Excluding pregnant volunteers

Of the total 41 volunteers, the day of ovulation was determined in 40 women; one woman attended the study site for trans-vaginal ultrasound to determine the day of ovulation.

Methods

A prospective study (NCT01802060) required women (aged 16–45 years) with natural menstrual cycles and no reported infertility to collect daily urine samples from the first day of their period (day 1 of their menstrual cycle) until the first day of their next period. Women attended the study site for trans-vaginal ultrasound to determine the day of ovulation. Where possible, visits were conducted every two days until the follicle size reached 16 mm; then visits were conducted daily, with subsequent scans carried out on days 7 and 9 following ovulation. Where ovulation occurred between two scan days, the day of ovulation was considered as half a day following the last day where a dominant follicle was present. Serum samples were collected on scan days for measurement of serum LH, estradiol and progesterone (ADVIA Centaur XP).

Urinary LH, estrone-3-glucuronide (E3G, a metabolite of estradiol), follicle stimulating hormone (FSH) and pregnanediol-3-glucuronide (P3G) were measured using in-house assays on AutoDELFIA (Perkin Elmer). Validation of these assays has previously been reported.1

Data was analysed using SAS version 9.2, to create normograms referenced to the day of ovulation.

Results

Of the total 41 volunteers, the day of ovulation was determined in 40 women; one woman had an anovular cycle. The mean age of the ovulatory volunteers was 28.9 years (SD 4.76, median 29.5, range 18–37); 95% and 5% of women were white and Asian, respectively. The menstrual cycle characteristics of the volunteers are described in Table 1.

Table 1: Characteristics of the menstrual cycles recorded in the study of volunteers whose data was used to produce the urinary hormone normograms.

<table>
<thead>
<tr>
<th></th>
<th>Median</th>
<th>Minimum</th>
<th>5th centile</th>
<th>25th centile</th>
<th>50th centile</th>
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<th>Mean</th>
<th>SD</th>
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<tbody>
<tr>
<td>Cycle length (days)</td>
<td>37.00</td>
<td>22.00</td>
<td>27.00</td>
<td>22.00</td>
<td>26.00</td>
<td>29.00</td>
<td>34.00</td>
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<tr>
<td>Day of ovulation</td>
<td>40.50</td>
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<td>26.50</td>
<td>11.00</td>
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Normograms consisting of the median hormone levels and 10th–90th centile ranges by day, relative to the day of ovulation observed by ultrasound, were derived for each urinary reproductive hormone measured (Figures 1–4).

Introduction

• Reference ranges of reproductive hormones in women with natural menstrual cycles and no reported infertility provide a valuable tool for understanding the normal range of hormones in relation to day of cycle
• However, due to variation in menstrual cycle length, alignment by cycle day obscures the endocrinology1
• Other researchers have used the day of the luteinising hormone (LH) surge, i.e. when LH levels peak, to create reference ranges.2 however this can still cause distortion of the hormonal profiles because:
  o There is an individual variation in time from peak LH to ovulation1
  o Different LH assays have different levels of sensitivity to the degradation products of LH, thus the timing of the LH peak is assay-dependent

Therefore, the most appropriate way to present reproductive reference ranges is as normograms referenced to the actual day of ovulation, as determined by an independent method
• Trans-vaginal ultrasound is an effective way to determine the day of ovulation if examinations are frequent enough
• This study sought to create new urinary reproductive hormone normograms in relation to the ultrasound-determined day of ovulation.

Methods

A prospective study (NCT01802060) required women (aged 16–45 years) with natural menstrual cycles and no reported infertility to collect daily urine samples from the first day of their period (day 1 of their menstrual cycle) until the first day of their next period. Women attended the study site for trans-vaginal ultrasound to determine the day of ovulation.

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Figure 1. Urinary LH normogram

Figure 2. Urinary E3G normogram

Figure 3. Urinary FSH normogram

Figure 4. Urinary P3G normogram

Conclusion

These are the first urinary reproductive hormone normograms referenced to the actual day of ovulation, and therefore provide the most robust reference ranges to examine menstrual cycle endocrinology.

References


Declaraton of interest

Sarah Johnson, Sarah Weddell and Sonya Godbert are employees of SPD Development Company Ltd., a fully owned subsidiary of SPD Swiss Precision Diagnostics GmbH, the manufacturers of Clearblue Pregnancy and Fertility tests. This study was funded by SPD Development Company Ltd.