Dermatologic Management of Hidradenitis Suppurativa and Impact on Pregnancy and Breastfeeding

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PRACTICE **POINTS**

- Some medications used to treat hidradenitis suppurativa (HS) may have teratogenic effects and be contraindicated during breastfeeding.
- We summarize what treatments are proven to be safe in pregnancy and breastfeeding and highlight the need for more guidelines and safety data for dermatologists to manage their pregnant patients with HS.

Hidradenitis suppurativa (HS) is a chronic inflammatory skin disease that most commonly affects women of childbearing age. The symptoms of the disease are managed with a multitude of topical and systemic medications. The course of HS changes during pregnancy, and some women can experience postpartum flares. Thus, it is important to be aware of how pregnancy may alter the treatment plan for women and impact their choice to breastfeed. The following review summarizes medical management for HS and its safety during pregnancy and breastfeeding.

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Hidradenitis suppurativa (HS) is a chronic inflammatory skin disease associated with hyperandrogenism and is caused by occlusion or rupture of follicular units and inflammation of the apocrine glands.[1-3] The disease most commonly affects women (female to male ratio of 3:1) of childbearing age.[1,2,4,5] Body areas affected include the axillae and groin, and less commonly the perineum; perianal region; and skin folds, such as gluteal, inframammary, and infraumbilical folds.[1,2] Symptoms manifest as painful subcutaneous nodules with possible accompanying purulent drainage, sinus tracts, and/or dermal contractures. Although the pathophysiology is unclear, androgens affect the course of HS during pregnancy by stimulating the affected glands and altering cytokines.[1,2,6]

During pregnancy, maternal immune function switches from cell-mediated T helper cell (T_H1) to humoral T_H2 cytokine production. The activity of sebaceous and eccrine glands increases while the activity of apocrine glands decreases, thus changing the inflammatory course of HS during pregnancy.[3] Approximately 20% of women with HS experience improvement of symptoms during pregnancy, while the remainder either experience no relief or deterioration of symptoms.[1] Improvement in symptoms during pregnancy was found to occur more frequently in those who had worsening symptoms during menses owing to the possible hormonal effect estrogen has on inhibiting T_H1 and T_H17 proinflammatory cytokines, which promotes an immunosuppressive environment.[4]

Lactation and breastfeeding abilities may be hindered if a woman has HS affecting the apocrine glands of breast tissue and a symptom flare in the postpartum period. If HS causes notable inflammation in the nipple-areolar complex during pregnancy, the patient may experience difficulties with lactation and milk fistula formation, leading to inability to breastfeed.[2] Another reason why mothers with HS may not be able to breastfeed is that the medications required to treat the disease are unsafe if passed to the infant via breast milk. In addition, the teratogenic effects of HS medications may necessitate therapy adjustments in pregnancy.[1] Here, we provide a brief overview of the medical management considerations of HS in the setting of pregnancy and the impact on breastfeeding.

MEDICAL MANAGEMENT AND DRUG SAFETY

Dermatologists prescribe a myriad of topical and systemic medications to ameliorate symptoms of HS. Therapy regimens often are multimodal and include antibiotics, biologics, and immunosuppressants.[1,3]

Antibiotics

First-line antibiotics include clindamycin, metronidazole, tetracyclines, erythromycin, rifampin, dapsone, and

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The eTable is available in the Appendix online at www.mdedge.com/dermatology.

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fluoroquinolones. Topical clindamycin 1%, metronidazole 0.75%, and erythromycin 2% are used for open or active HS lesions and are all safe to use in pregnancy since there is minimal systemic absorption and minimal excretion into breast milk.[1] Topical antimicrobial washes such as benzoyl peroxide and chlorhexidine often are used in combination with systemic medications to treat HS. These washes are safe during pregnancy and lactation, as they have minimal systemic absorption.[7]

Of these first-line antibiotics, only tetracyclines are contraindicated during pregnancy and lactation, as they are deemed to be in category D by the US Food and Drug Administration (FDA).[1] Aside from tetracyclines, these antibiotics do not cause birth defects and are safe for nursing infants.[1,8] Systemic clindamycin is safe during pregnancy and breastfeeding. Systemic metronidazole also is safe for use in pregnant patients but needs to be discontinued 12 to 24 hours prior to breastfeeding, which often prohibits appropriate dosing.[1]

