Pregnancy and Medication Safety for Dermatologists

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DISCLOSURE OF RELATIONSHIPS WITH INDUSTRY

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F038 – Cutaneous Disorders of Pregnancy
Pregnancy and Medication Safety for Dermatologists

DISCLOSURES
I do not have any relevant relationships with industry.
Pregnancy Rx Pitfalls

• Some physicians take a “hands-off” approach, are afraid to treat or under treat
• OB evidence = Largely expert opinion, based on experience
• No controlled human studies, most evidence is from animal studies
• Previous FDA Pregnancy Risk Categories are not precise
Historical FDA Pregnancy Risk Categories

- X – Contraindicated in pregnancy; there is no reason to risk use of drug in pregnancy
- D – Positive evidence of risk to human fetus, but benefits may outweigh risks of drug
- C – Risk cannot be ruled out; human studies may or may not show risk; potential benefits may justify potential risk
- B – No risk to human fetus despite possible animal risk; or no risk in animal studies and human studies not done
- A – Controlled studies show no fetal risk
FDA Pregnancy and Lactation Labeling Rule

- 66% of drugs are Pregnancy Category C
- Previous classification system is imprecise
- Risk of the drug often dependent on when the exposure happened, which trimester, not necessarily a global risk
- New labeling will include a fetal risk summary, clinical considerations, and data
- Effective 6/30/15 for newly approved medications
- All others must revise labeling and remove letter category within 3 years of this date
- www.fda.gov
Timeline for Risk

• For all female patients ask:
  – If sexually active
  – If trying to conceive or birth control method
  – If currently pregnant and which trimester
  – Sexually active women on no contraception = 85% chance of pregnancy within 1 year
Periods of Development

• Pre-implantation = 0 to 2 weeks
• Embryonic/organogenesis = 2 to 8 weeks
• Fetal = 9th week to birth
• Avoiding teratogenic medications during the embryonic period most important
• Brain, teeth, and bones do remain susceptible after 9 weeks
• WARNING!! – Home pregnancy test may not be positive until up to 5 weeks after conception!
Topical medications

• For most dermatologic conditions, safest choice and first-line
• Studies of various topicals estimate absorption from less than 4 to 25 %
• Less absorption for decreased BSA, lower potency, no occlusion
Systemic medications

• Can be used when necessary if practitioner knowledgeable about safety ratings and high-risk periods during pregnancy

• Those absolutely contraindicated during the entire pregnancy or those who could become pregnant:
  – Isotretinoin
  – Acitretin
  – Methotrexate
Acne and Rosacea

• Topical retinoids
  – Adapalene and tretinoin are Category C
  – Conflicting studies on whether topical tretinoin and adapalene are teratogenic in 1\textsuperscript{st} trimester but no problems reported in 2\textsuperscript{nd} or 3\textsuperscript{rd} trimester\textsuperscript{4}
  – Topical tazarotene is category X due to retinoid-like anomalies in animal studies\textsuperscript{4}
Acne and Rosacea

• Topical antibacterial agents
  – Topical clindamycin, erythromycin, and metronidazole category B
  – Topical dapsone is category C, no fetal risks reported in the literature
  – Dapsone = theoretical risk of hyperbilirubinemia in the neonate when used near delivery, consider stopping at 36 weeks
Acne and Rosacea

• Other anti-acne products
  – Sodium sulfacetamide and benzoyl peroxide category C without reported fetal risks, safe any trimester
  – Azelaic acid is Category B, less than 4% systemically absorbed, safe throughout pregnancy
  – Salicylic acid is category C, avoid applying over large areas to decrease systemic absorption, between 9 and 25% quoted in the literature$^{5-7}$
Acne and Rosacea

• Oral antibiotics
  – Tetracyclines are category D
    • Highest risk in 2\textsuperscript{nd} and 3\textsuperscript{rd} trimester
    • No associated anomalies in 1\textsuperscript{st} trimester
    • Dental staining and enamel hypoplasia
    • Associated with acute fatty liver in pregnancy
• Erythromycin is category B
  – 2 Swedish studies showed increased risk of CV malformations when used early in pregnancy\textsuperscript{8-9}
  – Rare reports of hepatotoxicity with prolonged use
• Azithromycin, Penicillins, and Cephalosporins are all category B
Acne and Rosacea

• Spironolactone
  – Off-label, Category C
  – Caused feminization of male rat fetuses and delayed sexual maturation of female rat fetuses in animal studies\textsuperscript{10}
  – No adverse effects seen in human pregnancies
  – Theoretical high-risk period would be after week 8
Psoriasis and Atopic Dermatitis

