Investigating the Cause of Hirsutism and Acne in Women

Last month in Clinical Chemistry, Fiet et al. described a method for the simultaneous measurement of eight steroids in women with hirsutism and acne (1). The method is simple and provides analytically specific results. Importantly, the authors tested the approach clinically, with encouraging results. The clinical evaluation of patients with androgen-related disorders is often challenging and new approaches are welcomed.

An assumption driving measurements of multiple steroids in patients with hirsutism and acne is that these conditions are androgen-related disorders, having as a common denominator an increase in ovarian or adrenal androgen production. Although it is important to rule out significant abnormalities in ovarian and adrenal secretion in patients complaining of such disorders, the tenet that these skin manifestations of androgen excess solely signify increased ovarian or adrenal androgen production is no longer valid.

The effects of androgen on the skin may be dissociated from other effects of androgen such as that on the hypothalamic–pituitary–ovarian axis (2). Thus, a woman who has hyperandrogenemia need not have hirsutism or acne: Witness the woman with polycystic ovary syndrome who is not hirsute (3, 4). On the other hand, many women with hirsutism or acne may have normal ovarian and adrenal androgen production. In this setting, enhanced activity of skin 5α-reductase appears to explain much of the abnormality, and specific markers of this activity in blood have been suggested as useful (3, 5–7).

Apart from these general considerations, practical clinical concerns must also be contemplated in advocating the measurement of multiple steroids. Ruling out the extremely rare patient with an adrenal tumor may be important, but a detailed assessment of adrenal androgen production to determine adrenal enzymatic activity may be unnecessary unless the concern of the patient is pregnancy. For the complaint of hirsutism, adrenal suppression with dexamethasone is not highly effective; using antiandrogen therapy without corticosteroids provides greater efficacy (8, 9). Thus, even in the setting of enhanced androgen production, blockade of androgen action may be more efficacious.

Nevertheless, the comprehensive data by Fiet et al. are noteworthy in that a simplified method of analysis with small volumes of sera has been described. Utilization of the SPA methodology greatly affects the efficiency of the assay. A potential concern, that a particular steroid may coelute into adjacent fractions, does not appear to be significant: The assays are highly specific and the reported recoveries appear to be good. The requirement of only small volumes (<1 mL) of serum or plasma may be valuable, particularly if this approach is used to make diagnoses in children. The method appears to be particularly valuable in the pre- and post-corticotropin (ACTH) testing of patients suspected of having an adrenal enzymatic deficiency state. This use may perhaps provide more utility than the routine use of baseline assessments alone. On this point, although dehydroepiandrosterone (DHEA) and 11β-hydroxyandrostenedione (11-HA) are primarily adrenal in origin, the ovary does secrete DHEA and on occasion may produce 11-HA as well (10, 11).

Clinical evaluation and subcategorization of patients resembling those studied by Fiet et al. is controversial. Clearly, clinicians should be able to diagnose patients with Cushing syndrome (group 3 of Fiet et al.) from the combination of clinical examination and urinary free cortisol alone. The additional steroids and ACTH testing are not helpful. Reliance on values of luteinizing hormone (LH) for diagnoses and the use of gonadotropin-releasing hormone-stimulated values are also controversial. Serum LH abnormalities neither absolutely rule nor rule out the diagnosis of polycystic ovary syndrome or ovarian hyperandrogenism (12, 13).

In the final analysis, as are all things in US medicine today, the cost-effectiveness of any approach must be considered. If this eight-steroid approach is similar in cost to more minimalist approaches, then the additional information obtained could be beneficial. If, on the other hand, the cost is eight times that of a single (perhaps direct) assay, it would be difficult to support this approach for routine baseline testing. However, as stated earlier, in patients suspected of having an adrenal enzymatic deficiency, or who may have been found to have an elevated value for early morning 17α-hydroxyprogesterone, this comprehensive assessment before and after ACTH may be warranted. Such patients may prove to be the group for whom this new test is most appropriate.

References

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