Short Report

The LH/FSH ratio has little use in diagnosing polycystic ovarian syndrome

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Abstract

Background The luteinizing hormone/follicle stimulating hormone (LH/FSH) ratio is often requested to help diagnose polycystic ovarian syndrome (PCOS) despite a recent consensus recommending against its use. This study aimed to compare the variability of the LH/FSH ratio in PCOS with that of normal menstruating women over a full cycle in order to establish the diagnostic utility, or otherwise, of the test.

Methods Twelve women with PCOS and 11 matched controls had blood collected at four-day intervals on 10 consecutive occasions over a complete menstrual cycle.

Results The median LH/FSH ratio for individual subjects did not differ significantly between the PCOS and the non-affected group (1.6 versus 1.2, $P = 0.14$). Only 7.6% of samples from PCOS patients had an LH/FSH ratio above three, compared with 15.6% of samples from normal subjects.

Conclusion This study confirms that measurement of the LH/FSH ratio is of limited use in the diagnosis of PCOS.

Ann Clin Biochem 2006; **43:** 217–219

Introduction

An elevated luteinizing hormone/follicle stimulating hormone (LH/FSH) ratio has been used as a diagnostic test for polycystic ovarian syndrome (PCOS) for many years.[1,2] Despite its continued use, concerns about the clinical utility of the ratio have led to the recent Rotterdam European Society for Human Reproduction and Embryology/American Society for Reproductive Medicine (ESHRE/ASRM) consensus statement on PCOS recommending against its inclusion. Only one previous study has evaluated the variation of the LH/FSH ratio in PCOS[3] and this was only from specimens collected at monthly intervals. Therefore, this study aimed to determine the variability of the ratio in women with PCOS in comparison with normal controls throughout a full menstrual cycle.

Methods

Twelve overweight Caucasian women with PCOS (median age 28 years, range 18–31 years) and eleven weight-matched non-affected Caucasian women (median age 30 years, range 19–33 years) with regular menses (every 28–30 days) and normal free androgen index (FAI) participated in the study. PCOS was diagnosed using the Rotterdam criteria.[4] The body mass index (BMI, calculated as weight [kg]/height [m]^2) in the PCOS group was not significantly different from that in the non-affected group (mean $\pm$ SD 33.2 ± 6.3 versus 29.9 ± 3.3, $P = 0.151$ using Mann–Whitney U test). Fasting venous blood was collected into serum gel tubes (Becton Dickinson, Cowley, Oxfordshire, UK) at the same time each day (08:00–09:00) on 10 consecutive occasions at four-day intervals to encompass measurement over at least a complete menstrual cycle. Samples were separated by centrifugation at 2000g for 15 min at 4°C, and stored at –20°C within 1 h of collection. All subjects gave written informed consent and the study had been approved by the local research ethics committee.

Aliquots were thawed and analysed in a single continuous batch of reagents. Serum FSH, LH and testosterone were measured using a two-step procedure that used microparticle immunoassay technology (Abbott Diagnostics, Maidenhead, UK). Sex hormone binding globulin (SHBG) and insulin were measured using

chemiluminescent immunometric assays on the DPC Immulite 2000 (Euro/DPC, Llanberis, UK). Plasma glucose was measured using a hexokinase method on the Synchron LX 20 analyser (Beckman Coulter, Inc., High Wycombe, UK). The FAI was calculated from total testosterone × 100/SHBG. Statistical analysis was performed using SPSS version 11.5.

Results

Four patients from the PCOS group showed biochemical evidence of ovulation (progesterone >16 nmol/L)[5] during the collection period, so a third comparison group of anovulatory PCOS patients ($n=8$) was added (Table 1). Overall, the median LH/FSH ratio for individual subjects did not differ significantly between the clinical PCOS and the non-affected groups (1.6 versus 1.2, $P=0.14$ using Mann–Whitney *U*-test), although the median ratio was higher in the anovulatory group than in controls (1.8 versus 1.2, $P=0.013$). LH concentrations alone were significantly higher in both clinical and anovulatory PCOS than in controls (Table 1). Tukey's test for indices of heterogeneity applied to the clinical PCOS and non-affected group showed no significant differences. The LH/FSH ratio exceeded three in only 9/119 samples (7.6%) in the clinical PCOS patients and in 17/109 controls (15.6%) ($\chi^2=2.047$, $P=0.153$). Two non-affected women had testosterone concentrations between 4.0 and 7.0 nmol/L among their 10 samples but had no clinical evidence of abnormal menstrual cycle or hyperandrogenism.

