

## Original Study

# Success of Treatment Modalities for Labial Fusion: A Retrospective Evaluation of Topical and Surgical Treatments

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**Abstract.** *Study Objective:* Standard treatment for girls with labial fusion has included topical estrogen cream, manual separation, or surgery. Side effects may limit the use of topical estrogen. Betamethasone has recently shown efficacy at separating labial fusion. Local irritation and inflammation may be an initiator of labial fusion. No adverse effects of betamethasone treatment have been documented. Long-term side effects are unknown. This study compares therapies for conservative management of labial fusion for efficacy and focuses on the response rate, time to separation, recurrence, and side effects of treatment.

*Design:* A retrospective chart review.

*Participants:* One hundred fifty-one prepubertal girls, mean age 3 years (range 0.25–8.75 years) diagnosed with labial fusion.

*Main Outcome Measures:* To investigate the incidence of related symptoms, length of topical estrogen or betamethasone treatment, side effects, rate of successful separation, rates of recurrence, percentage requiring surgery, and postoperative outcomes in patients with labial adhesion who underwent treatment.

*Results:* Of 151 patients with labial adhesion, 11 (7.3%) presented with urinary frequency, 30 (19.9%) with urinary tract infections, 13 (8.6%) with vaginitis, and 19 (12.6%) with post-void dripping. When compared to patients treated with betamethasone (1.3 months), patients treated primarily with premarin took nearly twice as long (2.2 months) for resolution of their adhesions. Rates of recurrence were lower for patients receiving betamethasone therapy. Side effects for estrogen therapy included breast budding and vaginal bleeding, and for betamethasone, local irritation was reported. Some patients went on to surgery and experienced recurrence after surgery.

*Conclusion:* Initial comparison of topical estrogen and betamethasone treatment of labial fusion suggests that betamethasone may separate fusion quicker with less recurrence and fewer side effects than topical estrogen therapy.

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**Key Words.** Labial fusion—Labial adhesion—Vaginoplasty—Vagina—Estrogen—Betamethasone—premarin

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### Introduction

Labial fusion is a common vaginal condition estimated to occur in 0.6%–5% of prepubertal girls.<sup>1–3</sup> Though it is often asymptomatic, it may be discovered when the fusion results in post-void dripping (urinary incontinence), urinary tract infections, vaginitis (vaginal irritation), hematuria, and urinary frequency. The inability of urine to exit the vaginal opening results in a pooling of urine. Urinary retention may cause colonization, leading to recurrent urinary tract symptoms in 20%–40% of these patients.<sup>4</sup> Labial fusion may be caused by inflammation and low prepubertal estrogen levels.<sup>4</sup> However, labial fusion has been noted in association with isolated premature thelarche, suggesting the existence of factors other than estrogen insufficiency.<sup>5</sup> Estradiol levels have been found to be slightly lower (but not meeting the level of statistically significant) in girls with labial fusion.<sup>6</sup> It has been postulated that in low-estrogen environments, the inflammatory cascade can progress with little to no restriction. This progression leads to an overactivation of macrophages, which are responsible for destroying the cells proximal to the site of inflammation. As the body attempts to repair the damaged areas of epithelium, new collagen fibers are laid down. Regarding estrogen effects on fibroblasts, at normal physiological (postpubertal) estrogen levels, there is a 40% decrease in collagen synthesis.<sup>7</sup> In prepubertal situations with exceedingly low levels of endogenous estrogen, there is an environment more conducive to fibrosis and eventual scarring.

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Labial fusion most commonly occurs between the ages of 2 and 7 years.<sup>1-3</sup> Until recently, topical estrogens and surgery were the mainstays of therapy. Typically, premarin vaginal cream is used. This cream is a mixture of conjugated estrogens from natural sources. The components are sodium estrone sulfate, sodium equilin sulfate, and the sodium sulfate conjugates 17  $\alpha$ -dihydroequilin, 17  $\alpha$ -estradiol, and 17  $\beta$ -dihydroequilin. The use of betamethasone as an initial intervention was recently reported by Myers.<sup>8</sup> Betamethasone dipropionate is a synthetic glucocorticoid that is used topically on the skin and has potent anti-inflammatory actions.

