Plasma and Saliva Concentrations of Progesterone in Postmenopausal Women after Topical Application of Progesterone Cream

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INTRODUCTION

Estrogen- and progesterone-containing hormone replacement therapy compensates for reduced ovarian secretion that occurs with the menopause. Because synthetic progestogens can be mildly androgenic and cause unpleasant side-effects, community attention has focussed on the use of "natural" progesterone skin cream. To date, there is no evidence that progesterone is absorbed through skin in sufficient amounts to be biologically effective. Nevertheless, salivary progesterone has been promoted as a novel medium to monitor women using progesterone cream. During natural menstrual cycles, salivary progesterone measurements follow plasma concentrations, albeit at much lower levels. However, there is controversy as to whether the progesterone sero-salivary relationship still holds after exogenous administration of progesterone in progesterone skin cream.

AIMS

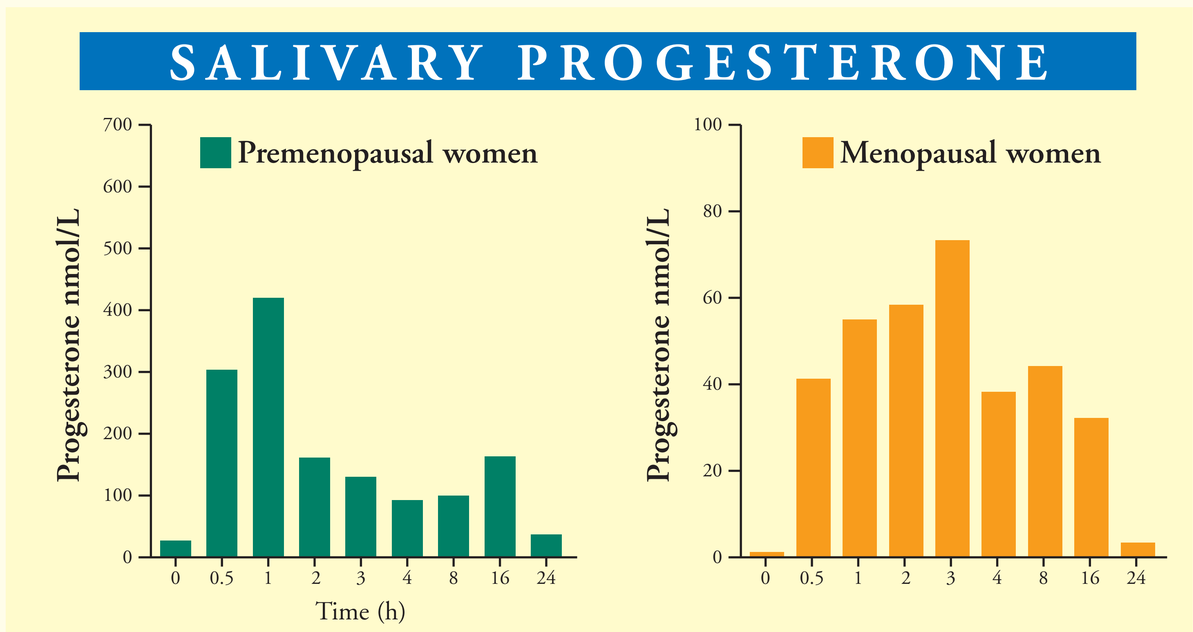
To determine if progesterone is absorbed transdermally and whether this absorption is influenced by menopausal status.

MATERIALS AND METHODS

Six menopausal and 4 premenopausal women were recruited into this study. The six menopausal women (≥2 years since last menses) had elevated serum gonadotrophins (LH ≥ 12 U/L, FSH ≥ 32 U/L), low serum estradiol (< 100 pmo/L) and progesterone concentrations (< 3 nmol/L) consistent with primary ovarian failure. The 4 premenopausal women had normal menstrual cycles and were studied in the mid-luteal phase (day 20-21). We measured serum and salivary progesterone concentrations before and up to 24 hours after topical application of 64 mg micronised progesterone cream (Pro-Feme®, Lawley Pharmaceuticals, Perth, Western Australia), Serum LH, FSH estradiol and progesterone were determined by Immulite (DPC).

RESULTS

In menopausal women, the basal serum progesterone (2.5 ± 0.2 nmol/L, mean±SEM) did not change significantly during the first 3 hours after treatment. Basal salivary progesterones were less than 3 nmol/L but increased significantly ($p < 0.05$) peaking at 3 hours (73 ± 24 nmol/L) and returning to baseline values (3.5 ± 0.7 nmol/L) at 24 hours (see figure).
In premenopausal women, serum progesterone concentrations did not alter after application of progesterone cream. However, salivary levels rose to a mean of 668 nmol/L at 4 hours, significantly higher ($p < 0.05$) than menopausal women at the same time and returned to baseline by 24 hours.



DISCUSSION

- We observed no change in serum progesterone concentrations after topical application of progesterone cream. Premenopausal women in the luteal phase had higher basal progesterone levels than menopausal women, but serum progesterones in both groups remained constant after application of progesterone cream.
- Salivary progesterone values rose significantly in premenopausal and menopausal women, peaking at 3-4 hours, suggesting that progesterone is absorbed through the skin and transported through the body.
- After administration of progesterone cream, salivary progesterones in premenopausal women in the luteal phase peaked at levels ten fold higher than reached by menopausal women.
- Assuming that progesterone secreted into saliva reflects exposure of other tissues to progesterone, then topically applied progesterone can reach target.
- Salivary progesterone measurements confirm transdermal absorption, but a relationship between progesterone dosage and salivary concentrations still needs to be established.

REFERENCES:

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