Taking the stress out of acne management

Tessa Laubscher MB ChB CCFP FCFP Loren Regier Margaret Jin PharmD CDE CGP Brent Jensen

Case 1

The first-year family medicine resident you supervise sees a 19-year-old woman in your clinic who requests treatment for facial acne. The patient is generally healthy, has no known allergies, and is taking Yasmin for contraception. She was hoping Yasmin would improve her skin, but after 6 months of use she is still getting frequent pimples. She washes her face with regular soap several times a day and uses a moisturizer and makeup daily. She uses benzoyl peroxide (she is uncertain of the strength) for "spot treatment" when new pimples appear. Last year she used a "vitamin A cream" prescribed by another physician; it didn't seem to help and it irritated her skin a bit. She asks about Proactiv, which she saw advertised on television. She has no acne lesions on her back or chest. The resident reports that the patient has mostly papules and pustules on her face along with some comedones. There is no scarring. He is uncertain how to describe the severity of the acne and how to treat it.

The presence of facial papules and pustules, few comedones, and no nodules or scarring suggests mild to moderate acne severity.[1] General measures and basic care are recommended at all levels of management. For this patient, limiting face washing to once or twice daily with mild soap (or soapless cleanser) is an important first step. Frequent washing causes ongoing trauma to the pores, which worsens the condition. It is also important to discuss use of noncomedogenic makeup products.

Options for initial therapy can include roles for topical products, such as benzoyl peroxide (BP), topical retinoids, topical or oral antibiotics, and combinations of the above.[2-8] Either BP or a topical retinoid (vitamin A cream) might be a good choice for initial therapy for mild to moderate acne; clinical trial evidence does not favour one over the other. Benzoyl peroxide has multiple mechanisms of action (including being anti-inflammatory), is not associated with any bacterial resistance, and is inexpensive. Topical retinoids are considered useful for comedonal lesions and long-term acne control; however, they are more expensive. Topical antibiotics are a potential step-up therapy in papulopustular (inflammatory) acne. To reduce bacterial resistance, topical antibiotics should be used in combination with BP. Response is often seen within 3 months, after which time the topical antibiotic can be discontinued and a topical retinoid or BP can be used for maintenance therapy.

In this case, the resident used the RxFiles "Acne—Topicals" chart to discuss the options of BP with or without a topical antibiotic for initial management. The chart provided information on benefits, harms, use, and comparative cost. The patient was counseled specifically on the need to apply topical therapy to the entire face each night and not just to "spot treat." When the resident was asked about Proactiv, he noted that it was a system of facial products containing 2.5% BP in a water-based formulation.

Bringing evidence to practice

- Products with greater than 5% BP are no more efficacious but cause more irritation than products with 2.5% to 5% BP.[9] To reduce irritation, start with a lower strength water-based product; apply every 2 to 3 nights, increasing the frequency as tolerated to nightly or twice daily. (Alternate initiation regimens are also possible.) Patients should be warned that BP can bleach clothing, bedding, and hair.
- Combination of BP and topical clindamycin is superior to use of either ingredient alone.[10] Topical antibiotic monotherapy is no longer recommended owing to resistance concerns.[7,11,12] If a topical antibiotic is prescribed, add BP or use a combination product such as BenzaClin or Clindoxyl. After the condition improves, stepping down to monotherapy with BP, a retinoid, or both can be considered.

Table 1[7,12-19] provides an overview of acne pharmacotherapy; the full version of the RxFiles chart is available from CFPlus.*

Case 2

David, a 17-year-old male patient, has been seeing his family physician for the past 4 years. Initially, David had mild inflammatory acne on his face and was treated successfully with clindamycin-BP gel. Two years ago his acne worsened, with comedones, papules, and pustules on his face and upper back. He was prescribed doxycycline (100 mg daily for 4 months). A dramatic response was seen and David resumed topical therapy. One year later he required another course of doxycycline; the acne improved somewhat, but within a few months he developed more papular and nodulocystic lesions with scarring on his face and upper back. He therefore returned to request a different antibiotic.

CFPlus GO

*The full version of the acne pharmacotherapy comparison chart and the patient follow-up sheet are available at **www.cfp.ca**. Go to the full text of the article on-line, then click on **CFPlus** in the menu at the top right of the page.

Is minocycline a better oral antibiotic for acne? Studies have not shown differences in efficacy among oral antibiotics.[15] Minocycline is not more efficacious but it is associated with a rare severe lupuslike reaction and it is more costly than tetracycline or doxycycline.