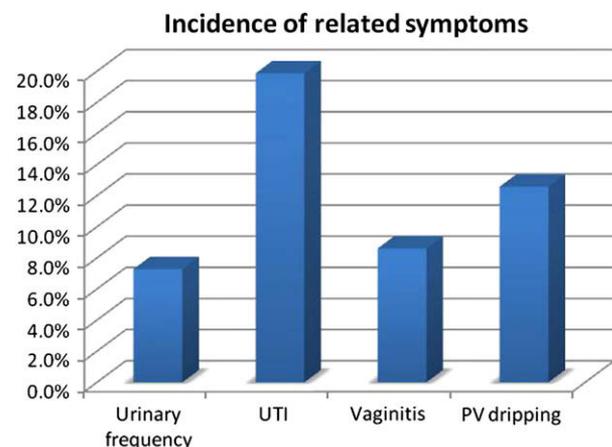
Topical therapy is the preferred initial form of treatment but is occasionally unsuccessful. Lysis of adhesions has been described both manually and surgically. Manual separation is sometimes attempted but may be painful. This problem is occasionally addressed with the use of topical lidocaine cream cream. Surgical separation is required for failure of medical therapy or manual separation in symptomatic cases, obviously scarred or thick adhesion, and for symptomatic cases in which parents (or child) refuse other forms of therapy. Recurrences are not uncommon with any form of therapy. Maintaining vaginal patency after surgery is not absolute. Fibrosis and scarring may increase with numerous attempts at manual disruption as well as surgical separation. Fibrosis can be attributed to a buildup of collagen as the repair process takes place. Primary goals for treatment are resolution of clinical symptoms. Topical therapies such as estrogen and betamethasone may resolve adhesions but may also minimize recurrences.

## Materials and Methods

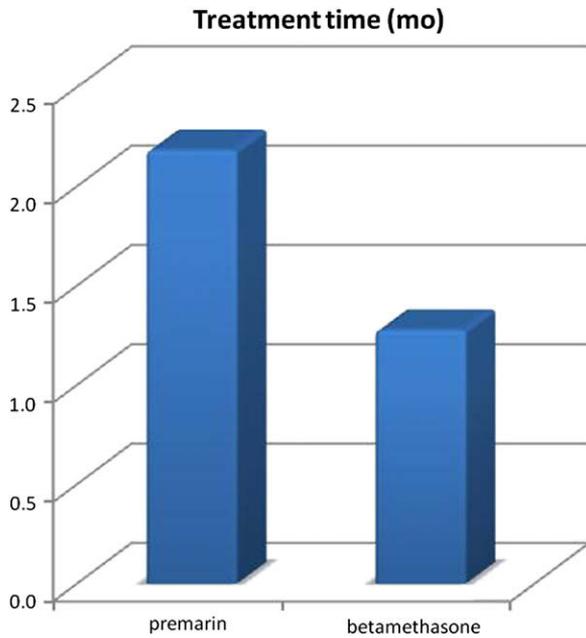
A comprehensive review of the medical literature was performed using PubMed. A 10-year retrospective chart review of all girls (151) presenting with labial adhesion as a secondary referral to a pediatric urology office was completed. The patients varied in age from 3 months to 9 years (mean 3 years). Primary treatment was daily application of either estrogen cream or betamethasone cream to the site of the adhesion and to follow the progress. If patients failed estrogen treatment, they had a trial of betamethasone; if they failed betamethasone, a trial of estrogen was given; upon medical treatment failure, they had the option of surgery. Data were collected on the incidence of related symptoms, length of topical estrogen treatment, length of topical betamethasone treatment, side effects of medical therapies, rate of successful separation, rate of recurrence, percentage requiring surgery, and postoperative outcomes (which included postoperative recurrence and treatment of labial fusion).

