SHBG PATTERN DURING THE MENSTRUAL CYCLE

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SUMMARY

The Authors evaluate the variation of Sex Hormone Binding Globulin during the menstrual cycle in 17 normal menstruating healthy women.

The resulting data seem to show not significant modification in the protein serum level, in agreement with most of the reports in literature.

A possible explanation might be the insufficient length of estrogen stimulation in the prolipherative phase.

This might lead to hypothesize that in presence of marked impairments of sex steroid metabolism SHBG levels may vary significantly.

In the last twenty years several investigations have been carried out in order to clarify the nature of the mechanisms which allow sex steroids to act in their target tissues.

As these hormones are unstable and insoluble in water solution, they are transported by plasma proteins in their migration throughout the organism. However, only the free share is biologically active as it is the only one able to enter the target cells.

The existence of a specific binding protein for sex hormones, the Sex Hormone Binding Globulin (SHBG) was hypothesized in 1958 [1] and proved in 1966 [2].

Thereafter the Searchers showed that both in males and in females the greatest part of androgens, at 37 °C, are linked to SHBG by a high affinity binding [3].

Only a small fraction of sex steroids is free in the plasma: 1% of total testosterone and 2-3% of total estradiol [4, 5].

The binding affinity of sex steroids for SHBG has been showed to be directly correlated to their biological activity "in vivo" [6, 7, 8].

Moreover, SHBG circulating levels are strictly correlated to androgen and estrogen production [9, 10, 11, 12, 13]; in fact, estrogens stimulate while androgens inhibit SHBG synthesis [12, 13].

For instance, when estradiol level increases we observe a rise in its free share; this fact, by enhancing the production of SHBG, leads to a fall in free testosterone level.

In this case the variation of SHBG acts as an estrogen-helper. Quite similar is the mechanism of androgen action.

Therefore, SHBG may be considered as an amplifier of the hormonal action of the steroids it binds [4].

Variations in the levels of SHBG, in turn. result in variations of free hormones levels [4].

"In vitro" studies demonstrated that an increase in the concentration of SHBG leads to a reduction of free testosterone

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and estradiol levels; the drop, however, was greater for testosterone than for estradiol ([4]).

All the above considerations lead us to believe that the study of SHBG may be of greatest interest in the different situations of gynecological physiopathology.

SHBG variations during the menstrual cycle have been studied by several Authors ([12, 13, 14, 15, 16]) with contrasting results: while in most of the studies ([12, 13, 14, 15]) SHBG levels did not exhibit statistically significant variations in the different phases of the menstrual cycle, Solomon *et al.* ([16]) showed a remarkable increase of SHBG levels during the prolipherative phase.

To understand better the physiopathologic aspects connected with sex steroids metabolism in the different periods of female reproductive life and to have personal data on SHBG variations during the menstrual cycle, we started the present study, the results of which may be the basis for further investigations.

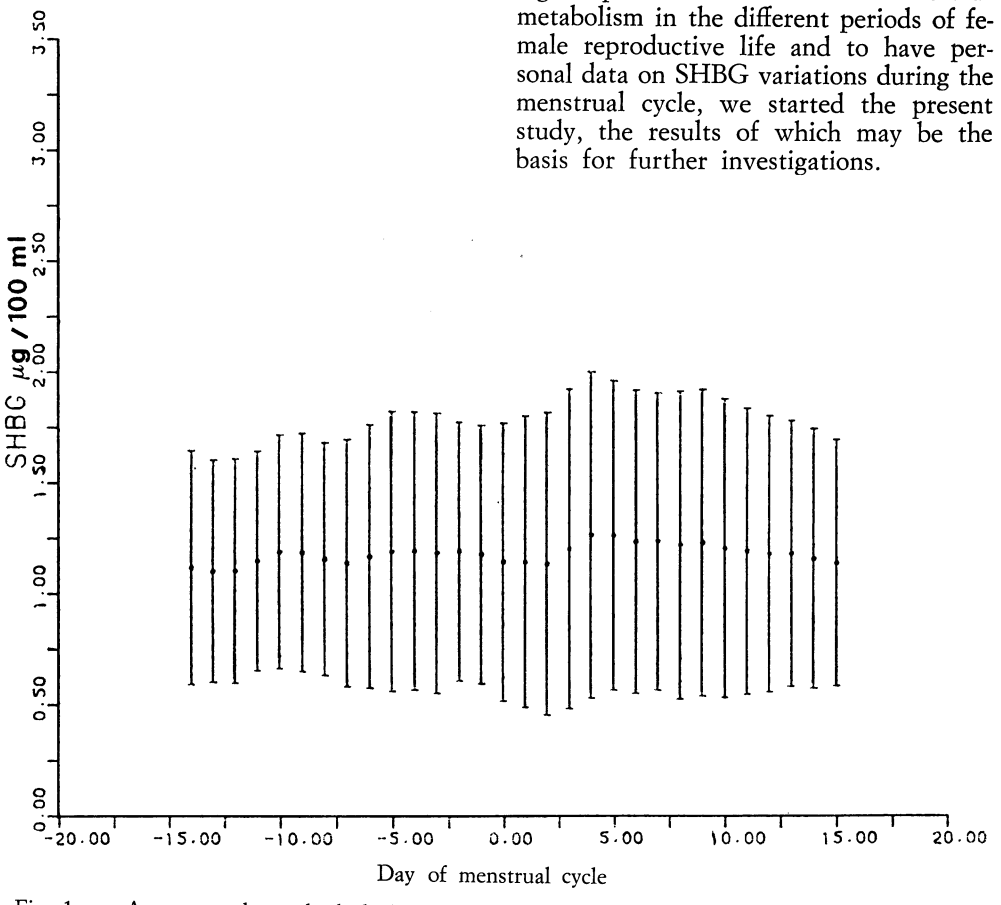

Fig. 1. — Average and standard deviation of SHBG levels for every day in the 17 examined women. The data were obtained by linear interpolation of the experimental values.

