LA was diagnosed for the first time in 65 patients. In the remaining 10 patients, LA recurred after manual separation of a complete LA in a different center. The mean reference age was 16 (range, 2–111) months. The most frequent (56%) reason for presentation (*n* = 42) was LA detected during the routine examination, whereas 20% of the patients with LA (*n* = 15) had complaints. The complaints and the reasons for presentation are shown in Table 1. All but 2 of the patients had complete LA. The average follow-up time period was 16 (range, 3–24) months.

The disease was divided into 4 subtypes according to their common characteristics, and are described in the following sections.

LA Type I (48%)

In LA type I, fusion tissue is translucent and in some instances so thin that it can separate only using minor traction of labial folds during examination. The reflections of the hymen and other vestibular structures can be easily visualized behind the thin and translucent line of adhesion (Fig. 1). Complete separation (100%) was obtained in an average of 2.5 weeks (range, 2–3 weeks) in all of these patients with the administration of 0.1% betamethasone ointment 2 times a day.

LA Type II (20%)

In LA type II fusion tissue is thick. The reflections of the hymen and other vestibular structures cannot be visualized (Fig. 2A). In the study, both patients with incomplete LA were type II patients. In 80% (*n* = 12) of the patients, 6 of them were the patients whose adhesions recurred after manual separation, with type II adhesion completely recovered with 3-week topical steroid therapy. For the remaining 20% (*n* = 3), the topical steroid therapy was extended by an additional 3 weeks. However, 2 of the patients could not comply with treatment after the fifth week of the therapy. The remaining 1 patient underwent surgical separation because of the absence of improvement after the sixth week of therapy. The 2 noncompliant families were reached by phone and stated that they had undergone manual separation at another center.

Table 1
Reason for Presentation of the Prepubertal Girls with Labial Adhesion

Reason for Presentation	n (%)
Incidental finding in the course of a medical check-up	42 (56)
Family notice	18 (24)
Irritation during urination	9 (12)
Strain during urination	3 (4)
Recurrent urinary tract infection	3 (4)
Total	75

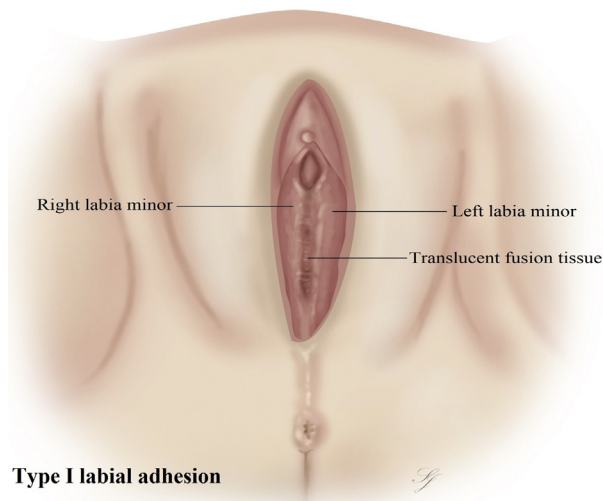


Fig. 1. Type I labial adhesion.

LA Type III (24%)

In LA type III fusion tissue is thick. The reflection of the vulvar components cannot be visualized. The most important issue that distinguishes type III adhesion from type II adhesion is that the hymen is slightly adherent to the labia minora (Fig. 3B). Sometimes during surgical separation, it can be noticed that the fibrotic tissues forming the fusion adhere firmly to the edges of the hymen. None of the patients with type III adhesion showed improvement at the third week of the topical steroid therapy. Therefore the therapy was extended up to 6 weeks. Only 12 (66%) of the patients, 4 of whom were the patients whose adhesions recurred after manual separation, complied with the 6-week therapy, and none of them showed improvement at the end of the sixth week. These patients underwent surgical separation. All of the noncompliant families were reached by phone and stated that they had undergone manual separation at another center.

