EFFECT OF THYROTROPIN-RELEASING HORMONE IN PITUITARY-THYROID SYSTEM FUNCTION IN FERTILE WOMEN AFTER SURGICAL CASTRATION

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SUMMARY

The Authors evaluate the effect of surgical castration on thyroid function of fertile women, and the response of TSH to TRH before and 30 days after castration.

INTRODUCTION

It is well known that, after castration, there is a fall in serum and tissue levels of gonadotropin-releasing factors and gonadotropins, which seems to result from the removal of negative feed-back inhibition of gonadal steroids normally exerted on the hypothalamus and pituitary ([7,10,12]).

Clinical and experimental studies have established that estrogens modulate the thyroid function, but the nature and significance of this influence have not been yet ascertained. A stimulatory effect of estradiol has been observed by Labrie *et al.* ([11]) on TSH secretion in the rat; the estrogens could stimulate the pituitary TRH receptor levels ([6]) or increase the ^{131}I uptake in thyroidal cells ([2]).

A decrease in the pituitary content of thyroid-stimulating hormone (TSH), following estradiol administration, has been reported by Simpson and Evans ([17]) and by Grumbrecht and Loeser ([9]) with increase of TSH plasma levels.

Ramey *et al.* ([13]) have shown that both ageing and ovarian function are involved in the modulation of the hypothalamic-pituitary-thyroid system function in the rat.

A possible effect of estrogens on TRH-induced TSH response was hypothesized by Sanchez-Franco *et al.* ([16]) in the follicular phase rather than in the luteal phase of the menstrual cycle.

It should be noted that prolactin, T_3, T_4 plasma levels were seen to be increased during and after surgery ([1,4]). Without post-operative complications, recovery of normal pituitary-thyroid function occurred after 4 to 7 days.

This study was carried out to evaluate the effect of surgical castration on thyroid function of fertile women and the TRH-induced TSH response before and 30 days after castration.

MATERIAL AND METHODS

Eight women, four eumenorrhoic and four hypermenorrhoic, aged from 42 to 52 years,

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underwent a total hysterectomy and bilateral salpingo-oophorectomy.

The surgery was carried out on the basis of the presence of uterine fibromioma (single or multiple nodules) in eumenorrhoic patients and hystologically determined cystic glandular hyperplasia in hypermenorrhoic patients. Surgery was carried out from the 9th to 11th day of the menstrual cycle. All the patients underwent TRH stimulation test 3 days before and 30 days after surgery.

Testing was done between 8 and 9 a.m. in bed. An indwelling cannula was inserted into the forearm vein and blood was withdrawn at −15 and at 0 min before the rapid i.v. injection of 2 ml of sterile saline containing 200 μg of TRH (Serono, Biodata, Italy) to obtain basal hormone levels and then blood samples were collected at 15, 30, 45, 60, 90 and 120 min after injection of TRH. Five and ten days after castration blood samples were drawn from the patients to obtain their basal hormone levels. The total T_4 and T_3 plasma levels were measured by a specific radioimmunoassay using tubes containing covalently bound antibodies on a defined-surface (Byk Gulden Mallinckrodt-SPAC-T_4 and SPAC-T_3 kits, Milan, Italy). The coefficient of variation in T_4 assay were 5% (within assay) and 9% (before assay) over the range 45-120 ng/ml and the sensitivity was 10 ng/ml. The same coefficients of variation in T_3 assay were respectively 4.5% and 8% over the range 0.6-1.7 ng/ml and the sensitivity was 0.5 ng/ml.

The TSH plasma concentrations were determined by a specific radioimmunoassay using a double antibody technique (RIA-Mat TSH, Byk Gulden Mallinckrodt).

The sensitivity was 0.6 U/ml while the coefficients of variation were lower than 10%.

The data were statistically analized by paired "t" test.

RESULTS

Figure 1 shows the effect of TRH on TSH levels 3 days before and 30 days after surgical castration. All the patients showed a rapid and significant increase of TSH plasma levels 15 min after TRH injection. After injection, before castration, TSH plasma levels starting from baseline levels of 3.3 ± 0.87 μU/ml reached 8.41 ± 1.1 μU/ml and 12.15 ± 1.3 μU/ml respectively at 15 and 30 min. Later the values gradually decreased until the end of observation (5.34 ± 1.3 μU/ml).

At the 5th and 10th day from castration, plasma TSH levels were 3.71 ± 0.7 μU/ml and 4.1 ± 0.54 μU/ml respectively. Therefore there was no significant difference between these data and pre-surgery basal values.

