

HORMONAL PROPHILE FOLLOWING TOTAL ABDOMINAL HYSTERECTOMY AND BILATERAL SALPINGO OOPHORECTOMY IN POST-MENOPAUSAL ENDOMETRIAL CARCINOMA

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SUMMARY

The Authors report the results of a study carried out on ten post-menopausal patients affected with endometrial carcinoma (FIGO stage I & II) who underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH & BSO).

Estradiol, Testosterone and Prolactin plasma levels were assayed before surgery and in the 2nd, 10th and 30th post-operative day.

The evaluation of the data supports the opinion that in postmenopause Estradiol origin is mainly extraglandular and the ovaries produce Testosterone; the evaluation of Prolactin levels before and after surgery, at last, cannot rule out the hypothesis of an hypothalamo-pituitary dysfunction in post-menopausal patients affected with endometrial cancer.

One of the most interesting problems of modern gynaecological oncology is undoubtedly the relation between hormones and cancer.

Hormone dependence of any degree seems to be excluded for cervical and vulvar neoplasia, whereas it may be hypothesized for ovarian epithelial neoplasia: quite recently, in fact, Progesterone-Receptors have been demonstrated in the affected tissues, and a better response to chemotherapy has been obtained in an encouraging number of cases when High-Dose MPA is administered in association⁽¹⁾.

However, debating about hormone dependent cancer means speaking of breast and endometrial neoplasia, as the hormonal stimulation on a prepared substrate is universally considered the main oncogen stimulus for them to develop.

In endometrial cancer, in particular, the finding of higher Estrogen levels associated with a higher incidence of obesity leads to consider estrogen stimulation the main oncogen factor⁽²⁻¹¹⁾ for neoplastic transformation.

Estrogens, in menopause, derive from the peripheral conversion in the fat-tissue, of androgens produced by the adrenals: the amount of end product is showed to parallel the bulk of fat-tissue, so that obese women will have higher Estrone levels due to higher conversion of Androstenedione; the subsequent hydroxylation of Estrone to Estradiol accounts for the increased levels of the latter: Estradiol stimulation unopposed by Progesterone would then lead to dysplastic and neoplastic growth.

Anyway, we should not underestimate the possible role of Prolactin in the pathogenesis of endometrial neoplasia: though *in vitro*, in fact, Prolactin has been showed to make non-hormone dependent tumours become hormone-dependent when it is present in the culture-medium^(12, 13, 14); besides, studies on Prolactin plasma levels in endometrial cancer affected patients⁽¹⁵⁾.

¹⁶⁾ lead to the hypothesis that an hypothalamic-pituitarian unbalance may be a joint-cause in the development of this malignancy.

Basing on these considerations, we carried out the present study, to improve

After a careful staging, they underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH + BSO). Blood samples were drawn from every patients's cubital vein between 08.00 and 10.00 of three non-consecutive days before surgery, and in the 2nd, 10th and 30th post-operative day.