LA Type IV (8%)

The most important characteristic of this subtype that differentiates it from the others is the fact that the fusion

area is lateralized to the right or left side, and not located in the midline (Fig. 4A). In such patients, adhesion occurs when one labia minora adheres to the inner surface of the other (Fig. 4B). None of these patients complied with the 6-week topical steroid therapy. All of them underwent surgical separation.

There was no statistically significant difference between the patients with different types of LA in terms of age, reason for presentation, symptoms, and presence of diaper usage.

Recurrence developed in 6 (8%) cases. All of the recurring patients had type III and IV adhesions. All of those with recurrent disease underwent surgical separation. No second recurrences were observed in these patients during the follow-up period.

Because incomplete LA cases are generally asymptomatic and this classification is made to protocolize treatment, and because the responses of incomplete cases ($n = 2$) are not different from the others, the amount of residual opening is not included among the classification criteria.

Discussion

The study has 2 main contributions to the literature. Primarily, to our knowledge, this is the first study to classify LA to guide treatment. Second, to our knowledge, this is the first study to protocolize treatment on the basis of classification of clinical findings.

LA is thought to develop during re-epithelization of microtraumatized hypoestrogenized labial skin.¹ Some of the causes of LAs include families' excessive desire to clean the perineum of their babies, and baby wipes used for this purpose, lichen sclerosis, infectious vulvovaginitis, genital trauma, sexual abuse, and others.^{4,5} LA is mostly seen in patients between 6 months and 2 years of age.⁶ In our study, 70% of the patients were younger than 2 years of age, which is consistent with the literature. The incidence of LA in the literature is between 0.6% and 5%.^{5–7} Because LA is usually asymptomatic, the actual incidence is considered to be higher. Twenty percent of the patients in our study presented with symptoms. In the literature, the reported incidence of symptoms in patients with LA is between 10% and 40%.^{8,9}

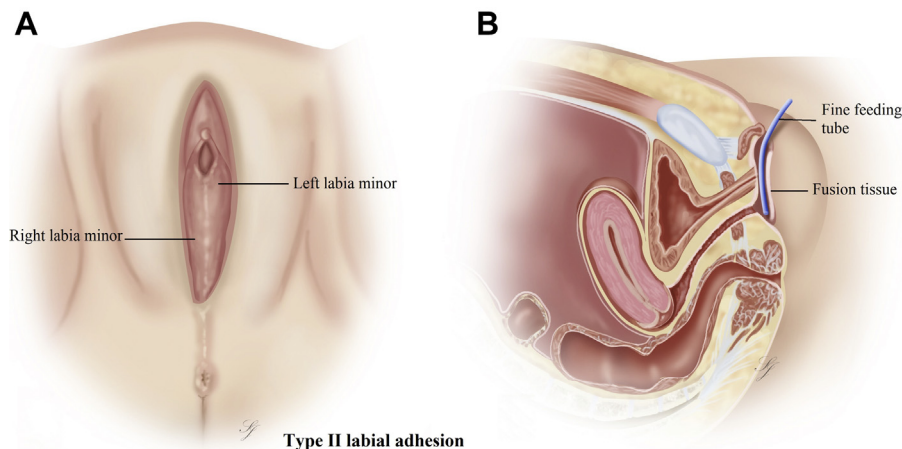


Fig. 2. Type II labial adhesion. (A) Anterior and (B) sagittal view.