• 50% of pregnant women with Psoriasis will improve, 20% worsen
• Topical steroids are first-line, a lot of data on use in pregnancy
• One review suggested a step-wise approach for psoriasis and pregnancy
  – Topical Steroids > topical calcipotriene > anthralin > tacrolimus\textsuperscript{10}
  – All are pregnancy Category C
  – Certain studies associated low birth weight with use of occlusion/large BSA with topical steroids
Psoriasis and Atopic Dermatitis

- Oral retinoids and methotrexate Category X
- Cyclosporine
  - Category C
  - Extensively studied in pregnant transplant patients with no specific birth defects identified
- Phototherapy
  - No adverse outcomes reported in studies
  - Avoid overheating during treatment, increased risk of NTDs if hyperthermia occurs during neural tube formation in the first 28 days of gestation
  - Ensure folic acid supplementation/prenatal vitamin
- Biologics
  - Category B but limited data, appear to be safe throughout pregnancy
  - Ixekizumab has no human data and inadequate data available to assess risk
- Apremilast
  - Risk of spontaneous abortion based on animal data, no human data available
Psoriasis and Atopic Dermatitis

• Oral steroids safe when used in moderate doses for the shortest duration possible
  – High doses in 3\textsuperscript{rd} trimester = potential for IUGR and inhibition of endogenous corticosteroid production
  – Not associated with congenital malformations when used for asthma or autoimmune disease during pregnancy\textsuperscript{10}
  – Mycophenolate mofetil = Category D
    • Do not recommend use in any trimester
    • Risk of miscarriage and anomalies of distal limbs, heart, esophagus, kidney, external ear, face
  – Anti-histamines = Category B
    • Potential risk for sedation of neonate in nursing mothers
Connective Tissue Disease

• Hydroxychloroquine
  – Category C, not associated with a specific congenital malformation
  – Experts recommend continuing therapy if already in use to avoid a lupus flare\(^1\)
  – More data are available on corticosteroid use in pregnancy, so may be more ideal for patients without systemic involvement
Bacterial infections

• Oral antibiotics previously discussed
  – Azithromycin, Penicillins, and Cephalosporins are all category B
• With the exception of Dapsone, all topical antibacterials are Category B
• Dapsone is Category C
  – Theoretical risk of neonatal hyperbilirubinemia if used near the time of delivery
Fungal infections

• Topical antifungals considered safer
• Two preferable options are clotrimazole and oxiconazole, both category B
• Topical ketoconazole and econazole are category C, limited data
• Topical ciclopirox, naftifine, terbinafine, butenafine, and nystatin all category B
Fungal infections

• Oral terbinafine = category B
  – Systemic treatment of choice for dermatophyte infection during pregnancy
  – Manufacturer does not recommend electively treating onychomycosis during pregnancy
• Griseofulvin = Category C
  – Risk of skeletal, CNS anomalies, fetal loss
• Ketoconazole = Category C
  – Sexual ambiguity of male fetus, interferes with implantation
• Itraconazole = Category C and lowest risk imidazole
• Fluconazole = Category C
  – Single dose safety confirmed in multiple studies
  – Large cohort studies indicate no teratogenicity
  – Some studies suggest prolonged high doses could increase the risk of fetal malformation
Parasitic infections

- Permethrin = Category B
  - Used extensively in pregnancy without evidence of fetal risk
  - Treatment of choice for scabies during pregnancy

- Ivermectin = Category C
  - Teratogenic to animals in high doses
  - Treat with permethrin instead
Dermatologic Surgery

• Non-emergent surgery of any kind = second trimester
  – Weeks 13 to 24 or postpartum
• Left lateral position if possible
  – Avoid supine positioning
• Prep with Alcohol or chlorhexidine
  – Povidone-iodine associated with fetal hypothyroidism
  – Hexachlorophene has caused fetal CNS toxicity
Dermatologic Surgery

• Lidocaine and Prilocaine = Category B
  – Multiple studies show no adverse effects in the fetus
  – Do not cross placental barrier

• Epinephrine = Category C
  – Decreased uterine blood flow in animal experiments
  – Dilution and small amounts in Dermatology = very minimal risk

• Local destruction of lesions without anesthesia is safe
  – Cryotherapy, laser ablation, application of TCA
Summary

• A conservative approach is always best!
• Topical medications are always first-line due to minimal systemic absorption
• Certain oral medications are safe when topical therapy fails
• Elective surgical procedures should be delayed until the post-partum period or performed during the 2nd trimester using local anesthesia

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Thank you!