Discussion

This study has shown that on an individual basis, the median and range of the LH/FSH ratio do not differ significantly between patients with or without clinical PCOS, indicating that the test does not have robust diagnostic utililty. Although the median of the LH/FSH ratio in the anovulatory PCOS group was statistically higher than in controls (1.8 versus 1.2), it is still much lower than the conventionally recommended cut-off of 3.0.[2] Indeed, numerically, there were fewer samples from PCOS patients with a ratio in excess of three than from the group of normally menstruating subjects. In fact, repeated measurement of just LH seemed better than the LH/FSH ratio at discriminating clinical PCOS from controls, although it would be premature to use our data to advocate such a use.

Confirmation of the unreliability of the LH/FSH ratio is important, as while the Rotterdam consensus[4] now does not recommend it as a diagnostic test, it is still often requested for that purpose. For example, in our institution approximately 20% of the 12,000 annual requests for LH and FSH measurement indicated PCOS as a reason for the request, at a cost of over £20,000.

Table 1 *Biochemical features of clinical PCOS, anovulatory PCOS and non-affected group*

Analyte (reference range)	Non-affected (*n*=109)	Clinical PCOS (*n*=119)	*P*-value (clinical PCOS versus non-affected)	Anovulatory PCOS (*n*=80)	*P*-value (anovulatory PCOS versus non-affected)
Fasting glucose (mmol/L) (3.5–5.0 mmol/L)	4.7 (3.6–5.7)	4.9 (4.0–9.0)	<0.001	4.9 (4.0–6.2)	0.034
Fasting insulin (mU/L)	7.8 (2.0–19.2)	19.8 (5.6–153.0)	<0.001	22.0 (4.6–153.0)	<0.001
Testosterone (nmol/L) (0–4.1 nmol/L)	3.0 (1.4–7.7)	3.8 (2.2–6.0)	<0.001	3.8 (2.3–6.0)	<0.001
FAI (0–8%)	5.3 (1.7–22.5)	13.6 (2.6–40.1)	<0.001	13.0 (2.6–40.1)	<0.001
SHBG (nmol/L)	53.8 (18.9–153.0)	24.8 (12.8–141.0)	<0.001	25.8 (12.8–141.0)	<0.001
LH (U/L)	5.9 (0.7–82.6)	9.3 (1.1–54.8)	0.003	11.1 (1.4–22.2)	<0.001
FSH (U/L)	5.2 (1.3–13.2)	5.6 (1.7–11.0)	0.127	5.8 (3.3–8.4)	0.017
LH/FSH ratio	1.2 (0.3–11.0)	1.6 (0.3–6.2)	0.136	1.8 (0.4–4.0)	0.013

Data presented as median (range). *n* denotes the number of samples. LH, luteinizing hormone; FSH, follicle stimulating hormone; SHBG, sex hormone binding globulin and FAI, free androgen index

Our data are the first to look at the LH/FSH ratio over a complete menstrual cycle and are in accord with a previous study by Oei and Kazer,[3] who looked at the LH/FSH ratio variability by repeating LH and FSH concentrations once monthly for four consecutive months. Like ourselves, they also concluded that the LH/FSH ratio was too unreliable in distinguishing between PCOS and normal menstruating women in clinical practice.

The reasons for the apparently poor performance of the ratio must remain speculative. However, it is possible that the test has become less useful than it used to be because of changes to the diagnostic criteria for PCOS (leading to the inclusion of more ovulatory patients), as well as changes in the specificity of gonadotrophin assays.

In conclusion, our data have shown that variability in the LH/FSH ratio is at least as large for normal women as it is for those with clinical PCOS. In support of the recent Rotterdam ESHRE/ASRM consensus, this study therefore confirms that the ratio has little diagnostic utility in clinical practice.

References

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Accepted for publication 20 March 2006