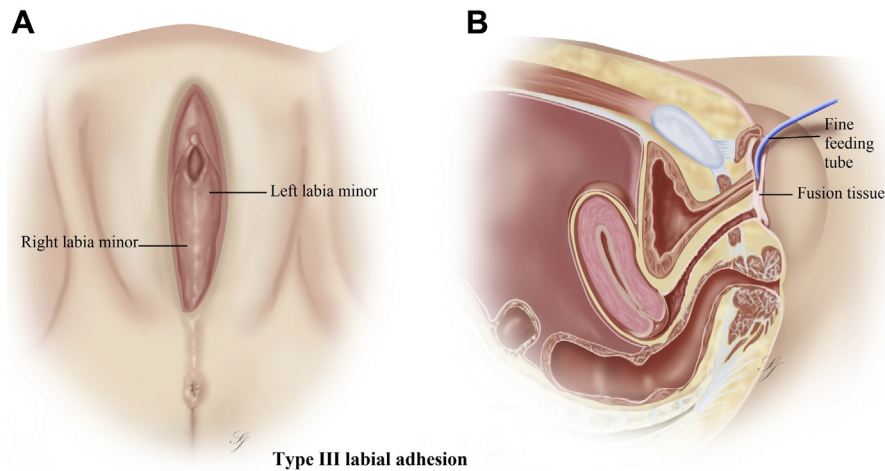


Fig. 3. Type III labial adhesion. (A) Anterior and (B) sagittal view.

There is a significant debate in the literature regarding which method should be used to treat LA during the prepubertal period. Although some authors recommend the interventional treatment option as the first-line treatment,^{10,11} follow-up without intervention is usually preferred in asymptomatic patients, and topical estrogen or betamethasone is considered as the first-line treatment in patients with an indication for treatment.^{5,9}

Because LA is rarely seen in newborns in mini puberty and during the postpubertal period, it is thought that LA is associated with the hypoestrogenic status in prepubertal girls.¹² This rationalizes the use of topical estrogen therapy to treat the disease. In the literature, 2-8 weeks of topical estrogen therapy was reported to be successful in 50%-88% of patients.^{13,14} Several studies suggest that hypoestrogenic status does not play a role in the etiology of the disease.¹⁵ Moreover, the use of topical estrogen has been reported in many studies to cause some side effects such as thelarche or vulvar pigmentation changes.^{13,16,17}

Topical betamethasone therapy provides a good alternative to topical estrogen in that it causes no or minimal side effects in the medical treatment of LA.¹³ In our clinical

practice, we prefer betamethasone for the medical treatment because of contradictory information relating to the role of estrogen in the etiology of LA, the systemic side effects of topical estrogen, and the success of betamethasone with minimal side effects.

The recurrence rate in our study was 8%. There are various data in the literature regarding recurrence rates, ranging from 0% to 76%.^{10,18} In an earlier study from our clinic in which we compared manual and surgical separation, recurrence rates were found to be 51.8% and 12.8% for manual and surgical separation methods, respectively.³ After detecting lower recurrence rates with the surgical separation method, it became our interventional method of choice. When we add type I cases that show 100% recovery and no recurrence with topical steroid therapy to our former data, we can explain our current low recurrence rate as an overall 8%. In our former study, we detected recurrences after the 11th month on average. In the current study, the number of patients with a follow-up period younger than 11 months was quite low. However, there still might have been some missed recurrences.

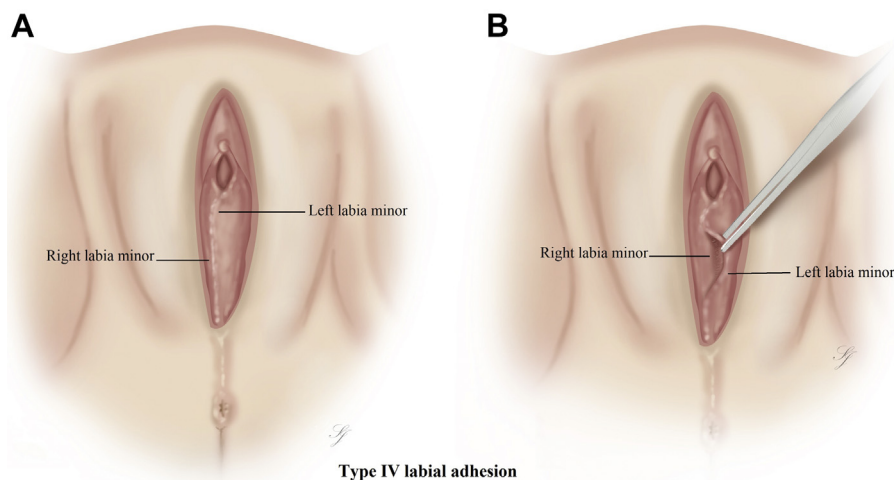


Fig. 4. Type IV labial adhesion. (A) Anterior view and (B) view during surgical separation.