Systemic Erythromycin—There are several forms of systemic erythromycin, including erythromycin base, erythromycin estolate, erythromycin ethylsuccinate (EES), and erythromycin stearate. Erythromycin estolate is contraindicated in pregnancy because it is associated with reversible maternal hepatoxicity and jaundice.[9-11] Erythromycin ethylsuccinate is the preferred form for pregnant patients. Providers should exercise caution when prescribing EES to lactating mothers, as small amounts are still secreted through breast milk.[11] Some studies have shown an increased risk for development of infantile hypertrophic pyloric stenosis with systemic erythromycin use, especially if a neonate is exposed in the first 14 days of life. Thus, we recommend withholding EES for 2 weeks after delivery if the patient is breastfeeding. A follow-up study did not find any association between erythromycin and infantile hypertrophic pyloric stenosis; however, the American Academy of Pediatrics still recommends short-term use only of erythromycin if it is to be used in the systemic form.[8]

Rifampin—Rifampin is excreted into breast milk but without adverse effects to the infant. Rifampin also is safe in pregnancy but should be used on a case-by-case basis in pregnant or nursing women because it is a cytochrome P450 inducer.

Dapsone—Dapsone has no increased risk for congenital anomalies. However, it is associated with hemolytic anemia and neonatal hyperbilirubinemia, especially in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency.[12] Newborns exposed to dapsone are at an increased risk for methemoglobinemia owing to increased sensitivity of fetal erythrocytes to oxidizing agents.[13] If dapsone use is necessary, stopping dapsone treatment in the last month of gestation is recommended to minimize risk for kernicterus.[9] Dapsone can be found in high concentrations in breast milk at 14.3% of the maternal dose. It is still safe to use during breastfeeding, but there is a risk of the infant developing hyperbilirubinemia/G6PD deficiency.[1,8] Thus, physicians may consider performing a G6PD screen on infants to determine if breastfeeding is safe.[12]

Fluoroquinolones—Quinolones are not contraindicated during pregnancy, but they can damage fetal cartilage and thus should be reserved for use in complicated infections when the benefits outweigh the risks.[12] Quinolones are believed to increase risk for arthropathy but are safe for use in lactation. When quinolones are digested with milk, exposure decreases below pediatric doses because of the ionized property of calcium in milk.[8]

Tumor Necrosis Factor α Inhibitors—The safety of anti–tumor necrosis factor (TNF) α biologics in pregnancy is less certain when compared with antibiotics.[1] Anti–TNF-α inhibitors such as etanercept, adalimumab, and infliximab are all labeled as FDA category B, meaning there are no well-controlled human studies of the drugs.[9] There are limited data that support safe use of TNF-α inhibitors prior to the third trimester before maternal IgG antibodies are transferred to the fetus via the placenta.[1,13] Anti–TNF-α inhibitors may be safe when breastfeeding because the drugs have large molecular weights that prevent them from entering breast milk in large amounts. Absorption also is limited due to the infant's digestive acids and enzymes breaking down the protein structure of the medication.[8] Overall, TNF-α inhibitor use is still controversial and only used if the benefits outweigh the risks during pregnancy or if there is no alternative treatment.[1,3,9]

Ustekinumab and Anakinra—Ustekinumab (an IL-12/IL-23 inhibitor) and anakinra (an IL-1α and IL-1β inhibitor) also are FDA category B drugs and have limited data supporting their use as HS treatment in pregnancy. Anakinra may have evidence of compatibility with breastfeeding, as endogenous IL-1α inhibitor is found in colostrum and mature breast milk.[1]

Immunosuppressants

Immunosuppressants that are used to treat HS include corticosteroids and cyclosporine.

Corticosteroids—Topical corticosteroids can be used safely in lactation if they are not applied directly to the nipple or any area that makes direct contact with the infant's mouth. Intralesional corticosteroid injections are safe for use during both pregnancy and breastfeeding to decrease inflammation of acutely flaring lesions and can be considered first-line treatment.[1] Oral glucocorticoids also can be safely used for acute flares during pregnancy; however, prolonged use is associated with pregnancy complications such as preeclampsia, eclampsia, premature delivery, and gestational diabetes.[12] There also is a small risk of oral cleft deformity in the infant; thus, potent corticosteroids are recommended in short durations during pregnancy, and there are no adverse effects if the maternal dose is less than 10 mg daily.[8,12] Systemic steroids are safe to use with breastfeeding, but patients should be advised to wait 4 hours after ingesting medication before breastfeeding.[1,8]

