

ACNE AND THE ADULT FEMALE

TIPS ON WHEN AND HOW TO USE HORMONAL THERAPY.

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When treating acne in the adult female patient, conventional therapy is a good place to start — a topical retinoid, a benzoyl peroxide and an antibiotic. Depending on the severity of the acne, that antibiotic can either be topical or oral. If these treatments provide no improvement for a patient, and if there are other signs of androgenism, then I would do a hormone evaluation. Based on find-

ings from the evaluation, I would then consider adding hormonal therapy to the regimen. In my experience, though, I have found that hormonal therapy by itself is not highly effective, so I typically use it as an adjuvant to conventional therapy.

PATHOGENESIS OF ACNE

We know that follicular keratinization exists, and this is the area that's targeted by topical retinoids because topical retinoids work very well at normalizing the follicle. We also know that *Propionibacterium acnes* causes inflammation. Interestingly, Jenny Kim, M.D., Ph.D., of the David Geffen School of Medicine at UCLA, found that *P. acnes* bacteria can activate the Toll-like receptor 2 (TLR2) that sits on the surface of an inflammatory cell — when the *P. acnes* bacteria activates the TLR2, it tells that inflammatory cell to make cytokines. We have seen that topical retinoids, such as adapalene and tretinoin, have been shown to decrease the expression of the TLR2 on inflammatory cells, so that may be one of the mechanisms by which retinoids can contribute to reducing inflammation.

In terms of sebum production, we know that this is a key component of the pathogenesis of acne. There are really only two approaches that make a significant difference for sebum production. One is the use of isotretinoin, and the other is

hormonal therapy, which can only be used in women. The indications for hormonal therapy to reduce sebum production are hormonal abnormalities in the patient. However, hormonal therapy, is a very useful adjuvant to conventional therapy, and it can be used and is effective even in women who have normal levels of androgen. For example, if I have a patient with moderate to severe acne for whom I'm considering isotretinoin, I initially may start her on an oral contraceptive. Many times, oral contraceptives added to a conventional regimen are effective enough that the patient doesn't need to start isotretinoin. Hormonal therapy may be an alternative to repeat courses of isotretinoin in some patients.

HORMONAL THERAPY INDICATIONS

There are signs that may cause you to suspect an abnormal hormone level in a patient. For instance, if a woman in her 30s who never really had acne presents with severe acne with a sudden onset, you should be concerned that there could be an hormonal problem, or if the acne is associated with other signs of excess androgens, such as hirsutism, irregular menstrual periods and signs of hyperandrogenism.

The suggested work-up for an endocrine disorder includes serum dehydroepiandrosterone sulfate (DHEAS), total and free testosterone, LH/FSH ratio, and 17-hydroxyprogesterone. It's important to remember that patients must not be taking oral contraceptives when they are tested for an endocrine disorder — they need to be off oral contraceptives for at least 6 weeks prior to testing. It's also important not to test near ovulation — have patients tested during their period or the week prior.

DHEAS is produced by the adrenal gland, so if there's congenital adrenal hyperplasia, DHEAS is going to be elevated. Results of >8000 ng/ml indicate adrenal tumor while results of 4000 ng/ml to 8000 ng/ml indicate congenital adrenal hyperplasia. Results of total and free testosterone of 15 ng/dl to 200 ng/dl indicate an ovarian tumor and mild elevations sug-

gest polycystic ovary disease. LH/FSH ratio >3 also indicates polycystic ovary disease. The 17-hydroxyprogesterone can help you to distinguish whether the source of androgen is from the adrenal or from the ovary.

HORMONAL THERAPY

Hormonal therapies consist of oral contraceptives that block the ovarian production of androgens, glucocorticoids that block the adrenal production in patients with congenital adrenal hyperplasia, and antiandrogens that block effects on skin, though there are not many of these available in the United States. Spironolactone functions as an antiandrogen, so oftentimes we use that off-label.

Spironolactone. Many patients with chronic adult acne, with intermittent (2 to 5 per month) tender nodules, respond quite well to treatment with spironolactone. Dosing is typically 25 mg to 100 mg twice a day, much lower than the doses used for hirsutism or androgenic alopecia. Side effects include breast tenderness and menstrual irregularity, and it's important to avoid pregnancy. Interestingly, spironolactone reduces sebum production when it's given in an oral form, though studies of topical spironolactone don't show any effect on sebum production.

Glucocorticoids. If a patient's lab results indicate a congenital adrenal hyperplasia (elevated serum DHEAS, 17-hydroxyprogesterone or testosterone), low-dose glucocorticoids may be prescribed, such as prednisone 2.5 mg to 5 mg daily at bedtime or dexamethasone 0.25 mg to 0.75 mg at bedtime. Be aware that there is an increased risk of adrenal suppression with dexamethasone.

ORAL CONTRACEPTIVES IN ACNE

This is an area that's always changing. In my practice, many patients are referred by gynecologists, who have already prescribed oral contraceptives for their acne. Patients present to me and complain that they were already taking something and not seeing any results. This really emphasizes the fact that hormonal therapy really needs to be part of a combination regimen. It's rare for hormonal therapy alone to be good enough for most patients.

Oral contraceptives basically work by inhibiting ovulation and reducing the production of androgens from the ovary. By reducing androgens, you can reduce sebum production and improve acne. All of the combination oral contraceptives have the same mechanism, so they all reduce ovarian androgens, and theoretically, they should all help to improve acne.

Oral contraceptives contain two agents: an estrogen and a progestin.

Over the years, because of safety reasons, the amount of estrogen in oral contraceptives has decreased. Most of the newer ones have 20 micrograms of estrogen, which is considered low dose. These included Alesse, Mircette, Loestrin, Estrostep, Ortho Tri-Cyclen Lo and Yaz.

Also, third-generation progestins have less cross-reactivity with the androgen receptor and are more "estrogenic" with higher levels of HDL and sex hormone-binding globulin. Oral contraceptives with third-generation progestins include Desogen, Ortho-Cept, Mircette, Ortho-Cyclen, Ortho Tri-Cyclen and Ortho Tri-Cyclen Lo.

There's a relatively new progestin called drospirenone. It is an analog of spironolactone, so there may be reason to think that this progestin has some of the benefits on acne that spironolactone has. There are two products that contain it — Yasmin and Yaz. Yaz is a new oral contraceptive that was approved as a contraceptive in April 2006 and FDA approved for use in acne in early 2007. One advantage of Yaz is that patients have only 4 days of a menstrual period.

As far as the oral contraceptives that have been studied in acne, we're all familiar with Ortho Tri-Cyclen. It was the one that was first approved for treatment of acne. Others have now been studied as well, and overall, all the trials were done as a single-agent trial, so the amount of lesion reduction was typically 30% to 40%, which again is why I think that oral contraceptives are effective as adjuvant agents, not as single agents.

THE IMPORTANCE OF A GOOD SKINCARE REGIMEN

When treating adults with acne, one of the most important things is to find a good regimen. The adult female patient wants to know how to clean her skin, what to put on, what time to put it on and how much to put on, so take the time to give recommendations about good skin care.

Recommend sun protection, the use of moisturizers, explain how to use medications and when to use them in conjunction with cosmetics. Explain the purpose of using a retinoid, the purpose of benzoyl peroxide, and effects to be expected with an antibiotic.

Go over all of these things, and let your patients know that it's going to take 8 to 10 weeks before they're going to notice the full effect of their current regimens and that if they're not happy after that time, there's plenty more that you can do. Like many treatments in dermatology, it's a matter of finding the right combination for each individual patient. ■

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