Table 2
Treatment Protocol for Labial Adhesion

Labial Fusion Type	Response to 0.1% Betamethasone treatment	Treatment Preference
Type I (48%)	100%	0.1% Betamethasone 2 × 1
Type II (20%)	80%	0.1% Betamethasone 2 × 1 If no response after 3 weeks, surgical separation
Type III (24%)	0%	Surgical separation
Type IV (8%)	0%	Surgical separation

In our literature search, we found limited information about the classification of LA. The present classifications are on the basis of the proportion of adherent labia or using terms such as “small opening,” “pinhole opening,” and “complete adhesion.”¹² Such classifications make no contribution to guide the treatment and to identify the treatment options.

The type I patients in our study constituted almost half of all LA patients. These patients showed complete response to the 0.1% betamethasone therapy of 2.5 weeks on average. Moreover, 80% of the type II patients showed complete response to the topical steroid therapy. Therefore, we believe that topical steroid therapy should be the first-line treatment in patients who meet the type I and type II LA criteria.

We observed that topical steroid therapy failed in 20% of the type II patients and in all of the type III and IV patients. Therefore, we believe that the first-line treatment should be surgical separation in type III and IV patients (Table 2). Because none of the type III patients were responsive to topical steroid treatment, they should be differentiated from the type II patients, who have an 80% response rate to topical treatment and might have an appearance similar to type III adhesions. According to our experience with the surgical separations for topical treatment-resistant type II and type III patients, hymenal adhesions were present with type III LAs, for which we recommend a thin (4-French) feeding tube being advanced through the opening below the clitoris to the back of the fusion tissue during the examination. The feeding tube is expected to show resistance in type III patients with adhesions between the fusion tissue and the hymen (Figs. 2B and 3B). No local anesthetic drug was used during the examination with the feeding tube. All patients tolerated this examination well. It was found that adhesion tissue was adhered to the hymen during surgical separation in all patients who were diagnosed with type III LA during the examination.

The main problem in type III, type IV, and unresponsive to topical steroid treatment type II patients is noncompliance with the treatment. In fact, a time period of 3 weeks seems to be a critical period for topical steroid therapy, because, on the basis of our experience, compliance with the treatment decreases after the third week of topical therapy. However, for patients whose parents agreed with extension of treatment after 3 weeks, no improvement was seen despite completion of the sixth week of the topical steroid therapy. None of the parents agreed with extension of treatment after 6 weeks. In other words, because all of

the treatment-responsive cases showed full recovery in 3 weeks and extension of treatment beyond 6 weeks showed no contribution to outcome, we do not recommend continuation of treatment beyond 3 weeks. That being said, treatment course can be extended with parental confirmation if there are signs of recovery as thinning of the fusion or conversion from a complete fusion to an incomplete fusion.

The most important information supporting our classification is, in our opinion, the different, somewhat incompatible and overlapping responses to topical steroid treatments in the literature. For example, there are studies that reported a 15%–36% response to topical estrogen treatment,¹⁹ and studies that reported that this response increased to 100%.²⁰ However, the average success is approximately 50%–70%.^{13,14,17} The same is also true for topical betamethasone treatment.^{9,17,21} The main event in these studies is which subtypes of LA in the selected patient population are predominant. The average success rate in the literature is 50%–70%, which corresponds to the success in our study (topical steroid success rate was 64% in our study, with all of these patients being type I and II patients). In other words, the most important factor determining the success level in these studies in the literature is the proportion of the type I and II patients in the selected patient population.

The use of betamethasone valerate as the only topical treatment in our study is the main limitation of the study because estrogen treatment is still considered the mainstay of treatment for LAs, and some practitioners continue to use this as primary treatment.

Conclusion

Classification of LA patients into subtypes and determination of treatment on the basis of this classification make a major contribution in planning the treatment of patients, not by trial-and-error, but using a predetermined strategy. Initiation of treatment with a predetermined strategy provides a major advantage with respect to trust relationships between patient and physician, and compliance of patients/patient relatives with treatment.

