

10 Misadventures in Treating Acne



VOLUME: 13 PUBLICATION DATE: Aug 15 2005

Issue Number:

Volume 13 - Issue 8 - August 2005

author:

By Noah Scheinfeld, M.D.

It has been estimated that patients who have acne vulgaris represent as much as 20% of a typical medical dermatology practice.¹ No doubt, this is a condition for which you write many prescriptions, including oral antibiotics such as minocycline, doxycycline, tetracycline, erythromycin, azithromycin, cotrimoxazole and trimethoprim-sulfamethoxazole. Because of high volume of prescriptions for this condition, we should remember to consider possible errors or overlooked treatments when managing patients who have acne. This article will consider 10 common misadventures to avoid for better patient outcomes.

1. Failure to Use Benzoyl Peroxide as an Acne Treatment

Benzoyl peroxide is the cheapest effective treatment of acne. If patients can tolerate it, it should be part of their therapeutic regimen. Not using it when possible is a misadventure in the treatment of acne. As monotherapy benzoyl peroxide is basically as effective as any other agent.² Combining a topical antibiotic with benzoyl peroxide may increase the bactericidal effect of the antibiotic and reduce the potential for bacterial resistance.³ In moderate acne vulgaris, 3% erythromycin/5% benzoyl peroxide may provide a greater beneficial effect than 0.025% tretinoin/erythromycin 4%.⁴

Avoid misadventure and tell acne patients to use benzoyl peroxide, if they can tolerate this therapy.

2. Benzoyl Peroxide Causes Contact Dermatitis

Benzoyl peroxides cause both an irritant and contact dermatitis.⁵ Its estimated rate of causing contact dermatitis is 1% to 2% although studies have found rates much higher.⁶ So, although benzoyl peroxide should be the cornerstone of anti-acne therapy, if a patient's acne worsens or the patient develops a red face, benzoyl peroxide use should be discontinued and its continued use evaluated with patch testing and if a contact dermatitis is noted its use avoided.

3. Considering Pregnancies During Acne Therapy

Many patients with acne are fertile women. Failing to consider that pregnancy can occur in such women can result in misadventures in acne treatment. Considerations exist that effect treatment during pregnancy.

Ask female patients of childbearing age about the last menstrual period they had and possible existing pregnancies before using therapies. Oral tetracycline is associated with maternal liver toxicity and deciduous tooth staining in the infant, and tetracycline occasionally has been associated with other congenital anomalies. Topical acne medications never have been implicated as a cause of fetal deformities in human beings;⁷ however, several reports exist of birth defects in women who used topical tretinoin.^{8,9} Note that topical tazarotene is a pregnancy category X drug, and irregular periods can be a sign of hormonal abnormalities. **During pregnancy, the best antibiotic, if one has to be used, is erythromycin.**¹⁰ Erythromycin and azithromycin are both pregnancy category B.¹¹

It is not clear if antibiotics decrease the effect of birth control pills and can lead to pregnancy while taking such pills, but this should be discussed with patients.¹² Know about, discuss and document your discussions regarding pregnancy with acne patients to avoid problems later.

4. Isotretinoin and Pregnancy

As all dermatologists know, the worst side effect of isotretinoin is the induction of birth defects. Maternal isotretinoin ingestion is associated with major craniofacial and cardiac deformities, as well as other congenital anomalies. If isotretinoin is to be used, pregnancy should be strictly avoided and two forms of birth control used. The isotretinoin informed consent booklets have not eliminated birth defects associated with isotretinoin use. In recent years, 100 to 150 women became pregnant while taking isotretinoin. The registry program for patients using isotretinoin might finally eliminate this problem. (See the article beginning on page 56 for more information about the new guidelines.)

5. Isotretinoin and Other Rare Side Effects

It is best to discuss all possible side effects in patients who take isotretinoin even those for which no firm proof exists of a causal relationship. It might be considered for your records that the discussion of the following list of side effects culled from Web sites that seek to bring malpractice lawsuits against doctors be used.

- Central Nervous System Ailments
- Inflammatory Bowel Disease: Ulcerative Colitis/Crohn's Disease/Rectal Bleeding
- Hearing/Vision Problems
- Bone and Muscle Damage (Musculoskeletal Injuries)
- Liver Damage
- Pancreatic Damage
- Other Serious Injuries (including Abdominal Pain, Lupus, Immune System Disorders, Kidney Damage)
- Psychiatric Diseases, Depression, Suicidal Tendencies.

