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Short report

Unpredictable endocrinology of the menopause transition: clinical, diagnostic and management implications

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Abstract

The approach to menopause can be divided into the early (E) and late (L) menopausal transitions (MT) on the basis of menstrual irregularity (EMT) and subsequent observation of at least one episode of 60 or more days amenorrhoea (LMT). In total, 40–60% of cycles in the LMT are anovulatory, often with low oestradiol (E2) and high follicle-stimulating hormone concentrations. The ovulatory cycles have variable endocrine characteristics, none of which is specific to EMT or LMT. Hormonal measurements of FSH and E2 are thus of little diagnostic value because of their unpredictable variability. Symptoms during the transitions may result from high or low E2 and can often be satisfactorily managed with low-dose oral contraceptives, which suppress pituitary–ovarian function.

Keywords: Menopause transition, FSH, oestradiol, symptom management, menopause prediction

Key learning points

- (1) The onset of menstrual cycle irregularity, generally occurring in women >40 years of age, is the diagnostic criterion for the occurrence of the early menopause transition (EMT). There are no specific endocrine characteristics of the menstrual cycles occurring during that transition and the majority of cycles are ovulatory.
- (2) The occurrence of 60 days or more of amenorrhoea is a generally accepted marker of entry into the late transition (LMT), particularly if it occurs more than once and after previous cycle irregularity. In total, 40–60% of cycles in the late transition are anovulatory. However, the full range of cycle types, from cycles resembling those in mid-reproductive life to those showing luteal phase insufficiency, may occur during the late transition.
- (3) Because there are no predictable endocrine changes in the cycles during either EMT or LMT, the measurement of hormones, particularly follicle-stimulating hormone (FSH) and oestradiol during the follicular phase provides no useful diagnostic information as hormone levels fluctuate extensively during the transition.
- (4) Symptoms may vary during the transitions and they result from either high or low oestradiol concentrations.
- (5) Optimal management may be to suppress pituitary–ovarian function with the use of low-dose oral contraceptives.

Overview of the case

A lady aged 46 consulted her family doctor because of symptoms of flushing, sweats and at times painful breasts. She had noted that her menses had become irregular in the past 12 months. She requested blood tests to find a cause for her symptoms and to determine 'whether she was menopausal'. Her doctor ordered FSH and oestradiol. FSH was 15.6 (about double the normal follicular phase concentration) and oestradiol 950 pmol/L (a mid-cycle type level). The sample was taken the day before she experienced menstrual flow and similar results were obtained early in the following cycle.

Questions

- (1) Should her doctor have agreed to do blood tests?
- (2) How can the results obtained be explained?
- (3) Is she likely to experience her final menses within the next three months?

Management options

Consideration of questions posed

- (1) *Should her doctor have agreed to do a blood test?*

As outlined in the key learning points, hormone measurements are generally of little if any value during the menopausal transition because of the wide fluctuation in hormone levels.^{1,2} Therefore he should not have agreed to do so.
- (2) *How can the results obtained be explained?*

The results obtained in the lady described may be due to a second ovulation late in the menstrual cycle, leading to atypical oestradiol secretion and ovulation very close to the time of the next menses as described by Hale *et al.*³ Blood samples obtained during the menopausal transition may show a very wide range of FSH and oestradiol concentrations, which vary greatly from one cycle to the next and within the same cycle.
- (3) *Is she likely to experience her final menses within the next three months?*

It is impossible to predict from the data provided the likely occurrence of her final menses. She has experienced one year of menopausal symptoms and her history suggests that she is still in the EMT. The transition on average lasts about four years,⁴ and therefore the likelihood that she would experience final menses within the next three months is low.

Symptom management

This lady's history of flushing, sweats and at times mastalgia, given her age of 46 years and her recent history of irregular menstrual cycles makes variable ovarian function as occurs during the menopausal transition by far the most likely cause of her symptoms. If she is sexually active and a non-smoker, then optimal management may be with a low-dose oral contraceptive, which would result in the suppression of pituitary and ovarian function, and hence would tend to eliminate the widely fluctuating hormonal changes that are occurring. Such management can be continued until the average age of menopause, i.e. to age 50–52. If there are reasons that she should not consider oral contraceptives, e.g. a previous history of venous thromboembolism, or significant cigarette smoking, she would be advised to use a barrier form of contraception and to be treated with sequential hormone therapy using transdermal oestradiol and an oral progestin for 12 days per month, if possible, timed to her own cycle. Periods of low oestradiol in this lady may be associated with flushes, sweats and vaginal dryness, while periods of high levels of oestradiol, as found in her, may lead to symptoms such as headache, irritability, bloating, heavy bleeding and mastalgia.

Anti-Mullerian hormone, which is generally stable from one cycle to another, regardless of its ovulatory status, appears to be a promising index of ovarian reserve and an approximate indicator of when final menses may be expected. However, current use of this predictor still gives a wide range for the timing of final menses.⁵

Where further research is needed

Attempts at staging the approach to menopause were made at a workshop in 2001, the Stages of Reproductive Aging Workshop (STRAW).⁶ This provides the basis for the current definition of the EMT and LMT with other stages defined prior to and following those periods of the approach to menopause. Further research is needed to develop markers of approaching menopause in women who have been hysterectomized and to determine whether different definitions are required, e.g. in women with obesity or in cigarette smokers. It would also be useful to have a method of diagnosing approaching menopause in women who have been on long-term oral contraceptive therapy.

Conclusion

Menopausal transition is a time of unpredictable menstrual cycle endocrine patterns. Cycles may show normal ovulatory features or varying degrees of impairment of ovarian function. The unpredictability of the hormonal changes makes hormone measurements unreliable in characterizing an individual's status and variable hormone levels may give rise to variable symptoms. There are no specific endocrine features of cycles either in the early or in the late transition, although anovulatory cycles are frequent in the latter.

Competing interests: None declared.

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References

- 1 Robertson DM, Hale GE, Jolley D, Fraser IS, Hughes CL, Burger HG. A proposed classification system for menstrual cycles in the menopausal transition based on changes in serum hormone profiles. *Menopause* 2008;15:1139–44
- 2 Burger HG, Hale GE, Dennerstein L, Robertson DM. Cycle and hormone changes during the perimenopause: the key role of ovarian function. *Menopause* 2008;15:603–15
- 3 Hale GE, Hughes CL, Burger HG, Robertson DM, Fraser IS. Atypical estradiol secretion and ovulation patterns caused by luteal out-of-phase (LOOP) events underlying irregular ovulatory menstrual cycles in the menopausal transition. *Menopause* 2009;16:50–9
- 4 Burger HG, Robertson DM, Baksheev L, Collins A, Csemiczky G, Landgren BM. The relationship between the endocrine characteristics and the regularity of menstrual cycles in the approach to menopause. *Menopause* 2005;12:267–74
- 5 Broer SL, Eijkemans MJ, Scheffer GJ, *et al.* Anti-Mullerian hormone predicts menopause: a long-term follow-up study in normo-ovulatory women. *J Clin Endocrinol Metab* 2011;96:2532–9
- 6 Soules MR, Sherman S, Parrott E, *et al.* Executive summary: Stages of Reproductive Aging Workshop (STRAW). *Climacteric* 2001;4: 267–72