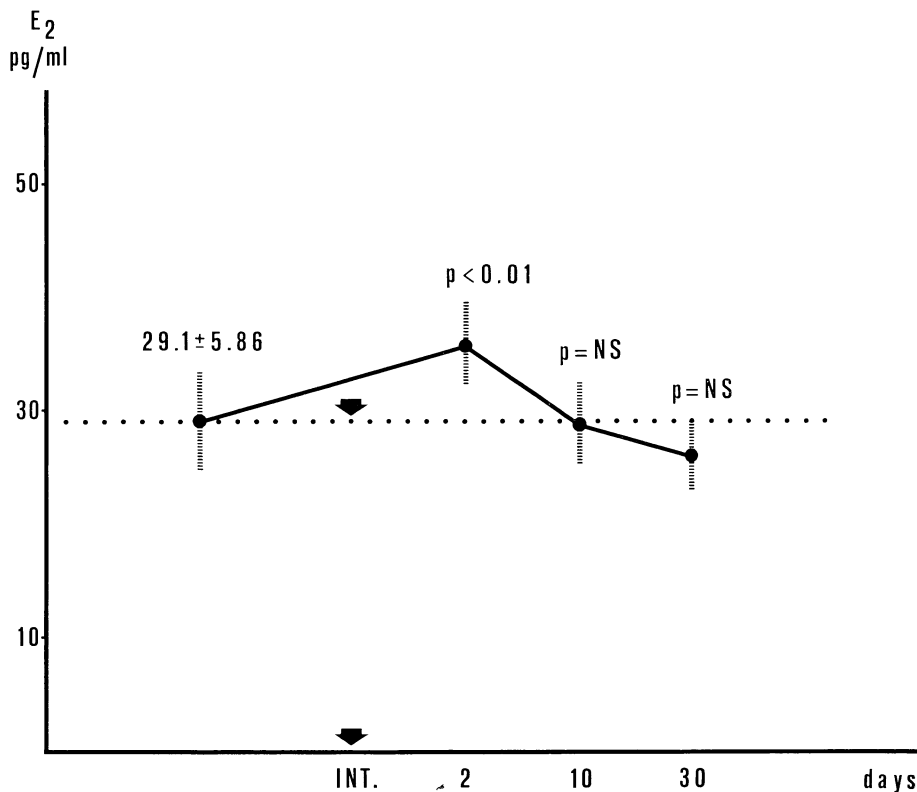


Fig. 1. — E₂ plasma levels before TAH & BSO and in the 2nd, 10th and 30th day from it.

our knowledge of this endocrine picture which seems to characterize this kind of neoplasia.

MATERIAL AND METHODS

We studied 10 patients admitted to the Obst. & Gyn. Dept. of Padua University because of an histologically proved endometrial cancer (FIGO stage I & II): their mean age was 65 ± 7.4 (S.D.) years and they all were above the 20% of their ideal weights.

After centrifugation, serum samples were stored at -20°C until the Radio Immuno Assay of FSH, LH, PRL, E₂, Testosterone. The Assay was performed as previously explained (²³). The statistical significance of the difference between the hormonal levels before and after TAH+BSO was evaluated by the Student's t paired test.

RESULTS

Gonadotropin levels before and after surgery were not significantly different.

Plasma Estradiol mean levels (pg/ml) before surgery and in the 2nd, 10th, 30th post-operative day were respectively (fig. 1):

29.1 ± 5.86 (S.D.);
 35.5 ± 4.55 (S.D.) ($t=2.72$; $p<0.01$);
 30.0 ± 3.43 (S.D.) ($p=N.S.$);
 26.8 ± 4.80 (S.D.) ($p=N.S.$).

Plasma Prolactin mean levels (ng/ml) before surgery and in the 2nd, 10th, 30th post-operative day were respectively (fig. 3):

8.57 ± 2.81 (S.D.);
 28.25 ± 14.21 (S.D.) ($t=4.3$; $p<0.001$);
 20.81 ± 16.84 (S.D.) ($p<0.001$);
 16.21 ± 10.83 (S.D.) ($p<0.001$)).