Cyclosporine—Topical and oral calcineurin inhibitors such as cyclosporine have low risk for transmission into breast milk; however, potential effects of exposure through breast milk are unknown. For that reason, manufacturers state that cyclosporine use is contraindicated during lactation.[8] If cyclosporine is to be used by a breastfeeding woman,

monitoring cyclosporine concentrations in the infant is suggested to ensure that the exposure is less than 5% to 10% of the therapeutic dose.[13] The use of cyclosporine has been extensively studied in pregnant transplant patients and is considered relatively safe for use in pregnancy.[14] Cyclosporine is lipid soluble and thus is quickly metabolized and spread throughout the body; it can easily cross the placenta.[9,13] Blood concentration in the fetus is 30% to 64% that of the maternal circulation. However, cyclosporine is only toxic to the fetus at maternally toxic doses, which can result in low birth weight and increased prenatal and postnatal mortality.[13]

Isotretinoin, Oral Contraceptive Pills, and Spironolactone

Isotretinoin and hormonal treatments such as oral contraceptive pills and spironolactone (an androgen receptor blocker) commonly are used to treat HS, but all are contraindicated in pregnancy and lactation. Isotretinoin is a well-established teratogen, but adverse effects on nursing babies have not been described. However, the manufacturer of isotretinoin advises against its use in lactation. Oral contraceptive pill use in early pregnancy is associated with increased risk for Down syndrome. Oral contraceptive pill use also is contraindicated in lactation for 2 reasons: decreased milk production and risk for fetal feminization. Antiandrogenic agents such as spironolactone have been shown to be associated with hypospadias and feminization of the male fetus.[7]

COMMENT

Women with HS usually require ongoing medical treatment during pregnancy and immediately postpartum; thus, it is important that treatments are proven to be safe for use in this specific population. Current management guidelines are not entirely suitable for pregnant and breastfeeding women given that many HS drugs have teratogenic effects and/or can be excreted into breast milk.[1] Several treatments have uncertain safety profiles in pregnancy and breastfeeding, which calls for dermatologists to change or create new regimens for their patients. Close management also is necessary to prevent excess inflammation of breast tissue and milk fistula formation, which would hinder normal breastfeeding.

The eTable lists medications used to treat HS. The FDA category is listed next to each drug. However, it should be noted that these FDA letter categories were replaced with the Pregnancy and Lactation Labeling Rule in 2015. The letter ratings were deemed overly simplistic and replaced with narrative-based labeling that provides more detailed adverse effects and clinical considerations.[9]

Risk Factors of HS—Predisposing risk factors for HS flares that are controllable include obesity and smoking.[2] Pregnancy weight gain may cause increased skin maceration at intertriginous sites, which can contribute to worsening HS symptoms.[1,5] Adipocytes play a role in HS exacerbation by promoting secretion of TNF-α, leading to increased inflammation.[5] Dermatologists can help prevent postpartum HS flares by monitoring weight gain during pregnancy, encouraging smoking cessation, and promoting weight and nutrition goals as set by an obstetrician.[1] In addition to medications, management of HS should include emotional support and education on wearing loose-fitting clothing to avoid irritation of the affected areas.[3] An emphasis on dermatologist counseling for all patients with HS, even for those with milder disease, can reduce exacerbations during pregnancy.[5]

CONCLUSION

The selection of dermatologic drugs for the treatment of HS in the setting of pregnancy involves complex decision-making. Dermatologists need more guidelines and proven safety data in human trials, especially regarding use of biologics and immunosuppressants to better treat HS in pregnancy. With more data, they can create more evidence-based treatment regimens to help prevent postpartum exacerbations of HS. Thus, patients can breastfeed their infants comfortably and without any risks of impaired child development. In the meantime, dermatologists can continue to work together with obstetricians and psychiatrists to decrease disease flares through counseling patients on nutrition and weight gain and providing emotional support.