David's physician decided isotretinoin pharmacotherapy would be preferable to another antibiotic. She reviewed important precautions and side effects with David, along with methods to manage them. She recommended 0.5 mg/kg of isotretinoin daily for the first month. David (who weighed 72 kg) was given a prescription for 40 mg daily and instructed to have laboratory work done (lipids, aspartate aminotransferase, alanine aminotransferase); therapy was not initiated until David's physician notified him that the laboratory results were within normal limits. David returned after 1 month, happy with the initial response to therapy.

Following initiation of isotretinoin, it is important to monitor side effects and make dosing adjustments as necessary. An isotretinoin patient follow-up sheet, available on CFPlus,* can assist with such follow-up visits; use of a follow-up sheet saves time and enhances communication with patients regarding therapy and management of side effects.[20]

David is pleased with the effect of isotretinoin on his acne, but is experiencing some muscle and joint pain that is worse after exercise. He is on the high school football team and is concerned that he will not be able to play if the arthralgia worsens. His physician therefore decides to continue the lower dose (0.5 mg/kg daily) in order to minimize side effects. David has no further problems and returns for monthly follow-up as recommended. After 4 months of taking isotretinoin, his skin is totally clear with no new acne lesions in the past 6 weeks. He has had no further side effects but continues to have mild leg arthralgia, and is hoping to discontinue therapy.

Bringing evidence to practice

- The total optimal cumulative dose of isotretinoin therapy is 120 to 150 mg/kg/course (equals 1 mg/kg daily over 120 to 150 days). More than 150 mg/kg/course offers no further benefit; less than 120 mg/kg/course increases rates of post-treatment relapse.[1,13] In most cases, after initiating isotretinoin at 0.5 mg/kg daily for 1 month, the dose should be increased to 1 mg/kg daily for approximately 4 to 5 months until the target cumulative dose is reached.[7] In a patient with limited tolerance of isotretinoin, continuing with or returning to the lower dose limits adverse effects; however, achieving the target cumulative dose will require a longer treatment period.
- While taking isotretinoin, other topicals are generally avoided, as they worsen the dryness that commonly occurs during therapy. Noncomedogenic moisturizing products might be useful. The beneficial

and drying effects of the isotretinoin persist several months after discontinuation. If a retinoid or BP is used for maintenance therapy after isotretinoin, delaying initiation for at least 4 months is often necessary while dry or sensitive skin and membranes persist.

Dr Laubscher is an Assistant Professor of Academic Family Medicine at the University of Saskatchewan in Saskatoon. **Mr Regier** is Program Coordinator