If these side effects occur after you have prescribed isotretinoin, litigation could occur, which is, of course, a serious misadventure.

6. Doxycycline Side Effects

The tetracycline group of antibiotics of which doxycycline is a part still remains among the most successful oral treatment for acne. Doxycycline is relatively free from side effects, apart from the occasional gastrointestinal upset or vaginal candidiasis, but rarer side effects include drug rashes and light-sensitive eruptions.

The incidence of light-sensitive rashes that occur with doxycycline at dosages of 100 mg daily is in the order of 3%. An increased incidence of light-sensitive eruptions occurs in patients receiving doxycycline at a daily dose of 150 mg or above.¹³ Doxycycline can also cause stomach upset and this should be discussed with patients. Some newer formulations indicate that this effect is diminished. There are even isolated reports of a doxycycline-induced gastric ulcer¹⁴ and esophageal ulceration.¹⁵ Just being aware of these side effects allows dermatologists to know to discontinue doxycycline if these side effects occur.

7. Trimethoprim-Sulfamethoxazole Package Insert and Possible Blood, Renal and Hepatic Side Effects

Most of you know that trimethoprim-sulfamethoxazole (Bactrim) is a very effective treatment for acne that it should not be given to patients who are allergic to sulfur medications and it can rarely cause severe skin rash such as Stevens-Johnson Syndrome.

However, you might not know that in 1998 the package insert warnings were changed due to rare cases of cytopenias to recommend "frequent" checks of patients' complete blood cell counts¹⁶ and that this medication can have hepatic and renal side effects. The package insert of Bactrim reads:

Bactrim is also contraindicated in patients with marked hepatic damage or with severe renal insufficiency when renal function status cannot be monitored.

Laboratory Tests: Complete blood counts should be done frequently in patients receiving Bactrim; if a significant reduction in the count of any formed blood element is noted, Bactrim should be discontinued. Urinalyses with careful microscopic examination and renal function tests should be performed during therapy, particularly for those patients with impaired renal function.

If your patient is undergoing treatment with trimethoprim-sulfamethoxazole, then just remember to monitor your patient's blood chemistries and complete blood cell count to avoid any problems.

8. Gram-Negative Folliculitis

I recently encountered a patient who had been on tretinoin gel, clindamycin and benzoyl gel and minocycline 100 mg twice a day for 3 months, and the patient had not experienced any change in her acne. I suspected it was gram-negative folliculitis, and her rash significantly improved with treatment with trimethoprim-sulfamethoxazole one double-strength tablet twice a day.

If acne does not respond to standard treatment, then consider an acne variant such as gram-negative folliculitis as the actual diagnosis and prescribe appropriate therapy such as isotretinoin or trimethoprim-sulfamethoxazole.

9. Minocycline Side Effects

Minocycline is likely to be an effective treatment for moderate acne vulgaris, but it is expensive and it can have side effects.¹⁷

Minocycline can cause a hypersensitivity syndrome. Current use of minocycline increased the risk of developing lupus-like syndrome 8.5-fold in a cohort of young acne patients. The effect was stronger in longer-term users. However, the absolute risk of developing lupus-like syndrome seems to be relatively low.¹⁸ Pigmentation on the face, mucosa and shins can occur with minocycline. It remains to be proven that minocycline has an effect on the effectiveness of birth control pills, and patients should be warned that this is unlikely but possible.¹⁹ Stopping minocycline eliminates the side effects, so be aware of minocycline's side effects and avoid misadventure.

10. Consideration of More Aggressive Treatment for People of Color Because Acne Leaves Marks

Acne vulgaris occurs in people of all ethnicities and races. Although the pathophysiology and treatment options are similar in all skin phototypes, darker-skinned patients have higher incidence rates of two sequelae of acne: post-inflammatory hyperpigmentation and keloidal scarring.²⁰ Post-inflammatory hyperpigmentation may also be triggered by skin irritation.

In choosing therapies for patients of color, therefore, clinicians must find a balance between aggressive early intervention to target inflammatory acne lesions, and gentle treatments to increase tolerability and avoid skin irritation. For most patients, a combination of topical retinoids, and topical or oral antibiotics with hydroquinone (as needed) to control hyperpigmentation will be successful. To avoid the misadventure of dyspigmentation appropriate and forceful treatment for acne should be used in patients of color.

