

The natural history of the physiological and endometrial dynamics during the perimenopause.

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Introduction

The perimenopause or menopause transition, is characterised by irregularities in ovarian function. Highly erratic oestrogen levels and inconsistent progesterone levels create a disturbance in the normally highly regulated hormonal balance [1]. In this study we explore these changing hormonal dynamics in early and late perimenopause in relation to the symptoms that women experience and the effects on the endometrium and menstrual patterns. We are particularly interested in whether these hormonal disturbances tip the balance towards oestrogen dominance and thus favour the development of endometrial pre-cancers [2]. Recently constructed perimenopause staging criteria will be used to classify participants into early, mid and late perimenopause, enabling us to further clarify the hormonal characteristics associated with each of the perimenopausal stages.

Method

Data presented here are the preliminary observational findings from a group of 54 perimenopausal women taking part in the 3-year comparative and longitudinal study. Participants recorded scores for 21 different experiences, menstrual patterns and basal temperatures using the Daily Perimenopause Diary (© J Prior, 1992) over 2-5 consecutive menstrual cycles. Menstrual blood loss was measured by colorimetric analysis of processed sanitary material from two menstrual periods. Blood samples were taken thrice weekly during one menstrual cycle (while recording Diary) and concluded with a transvaginal ultrasound and endometrial biopsy, the results of which are not yet available. Analyses of the Daily Diary experiences, the basal temperatures, menstrual blood loss and endometrial ultrasound findings are presented here.

Results to date

Fifty-four perimenopausal women aged between 44.5-55 years (mean 48.9) contributed a total of 225 Daily Diaries, 222 of which were complete (starting and ending with a menstrual period). According to new staging criteria, 16 women are early-perimenopausal, 8 are mid-perimenopausal and 31 are late-perimenopausal. The mean cycle length overall in the 222 complete cycles was 32.8 days (SD 16; range 14-120 days). The mean cycle length for each of the perimenopause stages were early: 26.8 (22-41); mid: 28.84 (16-69); late: 38.4 (14-120). Using the least means squares method of basal temperature determination, 78.7% cycles were deemed ovulatory, 15.1% were anovulatory and 6.2% had insufficient temp data for analysis. Ovulatory cycles were seen in 90.1%, 77.8% and 71.6% of cycles in early, mid and late perimenopause respectively. The mean menstrual blood loss was correlated to stage of perimenopause (39, 51 and 94 ml for early, mid and late perimenopause respectively). Vasomotor symptoms (VMS) were experienced by 81.5% women in at least one recorded cycle. Daytime and nighttime VMS was equally distributed across the stages of perimenopause, being in 45 and 48% of cycles from women in the early stage, 27 and 42% of cycles from women in mid stage and 51 and 50% of cycles from women in late stage. Overall, there were scores for VMS in 46.3% of ovulatory cycles and 58.8% anovulatory cycles. In ovulatory cycles, the mean number of daytime VMS scores per day was higher during the follicular phase than during the luteal phases but there was no phase effect across the cycle. Mid-follicular phase endometrial thickness measurements were no different between the stages of perimenopause, being, 5.8 mm (SD: 0.97) in early stage, 6.3 mm (SD: 0.76) in middle stage and 5.4 mm (SD: 1.3) in late stage perimenopause.

Discussion

The highly erratic hormonal milieu during the menopausal transition has yet to be fully characterised. With future hormonal analyses, this study will help our understanding these hormonal changes and the impact on perimenopausal experiences and menstrual patterns throughout the three stages. Analyses so far illustrate the high prevalence of “classical” menopausal experiences such vasomotor symptoms in ovulatory as well as anovulatory cycles. This suggests that changing relationships between oestrogen and progesterone as well as “absolute” levels of hormones play a role in these experiences. Oestrogen dominance in particular during the transition may play a role in both symptoms and the propensity for abnormal endometrial proliferation.

1.Prior, J.C. *Endocrine Reviews*, 1998. **19**(4): p. 397-428.

2.Hale, G.E., C.L. Hughes, and J.M. Cline *Journal of Clinical Endocrinology & Metabolism*, 2002. **87**(1): p. 3-15.

The menopause transition is characterised by complex hormonal changes and a wide variety of troubling experiences. This study aims to characterise these changing hormonal dynamic underlying these experiences and to investigate whether there is a unique perimenopausal predisposition to abnormal endometrial proliferation