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Salivary and Plasma Progesterone in Normal Women and in Patients with Benign Breast Disease

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Data on possible involvement of ovarian function by means of decreased progesterone production and/or imbalance in progesterone/estrogen ratio in the pathogenesis of benign breast disease have been reported in the literature (5). More recently, attention has been given to the possible role of prolactin on altered breast physiology (7); the influences exerted by this peptide on ovarian steroid hormone secretion (6) are generally acknowledged. Despite these observations, general agreement on the role of decreased levels of progesterone in the pathogenesis of cystic breast disease is lacking, owing to conflicting reports on hormonal profiles. Either normal (2) or low levels (5) of the gonadal steroid progesterone have been reported in women affected by fibrocystic mastopathy. A possible explanation of this discrepancy may be found in the involvement of different pathogenetical factors, but technical aspects also may be considered.

Usually employed radioimmunoassay methods give an estimate of the total levels of circulating steroid hormones, whereas only the non-protein bound, free fraction is known to yield biological activity. Different methods have been described for the determination of plasma steroid free fraction (1,8), but, at present, none is sufficiently accurate and easy to perform on a routine basis. However, recent data from others (9,10) and our laboratory have given an insight on apparent free levels of steroid hormones, and particularly testosterone (3) and progesterone (4), by means of salivary evaluations. This work was based on the facts that saliva contains very low amounts of proteins and that a close correlation between (at least) salivary testosterone values and plasma free testosterone values (as measured by equilibrium dialysis) has been shown (9).

In our study on 9 healthy, normally menstruating women (4), a marked rise in plasma progesterone levels (202% with respect to periovulatory values) was shown in the luteal phase, but such a rise was far less pronounced than that of salivary progesterone (2755%). These peak values were observed both in plasma and in saliva 8 days after the ovulatory peak.

This chapter presents preliminary data about progesterone salivary levels in a group of women affected by benign disease of the breast, as compared to a similar age-matched control group.

MATERIALS AND METHODS

Fourteen women (22 to 37 years) affected by benign disease of the breast (typical fibroadenosis) and 16 age-matched (23 to 36 years) controls volunteered for the study.

Diagnosis of fibroadenosis of the breast was performed by clinical examination and confirmed by at least two of the following laboratory procedures: contact thermography, X-ray, ecography, and biopsy. Both controls and patients had been free from any medication for at least 3 months prior to the present investigation and had regular menstrual cycles lasting for 26 to 30 days. The time of ovulation was assessed by means of mid-cycle LH/FSH peak, using a radioimmunoassay (RIA) method. In all the subjects, basal body temperature showed a typical biphasic pattern with a plateau lasting from 10 to 14 days.

Salivary and plasma samples were collected daily throughout the luteal phase. Both saliva and plasma were obtained between 7 and 9 a.m., following an overnight fast. Collection of saliva, performed over a period of 20 to 30 min by having the subjects spit directly into glass tubes, always preceded that of plasma samples in order to avoid a possible stress effect on salivary secretion. Evaluation of plasma and salivary progesterone was performed by radioimmunoassay technique, whose main technical characteristics are outlined in Table 1.

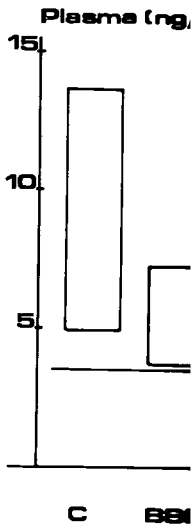
RESULTS

Figure 1 shows the results obtained. Plasma progesterone levels showed their peak values approximately 8 days after the LH peak. Ranges observed both for patients and controls (respectively, from 3.68 to 7.25, mean 5.5 and SD 1.2 ng/ml; and from 4.92 to 13.65, mean of 9.4 and SD of 2.9 ng/ml) were consistently above the lower limit of normality for our laboratory. In addition, a certain degree of overlapping between the two groups was shown, making it impossible to discriminate patients from normals based only on plasma measurements.

Data on saliva determination, however, showed that although saliva progesterone levels of control subjects were well above the lower limit of normal range (from 0.94 to 1.48 ng/ml, with a mean of 1.1 and SD 0.2), those of patients were below

TABLE 1. *Progesterone radioimmunoassay*

	Antiserum	Recovery %	Inter-assay %	Intra-assay %	Limit of detection ng/ml
Plasma	Biodata	93.8 ± 6.0	9.1	4.9	0.008
Saliva	Biodata	93.2 ± 6.3	9.4	5.2	0.008



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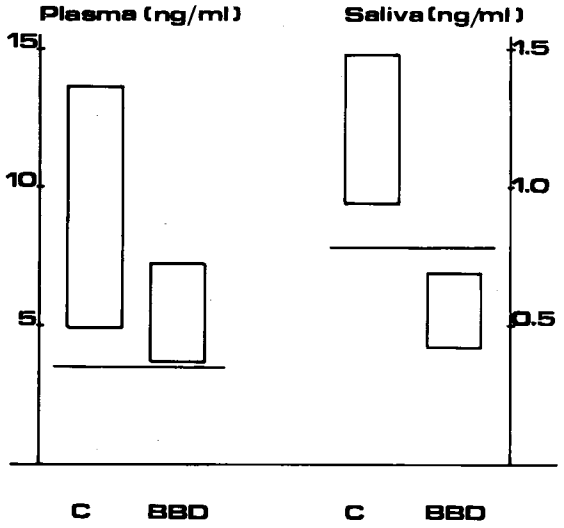

FIG. 1. Luteal phase plasma and salivary progesterone ranges (peak levels:ng/ml) in controls (C) and in patients with benign breast disease (BBD). Lower normal levels shown by continuous line.

such a limit, values ranging from 0.42 to 0.69 ng/ml, with a mean of 0.5 and SD of 0.1.

SUMMARY

Data obtained emphasize the clinical usefulness of salivary progesterone assay. In addition to methodological advantages, such as avoidance of venipuncture and evaluation of a longer observation period, salivary measurement appears to be more sensitive to physiopathological conditions such as benign breast disease, giving an evaluation of the free fraction of the circulating steroid.

These results, even if statistically significant, were drawn from a limited number of cases and need further confirmation in a larger experimental group. Moreover, information about other hormonal parameters, such as circulating estradiol and prolactin, is lacking, and work is needed to investigate further the hormonal patterns and their relationship with salivary progesterone levels.

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Fecal Steroid E
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