## Results

Of the 151 patients who presented with labial adhesion, 11 (7.3%) presented with urinary frequency, 30 (19.9%) with urinary tract infections, 13 (8.6%) with vaginitis, and 19 (12.6%) with post-void dripping (Fig. 1). Mean length of topical estrogen treatment was 2.2 months (range 0 to 24 months), with separation in 71.2% (104/146) of patients. Betamethasone therapy was used in 19 patients for a mean of 1.25 months (range 2 weeks to 12 weeks), with separation occurring in 78.9% (15/19) of patients (Figs. 2 and 3). One patient discontinued betamethasone and began premarin treatment because of related complaints of erythema and pain. Thirteen patients were started on premarin cream and were switched to betamethasone therapy (12 due to nonresponse of the adhesion to therapy, 1 due to side effects). Thirty-five percent (51/146) had recurrences of labial fusion with premarin. With betamethasone treatment, there was a recurrence rate of 15.8% (3/19) (Fig. 4). Surgery was required in 40 of 146 (27.4%) patients treated with premarin. Three of 19 patients (15.8%) in the betamethasone group were refractory to betamethasone treatment and required surgery (Fig. 5). Eleven of 43 (26%) patients who had surgical separation of the labial adhesion had recurrence postoperatively. These patients were treated with either topical estrogens (7 of 11 patients, or 64%), topical betamethasone (2 of 11 patients, or 18%), or a combination of the two (2 of 11 patients, or 18%). Eight of the 11 (73%) patients had resolution with medication, whereas 2 of the 11 (18%) patients with premarin-only treatment required a second surgical separation. Side effects of estrogen were minimal, with rash (5 of 146 patients, or 3%), breast development (7 of 146 patients, or 5%), and vaginal bleeding in 1 child (0.7%). Discontinuation of estrogen resulted in resolution of side effects. Betamethasone-related side effects included 1 instance



**Fig. 1.** Related clinical findings at presentation of labial fusion.

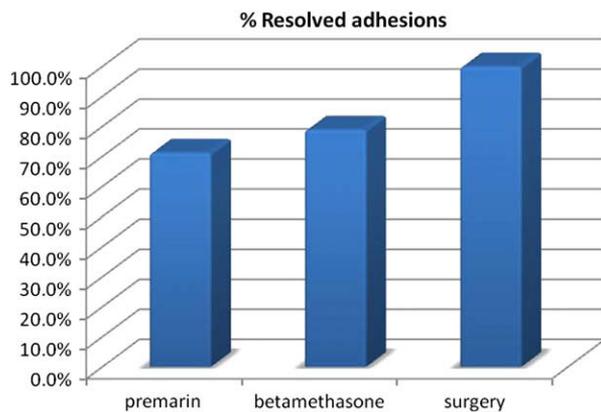


**Fig. 2.** Time to resolution of labial adhesion in patients treated with premarin and betamethasone.

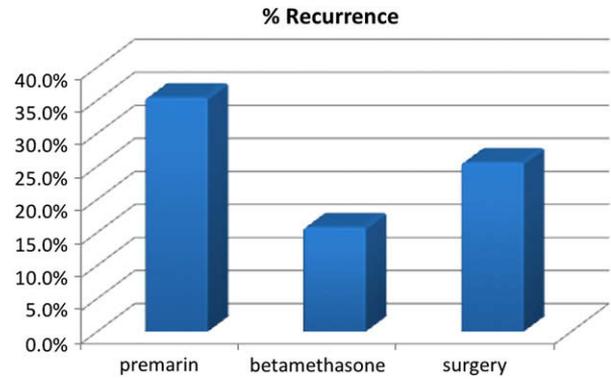
of fine pubic hair development and 1 case of mild erythema and pain of the area surrounding the vulva.

**Discussion**

Historically, medical treatment of labial adhesion involved a regimen of topical estrogen used for an unspecified period of time, with the physician determining response or nonresponse in separation of the adhesion. This choice of treatment was successful in approximately 50%-88% of patients,<sup>9,10</sup> resulting in separation of the adhesion in about 2-8 weeks. A review article by Tebruegge notes both success and short-term safety for use in treatment of prepubertal symptomatic girls. Estrogens need to be used for several weeks before separation.<sup>11</sup> In the past few years, betamethasone cream has been promoted as

