Treatment of Acne in the Pregnant Patient

Jonette E. Keri, M.D., Ph.D.
Associate Professor of Dermatology, University of Miami, Miller School of Medicine
Chief, Dermatology Service, Miami VA Hospital
Disclosures

• Hoffman-La Roche
Outline

• Why treat during this time
• Medications and Therapies that can be used
• Plan for your practice
• What if...
Acne

• Acne is a common problem
• Post-adolescent acne is more common in women
• Acne is commonly seen in pregnant women
• Causes significant psychological stress
How common is acne in pregnancy?

• Difficult to find consistent numbers
• Many references say common
How Common is Acne in Pregnancy?

• 400 women surveyed

• 75% Better after delivery
• 13% No change
• 12% Got worse

• Nussbaum, R. Clin Derm 2006; 24:133-141
How do we treat these patients?

• Get their acne as good as you can before they start to try to conceive

• Encourage them to get in the best health they can be prior to trying to conceive

• Discuss their expectations with them
How do we treat these patients?

- Topicals first
- Systemics second line
Topical Medications

• Over the counter or prescription?

• Most times by the time the patient comes to see you they have tried the over the counter medications AND they are looking for something more

  • This is an important time to discuss expectations
Pregnancy Categories

• I discuss the old Food and Drug Administration (FDA) pregnancy categories

• I do this during the expectation discussion
Risk Classifications

• United States Food and Drug Administration (FDA)
• New guidelines approved but still to be implemented for older drugs (drugs approved prior to June 30, 2015)

• There are other rating systems
  • Australian
  • Swedish
  • German
Old FDA pregnancy categories - simplified

- A = Safety established in human studies
- B = Presumed safety based on animal studies
- C = Uncertain safety; no human studies and animal studies show adverse effect
- D = Unsafe - evidence of risk that may in certain clinic circumstances be justifiable
- X = Highly unsafe – risk of use outweighs any possible benefit
New FDA Labeling

• New Pregnancy and Lactation Labeling Rule (PLLR)
• The new rule for newly approved prescription medications
• Staggered phase-in for older prescription drugs

New FDA labeling

• Pregnancy
• Lactation (instead of Breast-feeding)
• **Females and Males of Reproductive Potential – NEW**

Topical Medications for Acne
Topical medications
Category B versus Category C

• Generally use category B medications
• Topicals
  • Azeleic Acid
  • Clindamycin
  • Erythromycin

• Metronidazole
How about the topical category C medications?

- Benzoyl Peroxide
- Salicylic Acid
- Dapsone (topically)
Benzoyl Peroxide

- Benzoyl Peroxide
  - Most feel safe for use
  - Systemic Absorption is minimal
  - Over the counter preparations have no pregnancy warning
  - Benzoyl Peroxide is metabolized to benzoic acid (a food additive) in the skin*

Salicylic Acid

• Salicylic acid
  • Category C
  • Likely safe
  • Systemic absorption minimal over small areas
  • Low dose aspirin used for the treatment of pre-eclampsia in women*
  • **Key point** – concentration should be low and over limited body surface areas

Dapsone - topical

• Dapsone
  • Category C
  • Likely safe but studies are lacking
  • Oral dapsone is used to treat dermatitis herpetiformis in pregnancy

Topical Retinoids

• Tretinoin – Category C
  • One case report of otocerebral anomalies*

• Adapalene – Category C
  • One case report of anophthalmia and agenesis of the optic chiasma**

• Tazarotene – Category X
  • Contraindicated in pregnancy
Category N (Not Classified) Topical

• Glycolic Acid – best example and most well received
Glycolic Acid

- Glycolic Acid
- Thought to be safe as only a minimal amount is absorbed
  - Category - N
  - Up to 27% absorbed into the skin depending on pH, concentration and time* (in vitro)
  - Rats have some adverse reproductive effects, but the doses were much larger than used in humans, (300-600mg/kg/d orally)**


Systemic Medications
Systemic Medications – Category A

• Zinc supplements
  • Generally recommended 30-200mg a day
  • Gastrointestinal disturbances
  • 75mg/day of elemental zinc show no harm to the fetus*
  • Watch “overdose” – can lead to hypocupremia

Systemic Medications – Category B

- Cephalexin
- Cefadroxil  ** Severe acne patient
- Amoxicillin  ** Severe rosacea patient
- Azithromycin
- Erythromycin
  - AVOID Erythromycin Estolate – can be associated with hepatotoxicity in 10-15% of pregnant patients with prolonged use*
  - Unable to order/prescribe Estolate
  - Rare cases of pyloric stenosis in infants with other forms of erythromycin


Systemic Medications - Category C

- Prednisone when the patient has severe acne/scarring
- Work with the Ob/Gyn
- Dosing?
  - 0.5mg/kg or less in most cases
  - Weeks to months – duration
  - Combine with systemic antibiotic
  - Bone and Gastrointestinal prophylaxis
  - Work with Ob/Gyn
So in practice how do we decide?

- Discuss expectations with the patient
- First grade the acne – your grading system
  - Mild
  - Moderate
  - Severe – Look for scarring
- If acne is moderated to severe consider systemic medications
- Document discussions
Regimen

• Mild non-abrasive washes
• Washes with Glycolic Acid
• Topical Azeleic acid
• Topical Clindamycin
• Oral Antibiotics

• Physical sunscreen
Over the Counter Controversies

• Benzoyl Peroxide or not?
• Salicylic Acid as a wash or not?