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APPENDIX

eTABLE. Hidradenitis Suppurativa Therapies and Recommendations for Use in Pregnancy and Breastfeeding

HS drug	FDA category[3,a]	Pregnancy	Breastfeeding	Other
Benzoyl peroxide wash	C	Safe during pregnancy[7]	Safe during lactation, minimal systemic absorption[7]	
Topical clindamycin 1%	B	Safe during pregnancy, minimal systemic absorption[1]	Minimal excretion into breast milk[1]	
Systemic clindamycin	B	Safe during pregnancy[1]	Small concentration enters breast milk, safe[1,8]	
Topical metronidazole 0.75%	B	Safe during pregnancy, minimal systemic absorption[1]	Minimal excretion into breast milk[1]	
Systemic metronidazole	B	Safe during pregnancy[1]	Need to discontinue 12–24 h prior to breastfeeding[1]	
Topical erythromycin 2%	B	Safe during pregnancy, minimal systemic absorption[1]	Minimal excretion into breast milk[1]	
Systemic erythromycin	B	Safe during pregnancy[1]	Can use with caution and short term only; need to withhold for 2 wk after delivery due to risk of infantile hypertrophic pyloric stenosis[8]	Erythromycin ethylsuccinate is the preferred form for pregnant patients[11]
Tetracyclines	D	Contraindicated during pregnancy[1]	Contraindicated during lactation[1]	If used for >3 wk, can cause dental staining and poor bone growth in infants[1,8]
Rifampin	C	Safe during pregnancy[1]	0.05% of maternal daily dose excreted into breast milk, but no adverse effects[1,8]	Cytochrome P450 inducer, contributes to drug-drug interactions[1]
Dapsone	C	Safe during pregnancy, but need to stop in last month of gestation to minimize risk of kernicterus in infant[1,9]	Safe for use during lactation, but risk of hemolytic anemia in infant with G6PD deficiency[1,8,12]	Consider G6PD deficiency screening of infant prior to breastfeeding[12]
Quinolones	C	Used only for complicated infections[12]	Safe when digested with breast milk, exposure is far less than pediatric doses[8]	Can damage fetal cartilage if used during pregnancy[12]
TNF-α inhibitors	B	Safety uncertain[1,12]	Safety uncertain, no adverse effects reported[1,12]	

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eTABLE. (continued)

HS drug	FDA category[9,a]	Pregnancy	Breastfeeding	Other
Ustekinumab	B	Safety uncertain[1,12]	Limited data[1,12]	
Anakinra	B	Safety uncertain[1]	Limited data[1]	May be compatible with breastfeeding as endogenous IL-1α inhibitor is found in breast milk[1]
Systemic corticosteroids	C,[b] D[c]	Small risk of oral cleft deformity[1]	No adverse effects if maternal dose is 5–10 mg daily[8]	Advised to wait 4 h after ingesting medication before breastfeeding[1,8]
Topical corticosteroids	C	Safe during pregnancy, can be injected intralesionally[1,12]	Safe, exposure in breast milk is minimal[8]	Avoid applying high-potency topical steroids to nipple[8]
Cyclosporine	C	No evidence of teratogenicity in humans[1]	Contraindicated during lactation[8]	Need to monitor infant for cyclosporine toxicity (edema, hypertension, seizure) if mother chooses to breastfeed[8]
Oral contraceptive pills	X	Contraindicated during pregnancy[7]	Contraindicated during lactation[7]	Increased incidence of Down syndrome if used in early pregnancy[7]
Spironolactone	D	Need to avoid during pregnancy[7]	Need to avoid during lactation[7]	Associated with hypospadias and feminization of male fetus[7]
Isotretinoin	X	Teratogenic agent, contraindicated during pregnancy[7]	Need to avoid during lactation[7]	

Abbreviations: FDA, US Food and Drug Administration; G6PD, glucose-6-phosphate dehydrogenase; HS, hidradenitis suppurativa; TNF, tumor necrosis factor.

[a]Prior FDA pregnancy risk categories include A: well-controlled human studies indicate no fetal risk in all trimesters; B: animal studies indicate no fetal risk and well-controlled human studies are unavailable, or animal studies indicate fetal risk that has not been confirmed by human studies; C: animal studies indicate adverse effects to the fetus, or animal studies are unavailable and well-controlled human studies are lacking[d]; D: human studies indicate fetal risk[d]; X: studies in animals or humans indicate fetal risk that clearly outweighs potential benefits.[9]

[b]In second trimester.

[c]In first trimester.

[d]Potential benefits of the drug may warrant use in pregnant women despite potential risks.