MATERIAL AND METHODS

The study was carried out on 17 healthy women: their mean age was 35.2±3.6 years and their cycles were normal as to frequency (28±3 days), amount and duration of the menstrual flow.

Blood samples were drawn from the cubital vein between 08.00 and 11.00 a.m. every third day during a complete cycle.

After spontaneous coagulation blood was centrifuged and sera were stored at −18 °C until

SHBG assay; great care was put in avoiding sera unfreezing. SHBG was assayed according to a recent method [17] suitably modified: it is based on the separate precipitation of the complex SHBG-labeled hormone in a proper concentration of ammonium sulphate. At the same time we carried out the assay of FSH, LH, 17-β-estradiol, progesterone and testosterone by kits supplied by the Medical System.

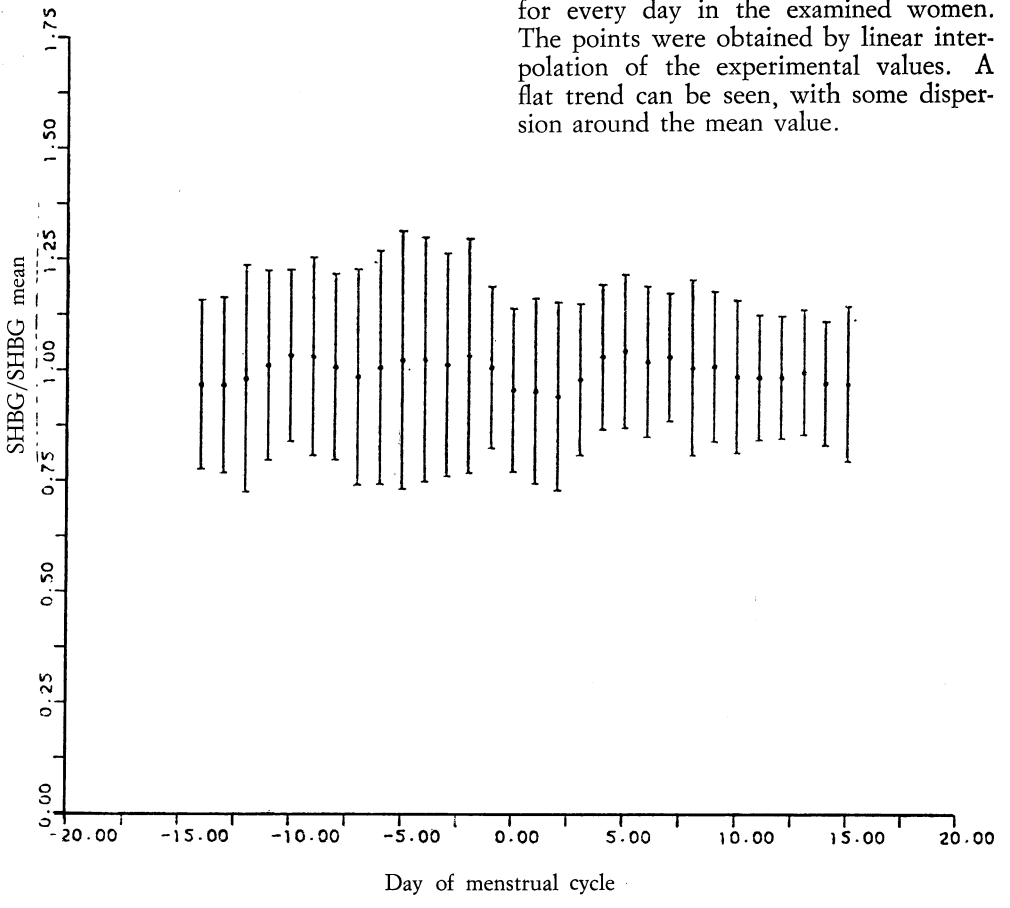

Fig. 2. — Experimental values for every day of the 17 examined women, normalized to the monthly average of every woman.

RESULTS AND DISCUSSION

SHBG serum levels did not show any significant fluctuation during the different phases of the menstrual cycle in the 17 patients we examined.

The assay of FSH, LH, 17-beta-estradiol, progesterone and testoserone gave results consistent with normal ovulatory cycles.

The first table (fig. 1) shows the average and the standard deviation of SHBG for every day in the examined women. The points were obtained by linear interpolation of the experimental values. A flat trend can be seen, with some dispersion around the mean value.

The second table (fig. 2) is similar to the first one, but the points were obtained by normalizing the experimental values to the monthly average of every woman. The trend is flat again with a lower dispersion around the mean value, which means the absence of periodic structures at least within 20%.

Basing on our data we can affirm, in agreement with most of the Authors, that:

1) the parameter SHBG is constant in the fertile age and does not vary throughout the menstrual cycle;

2) this might be explained by the possibility that the estrogen stimulation of the first phase is too short to induce significant responses in SHBG concentration;

3) as a consequence of this, significant modifications of SHBG levels might be supposed to occur when qualitative and quantitative alterations of sex steroids are persistent or when are present impairments of sex steroids metabolic processes.

The consideration might offer new important views in the field of gynecological diagnosis and physiopathology.

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