• Depends on the patient
• Many patients are very conservative

• Over the counter washes listed above are safe
What do I do?

• Talk to the OB/GYN
• Don’t be afraid to ask for help
• Consider prednisone in the severe patient
Is There Anything New?
Maybe not new, but not discussed in the past with respect to acne

- nbUVB
- Watch folate levels
Narrow band UVB for acne

• Pregnant patients
• Safe

• Zeichner, J. Narrow band UVB therapy for the treatment of acne vulgaris in pregnancy. Arch Derm 2011 147: (5); 537.
Folate reduction associated with nbUVB

- Studies using narrowband UVB showed mixed results, potentially explained by dose-dependent degradation of folate;
- Exposure >40 J/cm² cumulatively and >2 J/cm² per treatment were associated with 19%-27% decreases in serum folate levels, while lower doses did not affect folate levels.
- There is no evidence of decreased folate levels after UVA exposure.
- A lot of variability

Folate supplementation in nbUVB patients

Recommend all women of childbearing age on phototherapy take 0.8 mg/day of folate supplements, as suggested by current guidelines for women of childbearing age, to reduce the risk of neural tube defects in unplanned pregnancy.

Anything else new?
Case report using oral metronidazole along with prednisone for significant acne in pregnancy

- 30 year old woman
- 14 weeks gestation had significant acne
- treated with prednisone and then a variety of oral antibiotics including amoxicillin, erythromycin and cephalexin
- Initially got better but then got more acne, presumed steroid acne over the trunk and her prednisone dose was lowered and her erythromycin dose was increased
- Patient improved some and then was switched to metronidazole (?) 250mg twice daily and did well, but this was at 28 weeks

Why do I bring up the gestational age?

• Recent review in Canada of data in Quebec Canada from (1998-2009).
• Looked at spontaneous abortions (<20 weeks) in patients taking antibiotics
• Found macrolides (excluding erythromycin), quinolones, tetracyclines, sulfonamides and metronidazole during early pregnancy were associated with an increased risk of spontaneous abortion.

• However, residual confounding by severity of infection cannot be ruled out.
• They found cephalalexin, amoxicillin, erythromycin to be safe
Cosmetic procedures - peeling

• Glycolic acid peels: Relatively safe, limited dermal penetration.

• Lactic acid peels: Reports of safe use for gestational acne, limited dermal penetration.

• (Salicylic acid peels: Pregnancy category C, significant dermal penetration, limit use to small areas of coverage.) – Caution

What if.....??

The patient had an exposure....
Topical Retinoid Exposure

• The objective:

• Does exposure to topical retinoids lead to an increase in the risk of adverse pregnancy outcome

• Searched Medline, Embase, Web of Science and Cochrane Central Register of Controlled Trials databases from *inception to 4 December 2014*

Topical Retinoid Exposure

- Meta-analysis
- 654 pregnant women
- 1375 unexposed control pregnant women
- No significant differences among the studies evaluated

- Did not detect significant increases in:
  - congenital malformations
  - spontaneous abortions
  - stillbirth
  - elective termination of pregnancy
  - low birthweight
  - prematurity

What does this tell us?

• Use this result primarily to **reassure** women who may have had an inadvertent exposure.

• But…. there is not enough evidence (statistical power) to justify the use of topical retinoids during pregnancy.

Sulfonamide exposure

• Sulfonamide antibacterials are widely used in pregnancy, but evidence about their safety is mixed
• The objective of this study was to assess the association between first-trimester sulfonamide exposure and risk of specific congenital malformations

Sulfonamide Exposure

• METHODS:

• Mother-infant pairs were selected from a cohort of 1.2 million live-born deliveries (2001-2008) at 11 US health plans comprising the Medication Exposure in Pregnancy Risk Evaluation Program.

Sulfonamide Exposure

• **METHODS:**

• Mothers with **first-trimester** trimethoprim-sulfonamide (TMP-SUL) exposures were randomly matched 1:1 to:
  
  • a primary comparison group (mothers exposed to penicillins and/or cephalosporins)
  
  • a secondary comparison group (mothers with no dispensing of an antibacterial, antiprotozoal, or antimalarial medication)

Sulfonamide Exposure

• Overall, cardiovascular defects (1.52%) were the most common and cleft lip/palate (0.10%) the least common that were evaluated.

• TMP-SUL exposure was NOT associated with statistically significant elevated risks for:
  • Cardiovascular defects
  • Cleft lip/palate
  • Clubfoot
  • Urinary system defects

Sulfonamide Exposure

• CONCLUSIONS:

• First-trimester TMP-SUL exposure was not associated with a higher risk of the congenital anomalies studied, compared with exposure to penicillins and/or cephalosporins, or no exposure to antibacterials

After pregnancy, then what?

• LACTATION

PEARL:
Ask the Pediatrician
• American Academy of Pediatrics (AAP) has guidelines
AAP guidelines for medications prescribed to lactating mothers

• Medications divided into 3 groups

  1) Generally compatible with breastfeeding
  2) May be of concern
  3) Used with concern
Conclusions

• Define expectations
• Document discussions
• Don’t be afraid to treat
• Don’t be afraid to ask for help
  • OB/GYN
  • Pediatrician
  • Other Dermatologists
Treating Acne During Pregnancy and Lactation

• Editorial
• Significant psychological burden during these times (pregnant and post-partum periods)
• New FDA labeling may help after some initial “getting used to…”
• All pregnancies have a background risk of loss, birth defect, or adverse event

Thank you!