References:

References:

1. Duvauchelle SA. Topical treatment of acne vulgaris for the nurse practitioner. *Clin Excell Nurse Pract*. 1999 May;3(3):141-8.
2. Ozolins M, Eady EA, Avery AJ, Cunliffe WJ, Po AL, O'Neill C, Simpson NB, Walters CE, Carnegie E, Lewis JB, Dada J, Haynes M, Williams K, Williams HC. Comparison of five antimicrobial regimens for treatment of mild to moderate inflammatory facial acne vulgaris in the community: randomised controlled trial. *Lancet*. 2004 Dec 18;364(9452):2188-95.
3. Ozolins M, Eady EA, Avery A, Cunliffe WJ, O'Neill C, Simpson NB, Williams HC. Randomised controlled multiple treatment comparison to provide a cost-effectiveness rationale for the selection of antimicrobial therapy in acne. *Health Technol Assess*. 2005 Jan;9(1):1-212.
4. A randomized, double-blind, multicenter, parallel group study to compare relative efficacies of the topical gels 3% erythromycin/5% benzoyl peroxide and 0.025% tretinoin/erythromycin 4% in the treatment of moderate acne vulgaris of the face. *J Cutan Med Surg*. 2003 Jan-Feb;7(1):31-7.
5. Leyden JJ, Kligman AM. Contact sensitization to benzoyl peroxide. *Contact Dermatitis*. 1977 Oct;3(5):273-5.
6. Shwerek C, Lowenstein EJ. Delayed type hypersensitivity to benzoyl peroxide. *J Drugs Dermatol*. 2004 Mar-Apr;3(2):197-9.
7. Rothman KF, Pochi PE. Use of oral and topical agents for acne in pregnancy. *J Am Acad Dermatol*. 1988 Sep;19(3):431-42.
8. Lipson AH, Collins F, Webster WS. Multiple congenital defects associated with maternal use of topical tretinoin. *Lancet*. 1993 May 22;341(8856):1352-3.
9. Navarre-Belhassen C, Blanchet P, Hillaire-Buys D, Sarda P, Blayac JP. Multiple congenital malformations associated with topical tretinoin. *Ann Pharmacother*. 1998 Apr;32(4):505-6.
10. Meynadier J, Alirezai M. Systemic antibiotics for acne. *Dermatology*. 1998;196(1):135-9.
11. Gammon WR, Meyer C, Lantis S, Shenefelt P, Reizner G, Cripps DJ. Comparative efficacy of oral erythromycin versus oral tetracycline in the treatment of acne vulgaris. A double-blind study. *J Am Acad Dermatol*. 1986 Feb;14(2 Pt 1):183-6.
12. Rubin DF. Antibiotics and oral contraceptives. *Arch Dermatol*. 1981 Apr;117(4):189.
13. Layton AM, Cunliffe WJ. Phototoxic eruptions due to doxycycline--a dose-related phenomenon. *Clin Exp Dermatol*. 1993 Sep;18(5):425-7.

14. Sherman A, Bini EJ. Pill-induced gastric injury. *Am J Gastroenterol.* 1999 Feb;94(2):511-3.
15. Isler M. *Mil Med.* 2001 Mar;166(3):203, 222.
16. <http://www.fda.gov/medwatch/safety/1998/nov98.htm>
17. Gupta AK, Lynde CW, Kunynetz RA, Amin S, Choi K, Goldstein E, Garner SE, Eady EA, Popescu C, Newton J, Li WA. Minocycline for acne vulgaris: efficacy and safety. *Cochrane Database Syst Rev.* 2003;(1):CD002086.
18. Sturkenboom MC, Meier CR, Jick H, Stricker BH. Minocycline and lupuslike syndrome in acne patients. *Arch Intern Med.* 1999 Mar 8;159(5):493-7.
19. de Groot AC, Eshuis H, Stricker BH. [Inefficacy of oral contraception during use of minocycline] *Ned Tijdschr Geneeskd.* 1990 Jun 23;134(25):1227-9.
20. Callender VD. Acne in ethnic skin: special considerations for therapy. *Dermatol Ther.* 2004;17(2):184-95.