Pregnancy and dermatologic therapy

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Dermatologists should be familiar with medication safety in pregnancy to be able to prescribe safely and confidently to pregnant women or women who may become pregnant during the course of treatment for dermatologic conditions. Topical medications should be considered first-line therapy for pregnant women, but certain systemic medications are safe to use in pregnancy and may be prescribed if necessary. Dermatologic surgery may be performed during the second trimester of pregnancy with proper positioning, but elective procedures should be delayed until the postpartum period. (J Am Acad Dermatol 2013;68:663-71.)

Key words: dermatologic surgery; dermatologic therapy; medication safety; pregnancy; systemic medications; topical medications.

Women present to their physicians with a variety of skin disorders in the pregnant and nonpregnant state, with certain dermatoses encountered only during pregnancy.[1] These women typically present first to their obstetricians during routine visits, but they sometimes require referral to a dermatologist for continued treatment of pre-existing or new skin symptoms. Female dermatologic patients may also become pregnant during the treatment of their skin disease. It is important, therefore, for dermatologists to be able to prescribe safely and confidently to pregnant women and women who may become pregnant.

DRUG CLASSIFICATION FOR PREGNANCY

Birth defects related to the use of diethylstilbestrol and thalidomide in the mid-20th century led to the development of the Food and Drug Administration (FDA) Pregnancy and Lactation Categories.[2] One of 5 categories is assigned to each drug before it is released.[3] Because of the impossibility of conducting controlled studies with medication use in pregnant women, these categories reflect a risk-benefit ratio based on animal studies or epidemiologic data.[4] The classifications are included in Table I.[3]

Although the FDA pregnancy classifications are the most widely used, other sources for determining the safety of a medication during pregnancy include Teratogen Information Service, Reproductive Toxicology Service (www.reprotox.org), *Drugs in Pregnancy and Lactation* by Briggs et al,[5] *US Pharmacopeial Dispensing Information*,[6] and case reports.[3] Because the FDA can be slow to update the ratings based on the most recent data and research, sources such as the Reproductive Toxicology Service World Wide Web site may be more up to date.[1]

TIMELINE FOR RISK

When prescribing a medication, it is important to determine whether a patient is actively preventing pregnancy with contraception, trying to conceive or not preventing pregnancy, or is currently pregnant in a specific trimester and/or period of development (preimplantation, embryonic, or fetal).[1]

For sexually active women not on contraception, there is an 85% chance of becoming pregnant within 1 year.[7] Avoiding potentially teratogenic agents during the embryonic period, which is the second through the eighth week after conception when organogenesis occurs, is especially important.[1] Because some women will not have a positive home pregnancy test result until up to 5 weeks after conception, these patients should be treated with medications that are safe during pregnancy.[1] Although the highest period of risk is during organogenesis, certain structures, such as the brain, teeth, and bones, remain susceptible after 9 weeks. Thus, some medications that do not cause harm during

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organogenesis may cause complications later in pregnancy.[1]

TOPICAL MEDICATIONS DURING PREGNANCY

For most dermatologic conditions in pregnancy, topical treatments remain the safest choice and should be considered first-line therapy. Table II summarizes the pregnancy classifications and risks of each topical medication.

Acne and rosacea

For acne and rosacea, a plethora of topical medications are available, most of which are safe for use during pregnancy. The topical retinoids tretinoin and adapalene are category C. Some studies suggest that topical tretinoin is teratogenic in the first trimester,[8-10] but another study contradicts that finding.[11] Absorption is minimal, and risk is unlikely, but alternative treatments should be considered in the first trimester if they are available.[12] Adapalene, also category C, has minimal absorption, so use during pregnancy could be considered once the benefits and risks have been discussed with the patient.[12] Data suggest that the potential risk of teratogenicity of both agents is only during the first trimester, and no problems have been reported in studies where use occurs in the second and third trimester.[12] A practical approach would be to consider treatment with these agents after the first trimester in consultation with the patient's obstetrician. Topical tazarotene, on the other hand, is category X because of retinoid-like anomalies found in animal studies, so it is contraindicated.[12]

Antibacterial topical agents used for acne and rosacea include clindamycin, erythromycin, and metronidazole, all of which are category B and safe throughout pregnancy.[12] Topical dapsone, a category C medication, has been used safely as an oral medication in pregnancy for both leprosy and dermatitis herpetiformis, and no fetal risks are reported in the literature.[12] There is a theoretical risk of neonatal hyperbilirubinemia when used near the time of delivery, so the prescribing physician should consider stopping treatment before the last month of pregnancy.[12] Topical sodium sulfacetamide, on the other hand, is a category C medication that is not associated with hyperbilirubinemia, so its use is not contraindicated anytime during pregnancy.[12] The nonantibacterial antiacne product benzoyl peroxide is category C because human studies have not been conducted, but it is considered safe to use during pregnancy and is a treatment of choice for acne in pregnant patients.[1,4,12] Salicylic acid, another nonantibacterial antiacne product, is also category C. Although this is an nonsteroidal anti-inflammatory drug, which is generally contraindicated in pregnancy because of the potential for oligohydramnios and early closure of the ductus arteriosus in the third trimester,[1] the systemic absorption is estimated to be between 9% and 25%.[13-15] Because of its minimal absorption, there is a very low teratogenic potential,[16] and pregnant women should simply be advised not to apply topical salicylic acid for prolonged periods over large areas or under occlusive dressings, which would enhance systemic absorption. Azelaic acid is pregnancy category B because animal studies show no adverse effects, and less than 4% of the applied dose is systemically absorbed.[4,12,15]

CAPSULE SUMMARY

- There are 3 distinct periods of development during pregnancy: preimplantation (0-2 weeks), embryonic/organogenesis (2-8 weeks), and fetal (9th week to birth).
- The risk associated with any given medication varies substantially over the course of these periods, with some medications presenting risk primarily early in pregnancy and others presenting risk primarily late in pregnancy.
- With appropriate steps, dermatologic surgery and procedures can generally be safely performed during pregnancy when necessary.

Psoriasis and atopic dermatitis

For inflammatory skin conditions such as psoriasis, topical corticosteroids are considered first-line therapy in pregnant patients. A detailed review of pregnancy and psoriasis was performed by Tauscher et al[17] in which they outlined a stepwise approach for treatment. For localized disease in pregnancy, they recommended topical corticosteroids as first-line therapy followed by stepwise therapy with topical calcipotriene, anthralin, and tacrolimus.[1] Although all of these topical medications are category C, there are many data on corticosteroid use for a variety of medical conditions in pregnancy, so they are currently the preferred first-line therapy.

The absorption, and therefore the safety in pregnancy, of topical corticosteroids is related to a number of factors, including the vehicle of administration, amount applied, occlusion, and sites of application.[4] A practical approach to therapy with topical corticosteroids in pregnant women would be to advise them not to apply large amounts over extensive areas or under occlusive dressings to avoid excessive