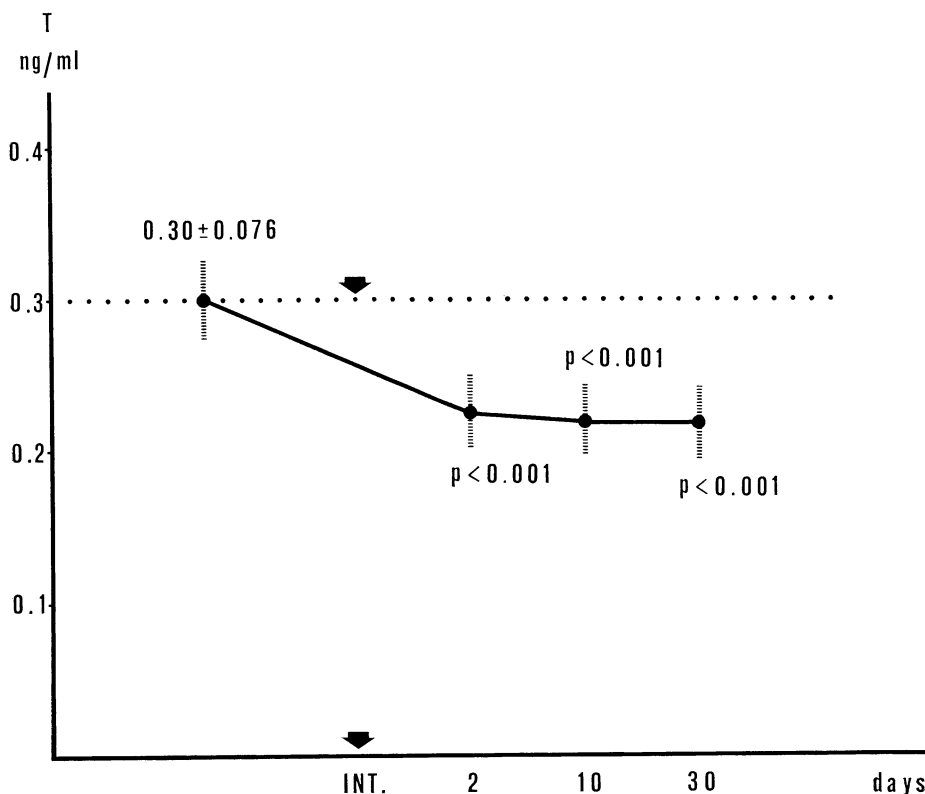


Fig. 2. — T plasma levels before TAH & BSO and in the 2nd, 10th and 30th day from it.

Plasma Testosterone mean levels (ng/ml) before surgery and in the 2nd, 10th, 30th post-operative day were respectively (fig. 2):

0.30 ± 0.076 (S.D.);
 0.16 ± 0.027 (S.D.) ($t=5.49$; $p<0.001$);
 0.14 ± 0.075 (S.D.) ($p<0.001$);
 0.14 ± 0.026 (S.D.) ($p<0.001$).

DISCUSSION AND CONCLUSION

The increased Estradiol levels in post-menopausal women affected with endometrial cancer seem due to the higher incidence of obesity in them than in controls (^{10, 11}), rather than to the presence of the malignancy itself. The most likely source of Estradiol in post-menopause is

the peripheral aromatization of Androstenedione; in this regard, James (¹⁷) believes that about 30% of circulating Estradiol derives from peripheral conversion of Estrone.

On the other hand, some share of Estradiol might derive from peripheral aro-

before and after TAH plus BSO in post-menopausal patients affected with endometrial cancer, seem to confirm the extraglandular origin of the hormone.

Particularly, the significant increase of Estradiol in the 2nd post-operative day might be explained by the adrenal stress