As in previous tests, 30 days after castration mean basal plasma TSH levels were 3.58 ± 0.6 μU/ml. That very day the TRH-test made clear TSH values higher than before surgery. Plasma TSH levels reached 13.8 ± 4.3 μU/ml at 15 min; 13.83 ± 2.81 μU/ml at 30 min; 13.46 ± 3.6 μU/ml at 45 min; 11.53 ± 2.0 μU/ml at 60 min; 10.15 ± 2.0 μU/ml at 90 min and 8.05 ± 1.13 μU/ml at 120 min.

Therefore, there was no significant difference at the statistical analysis, between these and the TSH responses before surgery (fig. 1).

After TRH injection, before castration plasma T_3 levels from 1.05 ± 0.1 ng/ml increased to 1.22 ± 0.06 ng/ml and 1.27 ± 0.06 ng/ml, respectively at 90 and 120 min (fig. 2). At the 5th, 10th and 30th day from castration, plasma basal T_3 levels were unchanged: 1.07 ± 0.1 ng/ml, 1.05 ± 0.5 ng/ml and 1.05 ± 0.07 ng/ml respectively. They showed, after TRH injection a response like those before surgery (1.17 ± 0.07 ng/ml at 90 min, 1.30 ± 0.07 ng/ml at 120 min) (fig. 2).

Three days before castration, plasma basal T_4 levels were 80 ± 11.8 ng/ml and, after TRH injection, showed any variation (fig. 2). At 5th day from surgery, T_4 levels showed a short increase (89.5 ± 6.2 ng/ml), whereas at 10th they were 80.1 ± 10.6 ng/ml.

At 30th day basal T_4 levels were 73.3 ± 10.8 ng/ml lower than basal values before surgery. Therefore this decrease was no significant at the statistical analysis, also at 30th day from surgery there was any TRH-induced T_4 response.

DISCUSSION

There are relatively few reports on the TSH response to TRH (Chen and Walpish, 1978)([4]) and on the variations of

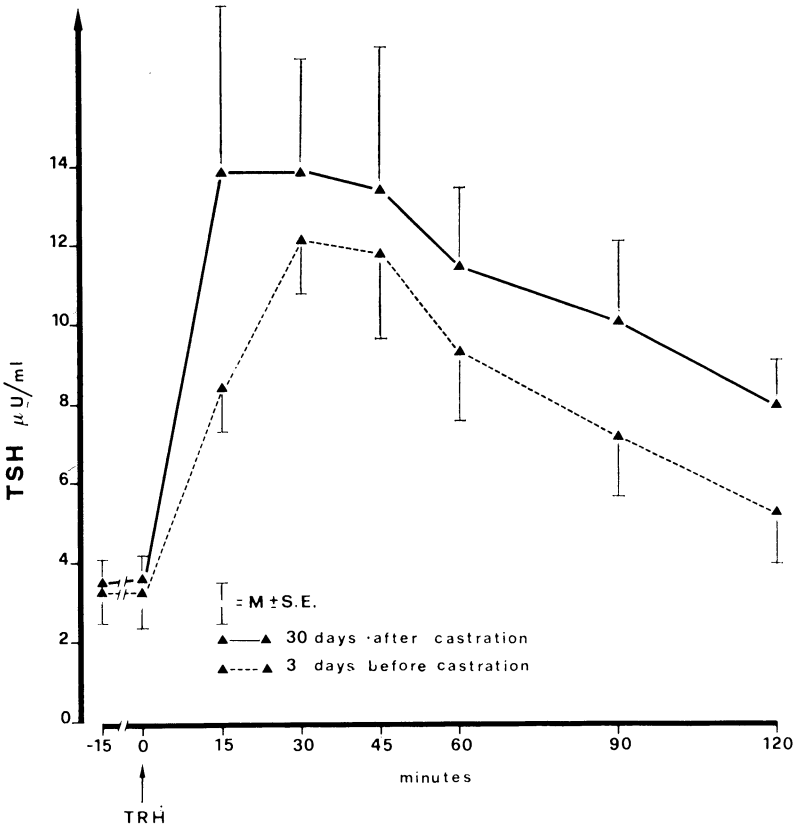

Fig. 1. — Effects of surgical castration on plasma TRH-induced TSH response in eight women. Arrow indicated time at which TRH injection was given and the results are reported as mean ± standard error. Note that the TSH response to TRH was higher 30 days after castration when compared with that before surgery. But this difference was not significant at the statistical analysis.

basal TSH, T_3, T_4 plasma levels with age in rat ([8]).

In man, Snyder and Utiger ([18]) reported TRH-induced TSH response in women is not related with the age, whereas ([19]) in men decreases with age. It has been reported that estrogens have a stimulatory effect on TRH and TSH secretion ([6]) and in female rats the castration determines a decrease both in the TSH response to TRH and in T_3 and T_4 basal levels ([4]). Roti *et al.* ([15]) reported that in the rat castration decreases basal TSH levels and TRH-induced TSH response.