Table 1. Overview of acne pharmacotherapy*

TREATMENT	ROLE	COMMENTS	USE
Topicals: applied to entire affected area[13]			
BP • Water-based 2.5%, 4%, 5%, 8%, 10% • Other (alcohol-based, acetone-based, lotion, soap, washes)	Mild to moderate acne; monotherapy or in combination regimens; prevents bacterial resistance[7,12,13]	Water-based formulations (eg, creams) are less drying or irritating; initial worsening for 2-4 wk; improvement <3 mo	Start with lower strength (2.5%-5%) or less frequent nighttime application; increase strength or frequency if tolerated; water-based BP preferred for dry skin
Retinoids • TRE 0.01%, 0.025%, 0.05%, 0.1% • Adapalene 0.1% cream; 0.3% gel • Tazarotene 0.05%, 0.1% cream, gel	Mild to moderate acne, especially comedonal; maintenance therapy (can step down to less frequent use)	Some guidelines suggest as first-line[13]; irritating and drying (adapalene might be better tolerated); initial worsening for 2-4 wk; improvement <3 mo	Apply minimal amount to cover area; start with lower strength tretinoin 0.01%-0.025% or adapalene 0.1% applied every 2-3 nights; gradually increase frequency or strength; AEs subside over time
Topical antibiotics • CLI 1% solution • ERY 2% gel	Mild to moderate inflammatory acne	Use in combination with BP to minimize resistance concerns	Apply twice daily; avoid long-term use if possible; step down to BP or retinoid only
Combination topical gels • Benzamycin (BP 5% and ERY 3%) • BenzaClin, Clindoxyl (BP 5% and CLI 1%) • Stievamycin (TRE and ERY 4%)	Mild to moderate inflammatory acne when more intensive therapy is desired	More effective than monotherapy; response might be seen in 2-3 wk; optimal results in 8-10 wk; convenient but more expensive	Apply 1-2 times daily (begin with nighttime administration); after response, step down to maintenance with BP or retinoid
Orals			
Oral antibiotics • Tetracycline 250-mg capsule • Doxycycline 100-mg capsule • MIN 50- or 100-mg capsule • ERY 250 mg, 333 mg, 500 mg	Moderate to severe inflammatory acne if topical agents are not effective or practical; use with BP	Little or no difference in efficacy[14]; MIN has AE concerns (eg, rare lupuslike reaction) and is expensive[15]	To minimize resistance, use for 2-4 mo then step down to topical agents; dosing: doxycycline 100 mg daily (see CFPlus for other dosing)
Hormonal contraceptives • Tri-Cyclen, Alesse, Aviane, Yasmin (have acne indication) • Diane-35, Cyestra-35 (acne but no contraception indication)	First-line in women if also desired for contraception; antiandrogen effect; useful in combination with other therapies	Acne might worsen early in cycle; allow 3-6 mo for response; any COC might be beneficial owing to estrogen's effect on sex hormone binding globulin, but some might make acne worse[16,17]	Generally used in typical cyclic fashion; daily for 21 d, followed by 7-d hormone-free interval
Spironolactone • 25- or 100-mg tablets	Adult or late onset acne in women; hirsutism	Antiandrogen effect; 2-3 mo for optimal response	Usual dose is 50-100 mg/d
Isotretinoin (Accutane, Clarus) • 10- or 40-mg capsules (10-mg capsules relatively expensive)	For more severe acne (eg, nodulocystic, scarring)	Very effective, but must balance with AEs, contraindications, side effect management, and follow-up; **teratogenic in pregnancy**	Low dose for 1 mo; increase (or decrease) as tolerated; optimal cumulative dose: 120-150 mg/kg/course; see monograph for pregnancy testing and contraception requirements

AE—adverse effect, BP—benzoyl peroxide, CLI—clindamycin, COC—combination oral contraceptive, ERY—erythromycin, MIN—minocycline, TRE—tretinoin.
*Table is adapted from the RxFiles Acne Pharmacotherapy Comparison Chart[18] and the Dalhousie CME Academic Detailing Service Acne Review 2008.[19]

of the RxFiles Academic Detailing Program for Saskatoon Health Region. **Dr Jin** is a clinical pharmacist and Program Coordinator of the Academic Detailing Program for the Hamilton Family Health Team in Ontario. **Mr Jensen** is a pharmacist for the RxFiles Academic Detailing Program.

Competing interests

RxFiles and contributing authors do not have any commercial competing interests. RxFiles Academic Detailing Program is funded through a grant from Saskatchewan Health to Saskatoon Health Region; additional "not for profit; not for loss" revenue is obtained from sale of books and on-line subscriptions.

Correspondence

Mr Regier, Saskatoon Health Region, RxFiles Academic Detailing, c/o Saskatoon City Hospital, 701 Queen St, Saskatoon, SK S7K 0M7; telephone 306 655-8505; fax 306 655-7980; e-mail **regierl@rxfiles.ca**; website **www.rxfiles.ca**

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RxFiles is an academic detailing program providing objective comparative drug information to physicians, pharmacists, and allied health professionals. The program began in 1997 as a service to family physicians in Saskatoon, Sask. In 2000, the program was expanded to provide service to physicians throughout Saskatchewan. Efforts to keep the drug selection tools up-to-date resulted in the publication of the *RxFiles Drug Comparison Charts*, beginning in 2001. The book has become a practical tool for evidence-based and clinically relevant drug use information throughout Canada.

RxFiles charts begin with input from family physicians, other specialists, and pharmacists on current questions, information needs, and practice gaps. An extensive review of the literature provides the foundation for incorporating evidence and information relevant to prescribing decisions. The review looks to systematic reviews, original landmark trials, clinical practice guidelines, and many other information sources. An emphasis is placed on noting the most important clinical outcomes, risk-benefit assessment, patient safety, and cost considerations.

RxFiles continues to serve health providers and educators through newsletter reviews, question-and-answer summaries, trial summaries, and up-to-date drug comparison charts. The clinical relevance of these materials comes from their initial focus as academic detailing tools for front-line practitioners wanting to provide the best possible drug therapy for their patients.