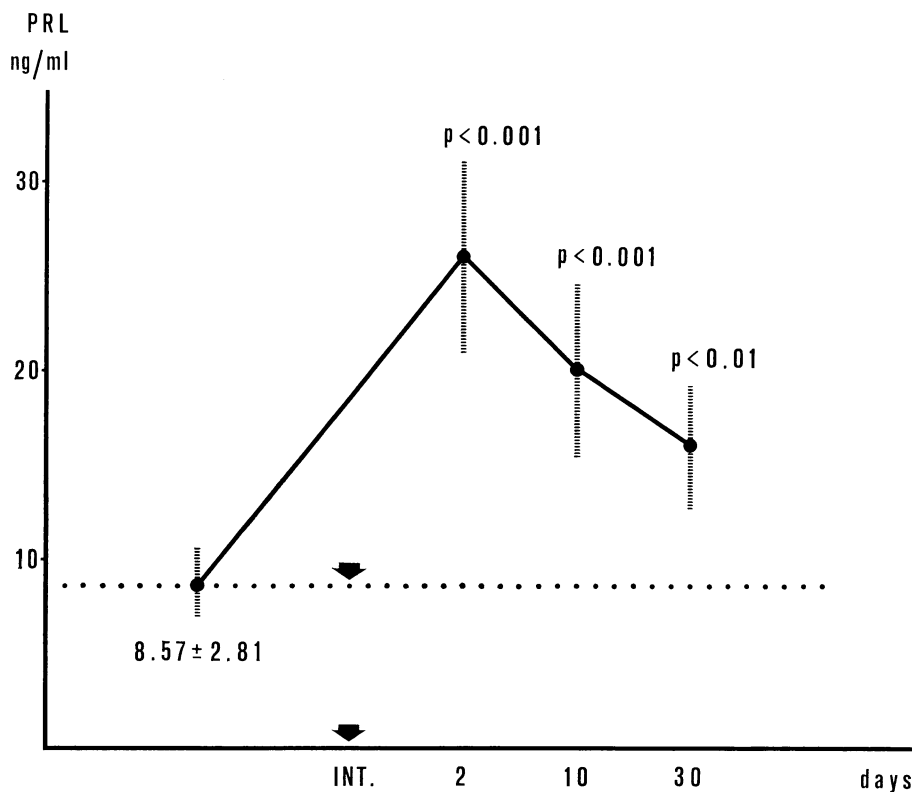


Fig. 3. — PRL plasma levels before TAH & BSO and in the 2nd, 10th and 30th day from it.

matization of Testosterone (^{18, 19}), even if this way is considered secondary (¹⁷).

Also the ovary (²⁰) has been showed to produce Estradiol in post-menopause in cases of gonadal stromal hyperplasia, but additional data should be required.

Though theoretically Estradiol may derive either from direct gonadal synthesis or from extraglandular production, our data (fig. 1) on hormonal plasma levels

and the consequent increase of circulating Androstenedione disposable for aromatization to Estrone and, then, to Estradiol; recent reports in literature (²¹) seem to support our results.

The extraglandular origin of Estradiol is furtherly supported by the finding of no significant difference between its levels before surgery and in the 10th and 30th post-operative day; the presence or ab-

sence of the ovary then would not influence in any way post-menopausal Estradiol plasma levels^(9, 21, 22).

Testosterone plasma levels in menopause depend on both ovarian and adrenal production⁽²²⁾; this fact is furtherly supported by our data (fig. 2), which indirectly lay stress on the importance of BSO as an advisable complement to TAH in the surgical treatment of post-menopausal endometrial carcinoma; the smaller amount of circulating Testosterone would lead to a reduction of its conversion to Estradiol.

As to Prolactin (fig. 3) our data seem to agree with the reports, frequent in literature, according to which its levels increase in stress-conditions.

On the other hand, if Prolactin increase in the 2nd post-operative day may be explained by the stress, it is difficult to interpret its persistence in the 10th, and 30th post-operative day.

The small number of cases we studied let us draw no conclusions about the possible interference of Prolactin in the pathogenesis of endometrial cancer, even if our results make us suggest the opportunity of further investigations on the hypothalamo-hypophyseal function in women affected with this malignancy.

The overall evaluation of our results leads us, at last, to the following conclusions: 1) Estradiol in post-menopause has an extraglandular origin, though indirectly it derives from the peripheral aromatization of adrenal androstenedione; 2) Testosterone plasma levels in post-menopause significantly decrease after BSO; this means that a share of its production is to be ascribed to the ovaries; 3) the persistence of high Prolactin levels even long after surgery may lead to hypothesize that a dyencephalon-hypophyseal unbalance may have a role in the pathogenesis of post-menopausal endometrial adenocarcinoma.

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