In the present study we observed that the TRH-induced TSH response 30 days after castration was higher before surgical treatment, but this difference was no significant at the statistical analysis. Also, during the same period of observation, the TRH induced no variation on T_3 and T_4 response; it was observed only a short decrease of basal T_4 levels at 30th day from castration, whereas at 5th day, according to Adami *et al.* ([1]) and Chen *et*

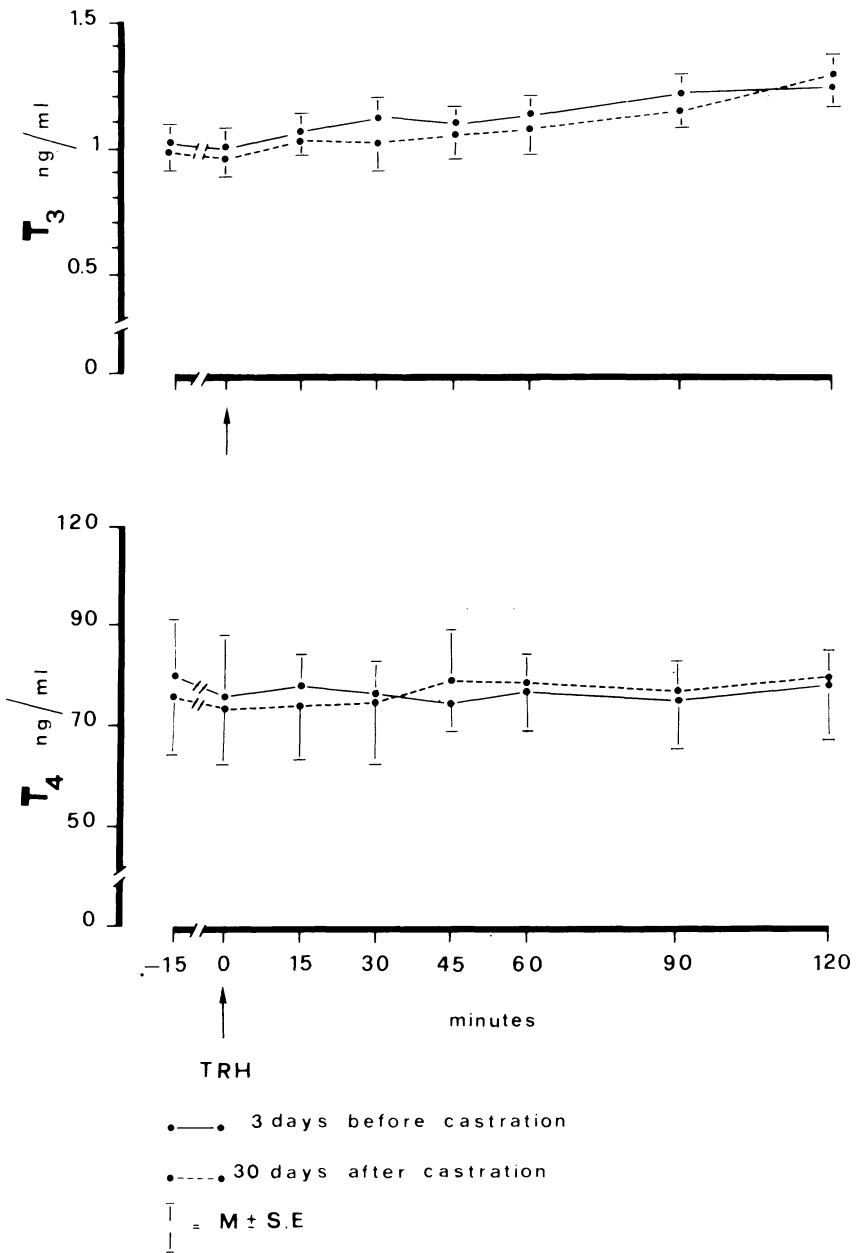

Fig. 2. — In eight women, the TRH test (200 μg i.v.) induced a similar T_3 response before and after castration. Note that the T_4 response was absent. The values are reported as mean ± standard error.

al. ([4]), they were higher than before surgical removal. Chen and Walpish ([5]) and Valueva e Verzhikovskava ([20]) reported the significantly higher basal serum TSH concentrations in intact old male rats: it could represent a compensated response of the pituitary-thyroid system to an early phase of thyroid gland failure.

Our results showed that surgical castration in fertile women determined a larger TSH reserve with a wide standard deviation (fig. 1), according to Riva and Mazzi ([14]) who observed the same results in post-menopausal women.

In conclusion, the different results of various AA. can be explained owing to the different times of observation: in fact, in this situation, the hypothalamo-pituitary and thyroid system comes to a new endocrinological balance. Further investigations are required on hypothalamic and pituitary steroidal receptors to explain the different results reported by several AA. in the last years.

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