References

1. Eyk NV, Allen L, Giesbrecht E, et al: Pediatric vulvovaginal disorders: a diagnostic approach and review of the literature. *J Obstet Gynaecol Can* 2009; 31:850
2. Bacon JL: Prepubertal labial adhesions. Evaluation of a referral population. *Am J Obstet Gynecol* 2002; 187:327
3. Huseynov M: Pre-pubertal labial adhesion surgery: the first study to compare manual or surgical separation. *Ann Med Res* 2019; 26:991
4. Celayir AC, Oral M: What is the real cause of labial synechia. *Zeynep Kamil Tıp Bülteni* 2005; 36:161
5. Bacon JL, Romano ME, Quint EH: Clinical recommendation: labial adhesions. *J Pediatr Adolesc Gynecol* 2015; 28:405
6. Leung AKC, Robson WLM, Tay-Uyboco J: The incidence of labial fusion in children. *J Paediatr Child Health* 1993; 29:235
7. McCann J, Wells R, Simon M, et al: Genital findings in prepubertal girls selected for nonabuse: a descriptive study. *Pediatrics* 1990; 86:428
8. Rubinstein A, Rahman G, Rizzo P, et al: Labial adhesions: experience in a children's hospital. *Arch Argent Pediatr* 2018; 116:56
9. Mayoglou L, Dulabon L, Martin-Alguacil N, et al: Success of Treatment modalities for labial fusion: a retrospective evaluation of topical and surgical treatments. *J Pediatr Adolesc Gynecol* 2009; 22:247

10. Hutson JM, O'Brien M, Beasley SW, et al: Part IV: abdomen: anus perineum and female genitalia. In: Hutson JM, O'Brien M, Beasley SW, et al, editors. *Jones' Clinical Paediatric Surgery*. Oxford, Wiley-Blackwell, 2015, pp 164–171
11. Nurzia M, Eickhorst K, Ankem M, et al: The surgical treatment of labial adhesions in pre-pubertal girls. *J Pediatr Adolesc Gynecol* 2003; 16:2
12. Norris JE, Elder CV, Dunford AM, et al: Spontaneous resolution of labial adhesions in pre-pubertal girls. *J Paediatr Child Health* 2018; 54:748
13. Muram D: Treatment of prepubertal girls with labial adhesions. *J Pediatr Adolesc Gynecol* 1999; 12:67
14. Khanam W, Chogtu L, Mir Z, et al: Adhesion of the labia minora-a study of 75 cases. *Obstet Gynecol Surv* 1978; 33:364
15. Çağlar MK: Serum estradiol levels in infants with and without labial adhesions: the role of estrogen in the etiology and treatment. *Pediatr Dermatol* 2007; 24: 373
16. Capraro VJ, Greenberg H: Adhesions of the labia minora. A study of 50 patients. *Obstet Gynecol* 1972; 39:65
17. Eroglu E, Yip M, Oktar T, et al: How should we treat prepubertal labial adhesions? Retrospective comparison of topical treatments: estrogen only, betamethasone only, and combination estrogen and betamethasone. *J Pediatr Adolesc Gynecol* 2011; 24:389
18. Watanabe T, Matsubara S, Fujinaga Y, et al: Manual separation followed by local cleanliness for pediatric labial adhesion. *J Obstet Gynaecol Res* 2010; 36:667
19. Dowlut-McElroy T, Higgins J, Williams KB, et al: Treatment of prepubertal labial adhesions: a randomized controlled trial. *J Pediatr Adolesc Gynecol* 2019; 32:259
20. Leung AK, Robson WL, Kao CP, et al: Treatment of labial fusion with topical estrogen therapy. *Clin Pediatr (Phila)* 2005; 44:245
21. Myers J, Sorensen C, Wisner B, et al: Betamethasone cream for the treatment of pre-pubertal labial adhesions. *J Pediatr Adolesc Gynecol* 2006; 19:407