Pituitary human chorionic gonadotrophin in reproductive ageing

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Introduction

- Production of non-pregnancy human chorionic gonadotrophin (hCG) by the pituitary gland can occur in older women: up to 8 mIU/ml in serum of women aged 45-55, and 13 mIU/ml in women aged >55.
- However, the association with reproductive rather than chronological age has not been examined, which is important because women aged 45-55 could be pre-, peri- or indeed post-menopausal.

Purpose of the study

- This study examined the relationship between pituitary hCG and reproductive hormones in daily urine samples from pre-, peri- and post-menopausal women.

Methods

- Volunteers were recruited into the following cohorts: pre-menopausal (regular menstrual cycles and no peri-menopausal symptoms), n=19; post-menopausal (last menstrual period >1 year ago), n=16; and peri-menopausal (irregular menstrual cycles and/or peri-menopausal symptoms), n=36.
- Daily urine samples were collected for complete menstrual cycles or for a minimum of 20 consecutive days of absent or erratic menses. hCG, follicle stimulating hormone (FSH) and luteinising hormone (LH) were measured using validated urinary AutoDELFIA assays (Perkin Elmer).

Results

- In pre-menopausal women, elevated pituitary hCG was rarely seen (maximal level 0.96 mIU/ml), and usually occurred on the day of LH surge.
- In post-menopausal women, elevated pituitary hCG was seen in conjunction with elevated FSH and LH (median: 0.85 mIU/ml, maximal level: 9.7 mIU/ml, 2% of samples had hCG >5 mIU/ml). An example of hCG production in a post-menopausal woman is shown in Figure 1.

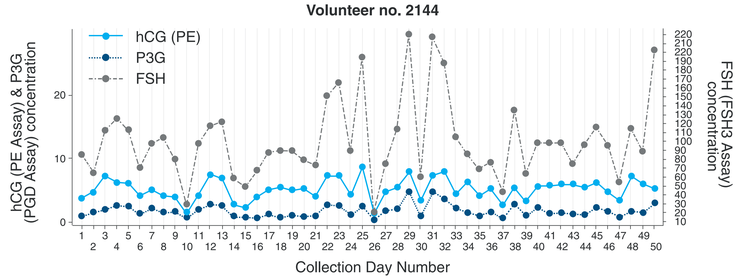

Figure 1: Hormone concentrations in a post-menopausal woman. hCG and FSH in mIU/ml, P3G (pregnanediol-3-glucuronide) concentration in µg/ml. This volunteer has no menstrual cycles; however, she is continually producing high concentrations of FSH and co-producing detectable quantities of hCG (2-8 mIU/ml). P3G levels remain consistently low.

- In the peri-menopausal cohort, 20% of women had hCG >1 mIU/ml and 1.3% >5 mIU/ml in at least one sample. Ten volunteers had normal menstrual cycles with no elevation of hCG, 16 volunteers had no menses with similar hormonal profiles to post-menopause (elevated hCG, FSH, LH), and 10 volunteers had erratic profiles typical of the changing ovarian activity of the peri-menopause. Elevated hCG was seen intermittently in these erratic profiles, in combination with elevated FSH and LH (Figure 2).

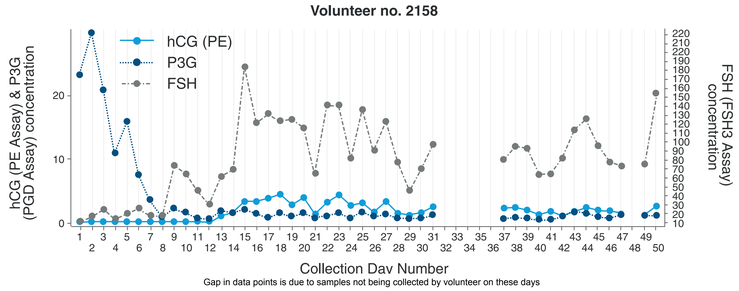

Figure 2: Hormone concentrations in a cycle from a peri-menopausal woman. hCG and FSH in mIU/ml, P3G concentration in µg/ml. It can be seen at the beginning of the cycle that P3G levels are falling whilst FSH levels are low and no hCG is present. FSH is then produced in very high concentrations and a small amount of hCG (2-8 mIU/ml) is co-produced. During this period of hCG production, P3G levels remain very low.

- In peri-menopausal women, hCG concentration was highest in the most aberrant profiles (up to 9.1 mIU/ml). Therefore, elevation of pituitary hCG appears to be directly related to reproductive age rather than chronological age.

Conclusions

- **Elevation of pituitary hCG is directly associated with reproductive age.**
- **An increasing incidence and absolute concentration of hCG is seen in conjunction with the erratic hormonal profiles that are characteristic of late peri-menopause and post-menopause. In contrast, elevated pituitary hCG is not seen in pre-menopause or non-aberrant cycles in peri-menopausal women.**
- **Elevated pituitary hCG could be misinterpreted as being indicative of pregnancy if not considered in the context of the woman's reproductive age. Chronological age should not be solely relied upon because of the inter-individual variability of age of entry to and from the peri-menopause.**

Study funding

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Declaration of interest

Sarah Johnson, Lorrae Marriott: Employees of SPD Development Company Ltd, a fully owned subsidiary of SPD Swiss Precision Diagnostics GmbH, the manufacturers of Clearblue pregnancy and fertility tests.

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