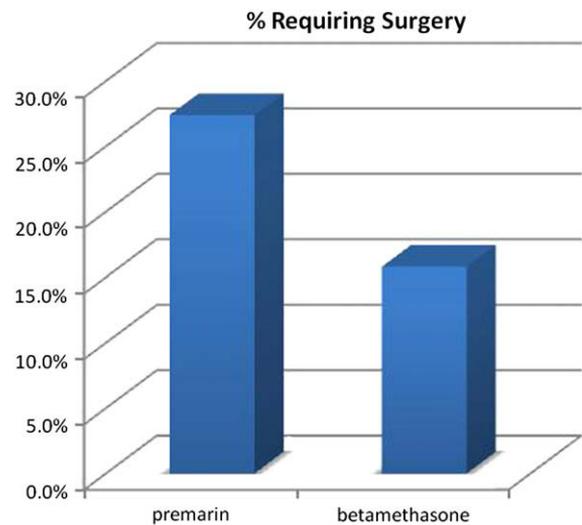


**Fig. 3.** Resolution of labial adhesion after treatment.



**Fig. 4.** Recurrence of labial adhesion after treatment.

a treatment modality in conjuncture with topical estrogen therapy.<sup>11</sup> Topical therapies are appropriate as first-line treatments for primary and recurrent labial adhesions and may be necessary after surgical separation. Topical estrogen therapy has also been found to improve outcomes after manual separation.<sup>12</sup> Recurrence is common, but adhesions tend to become thick and more difficult to separate with each subsequent attempt, more so if the adhesion is manually separated (more traumatic methods may result in more fibrosis). Surgical lysis of the adhesion can be attempted if medical therapy fails. Short-term side effects of topical estrogens include breast budding, rash or irritation, and vaginal bleeding. Short-term side effects of betamethasone include erythema, folliculitis, pruritus, vesiculation, fine hair growth, and skin atrophy. Long-term pharmacological treatment of labial fusion using either estrogens or betamethasone may have the potential for serious side effects. This risk is unknown. There is a potential for long-term risks of adrenal suppression, growth suppression, and possibly cancer in



**Fig. 5.** Refractory to therapy and required surgery.

chronic corticosteroid use, and for cancer in chronic estrogen use. Administration of these 2 topical medications should be limited to the smallest amount compatible with an effective separation followed by careful hygiene and bland emollients. Safety and efficacy in pediatric patients have not otherwise been established. Clinically, no guidelines have been structured for the duration or limits of topical therapy.

Labial adhesions have also been suggested to form in inflammatory conditions. There have been recorded instances of labial fusion following various insults to the vulvar tissue.<sup>9</sup> Following an insult resulting in irritation, vaginal tissue can become traumatized or inflammatory, resulting in adhesion during the healing process, due to an overactive healing response.

Labial adhesions do form most commonly in prepubertal girls, in which estrogen levels are low. They are rare after puberty. Many spontaneously resolve at the time of puberty. A study of estradiol levels in girls with and without labial adhesions found no significant difference.<sup>6</sup> Adhesions have been found in states of normal estrogenation; postpubertally, postpartum, and in premature thelarche. Thus, estrogen level alone is not responsible for this occurrence.

In a recent publication by Thornton targeting sex hormone dependent tissue of the dermal papilla cells,<sup>13</sup> the interrelationship of estrogen receptors and betamethasone was explored in greater detail. Neither androgens nor estrogens were found to alter estrogen receptor (ER)  $\alpha$  mRNA levels, but treatment with betamethasone significantly reduced ER  $\alpha$  levels to 38% of untreated controls. Estrogen receptor  $\beta$  levels were unaffected by any steroid treatment. Treatment with betamethasone significantly stimulated the expression of aromatase mRNA approximately 9-fold. These observations provide evidence for a glucocorticoid-dependent mechanism for selective action of estradiol via ER  $\beta$ . Up-regulation of aromatase combined with down-regulation of ER  $\alpha$  may provide a basis for selective action of estradiol produced locally by autocrine or paracrine mechanisms. Treatment with betamethasone may address both estrogen-related influence on the formation of labial adhesion and inflammatory-mediated causes as well.

In our study, we have found, as others have, that estrogen is indeed therapeutically successful for the separation of adhesions in a large number of (but not all) treated cases. Betamethasone is also successful therapeutically, when used primarily and also for medical failures of estrogen treatment. This study suggests that labial separation occurred more quickly and with less recurrence in the betamethasone group. But it should be recognized that significantly more cases were treated with premarin than with betamethasone. Evidence for these findings would be stronger in a prospectively designed, randomized study using a control

group. This is the first comparison study examining the outcomes of treatment with these 2 medications. Future comparison studies of these 2 topical therapies, using a randomized, prospective design, would be valuable.

## Conclusion

Topical estrogens and betamethasone were effective treatments for labial fusion in the majority of patients. Data collected within this study suggest that betamethasone as a primary method of treatment decreased the time necessary to treat by approximately half. The percentage of recurrence was less when using betamethasone when compared to premarin treatment. Side effects for short-term use were minimal for both. Labial fusion after surgical separation can also be successfully treated with topical therapy.

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