Androgen sulfate and glucuronide conjugates in nonhirsute and hirsute women with polycystic ovarian syndrome

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Peripheral androgen action largely determines the occurrence of hirsutism in women. Although serum 5α-androstane-3α,17β-diol (3α-diol) glucuronide signifies skin 5α-reductase activity and has been used as a marker of hirsutism and peripheral androgen metabolism, other C_{19} androgen conjugates have recently been measured and may also be useful markers of hirsutism in women. In addition to normal controls we studied both hirsute and nonhirsute patients with polycystic ovarian syndrome who had similar levels of circulating androgen precursors. In these three groups we measured various C_{19} sulfates and glucuronides including serum 3α-diol glucuronide. Serum androgen precursors were elevated, but were equal in the hirsute and nonhirsute patients. Serum androsterone sulfate and glucuronide, and 3α-diol sulfate and glucuronide clearly differentiated the hirsute from the nonhirsute group. Among the conjugates, androsterone glucuronide was most reflective of the difference between the two groups (100.3 ± 28.0 versus 42.9 ± 4.0 ng/ml, $p < 0.05$). In hirsute compared with nonhirsute patients with polycystic ovarian syndrome, serum 3α-diol glucuronide was increased by the smallest amount (32%), followed by androsterone sulfate (38%), 3α-diol sulfate (59%), and androsterone glucuronide with the largest increase (134%). Serum androsterone glucuronide and 3α-diol glucuronide both correlated with androstenedione and dehydroepiandrosterone sulfate in hirsute women but not in nonhirsute women. These data suggest that besides serum 3α-diol glucuronide, other C_{19} sulfate and glucuronide conjugates may reflect peripheral androgen action.

Depressive episodes in premenstrual syndrome

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Episodic depression, a prominent but poorly defined symptom of premenstrual syndrome, was quantitated in 24-hour cortisol secretory episodes (determined by sampling at 20-minute intervals) as biochemical markers, as well as the Beck Depression Inventory and Profile of Mood States as psychometric measures. Results of 16 patients with premenstrual syndrome were compared with six age-matched women with endogenous depression and 16 control women. On both the Profile of Mood States and Beck Depression Inventory, women with premenstrual syndrome showed a marked worsening of scores ($p < 0.01$) during the luteal phase compared with either their own follicular phase scores or the scores of controls in either cycle phase. However, Beck Depression Inventory scores were threefold higher ($p < 0.005$) in women with depression than in those with luteal phase premenstrual syndrome (33.7 ± 3.6 vs. 11.9 ± 2.5). The Profile of Mood States depression scale was also higher ($p < 0.05$) in women with depression than in those with premenstrual syndrome, while scores on other Profile of Mood States scales were similar. The numbers of cortisol secretory pulses identified by the cluster algorithm were similar (5 to 6 per 24 h) in all groups, and the times of circadian nadirs as determined by cosinor rhythmometry were comparable. While the mean amplitude and duration of the cortisol pulses were also similar in women with premenstrual syndrome and controls, both were significantly higher ($p < 0.05$) in women with depression. This resulted in markedly enhanced ($p < 0.005$) cortisol secretion during a given secretory episode in women with depression and in higher 24-hour transverse mean cortisol values in women with depression (87.8 ± 5.8 ng/ml) than in either those with premenstrual syndrome (66.7 ± 3.3 ng/ml) or controls (58.9 ± 3.3 ng/ml). These data affirm the clinical impression that depressive episodes occurring selectively in the luteal phase of the cycle in women with premenstrual syndrome are not present in controls and demonstrate, for the first time, that these episodes are distinct from endogenous depression as measured by both cortisol secretory parameters and psychological indices.

ONCOLOGY

Comparison of repeat smear, colposcopy, and colposcopically directed biopsy in the evaluation of the mildly adnormal smear

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Repeat smear, colposcopy, and colposcopically directed biopsy were performed in 161 patients referred to our department because of a Pap smear showing mild dysplasia (CIN 1). Colposcopically directed biopsies revealed the presence of CIN of different grades in 61 cases (37.5%). In 33 (20.4%) the CIN grade found at biopsy was higher than 1. Repeat smear confirmed the presence of CIN 1 in 67 women (47.2%). In this group of patients colposcopically directed biopsies showed a CIN grade greater than 1 in 12 (41.5%). The repeat smear was negative in 59 patients (41.5%). In this group, biopsy showed varying grades of neoplasia in 12 cases. Colposcopic examination indicated no dysplasia but the presence of minor cervical abnormalities in 76 women (47.2%): at biopsy a CIN grade higher than 1 was found in 9 cases (11.5%). These data suggest that the mildly atypical smear identifies a group of patients at increased risk of CIN but gives little or no information on the disease severity. Repeat smear and colposcopic examination alone appear inadequate to demonstrate the severity of the cervical lesion. Due to the high proportion of CIN 2 and 3 in patients with a mildly adnormal smear, the systematic biopsy of any colposcopically abnormal area seems essential to proper management of the patient.