Vian Hussam ALmansi ALqani et al /J. Pharm. Sci. & Res. Vol. 9(9), 2017, 1651-1653

ISSN:0975-1459
Journal of Pharmaceutical Sciences and Research
www.jpsr.pharmainfo.in

High serum LH is a Reliable Predictor of Successful Ovulation in PCOS Women Undergoing Surgical Ovarian Drilling

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Abstract

Background: A variety of medical and surgical option are present nowadays to induce ovulation and enhance fertility of women with PCOS; however the outcome is variable and unpredictable in a large proportion of patients. Of these predictors serum LH has been postulated to predict ovulation and the presence of sufficient controversy in published literatures made this study to be designed.

Objective: To evaluate the role of pre-operative serum LH in predicting ovulation in PCOS women undergoing ovarian drilling.

Patients and methods: The present cross sectional study enrolled 58 PCOS women undergoing surgical ovarian drilling, 29 women with low serum LH and 29 women with high serum LH. The study was carried out in Al-Dewaniyah Maternity and Children teaching hospital in Al-Dewaniyah province in Iraq and extended from January 2016 through June 2017.

Results: Ovulation was reported in 20 out of 29 women in group of high serum LH accounting for 68.9% ovulation rate and in 11 out of 29 women in group of low serum LH accounting for 37.9% ovulation rate. The difference in rate of ovulation was significantly higher in group of high serum LH than that of group with low serum LH (P=0.018).

Conclusion: Pre-operative serum LH is a reliable predictor for ovulation in PCOS women undergoing ovarian drilling.

Key words: PCOS, serum LH, ovarian drilling

INTRODUCTION

Infertility is an important problem facing couples after marriage and polycystic ovary syndrome (PCOS) is a frequent cause of anovulation and infertility (1). Despite discovered more than 70 years ago, great controversy about exact definition of polycystic ovary syndrome (PCOS) is still present and the most recent and used definitions are the National Institute of Health (NIH), Rotterdam, and Androgen excess and PCOS society (AES) criteria, where all are presently used in clinic (1). For that reason the exact prevalence of the disease is difficult to be estimated and it ranged from 6 to 20 %depending on the criteria used for diagnosis (2, 3). Although being of relatively high incidence, the disease etiology is still vague. The clinical manifestations of the disease usually start around the age of puberty (4). One of the most frequent abnormalities is insulin resistance (85%), the other common one being is high androgen level (60-80%) and lead to acne, hirsutism and alopecia (5). Serum concentrations of estrogens, androgens, sex steroid precursors and glucuronidated androgen metabolic products have been reported to be high (6). The sources of high androgen levels are mainly ovaries and followed by adrenal cortex (7). For that reason insulin and androgens have been regarded as key players in the pathogenesis of PCOS. Exposure to androgens in the prenatal period is a well established theory explaining pathogenesis in experimental animals; however, estimation of newborn umbilical venous blood failed to show consistent androgen elevation in humans (8-10). On the other hand, the exposure to androgens in the postnatal life and before the onset of puberty have been tested in experimental animals and gained some acceptance (11, 12). There strong evidence of raised both frequency and amplitude of pulsatile luteinizing hormone (LH) secretion by the anterior pituitary gland with subsequent increases in androgen production by theca cells, whereas low follicle stimulating hormone (FSH) level results in underdevelopment of ovarian follicles and retarded ovulation (1). The possible explanation for high LH concentration is either the high sensitivity of pituitary gland to normal gonadotropin releasing hormone (GnRH) or alteration in GnRH pattern of secretion (1, 13). On the other hand the concentration of FSH in PCOS patients is ether lower than normal or within the lower normal limit (1). The ovulatory dysfunction in PCOS is summarized as extensive early development of ovarian follicles followed by underdevelopment in later stages of follicle maturation (14). This pattern of growth will result in aggregation of small sized follicles together with the phenomenon of under ovulation (1). Ovarian synthesis and secretion of steroid hormone is the result of interaction between theca and granulose cells; Theca cells produce androstenedione from cholesterol, either by the Δ4 or Δ5 pathway, and the conversion to estrone and estradiol thereafter is exclusively acknowledged aromatase cytochrome P450 hydroxylase (CYP19) containing granulosa cells (15).

A variety of medical and surgical option are present nowadays to induce ovulation and enhance fertility of women with PCOS; however the outcome is variable and unpredictable in a large proportion of patients (16). Several predictors like LH/FSH ratio, serum testosterone, serum and follicular activin and inhibin were tested to predict pregnancy in PCOS woman undergoing controlled ovarian stimulation and assisted reproductive technology (17). Of these predictors serum LH has been postulated to predict ovulation and the presence of sufficient controversy in published literatures made this study to be designed. So the aim of the present study was to evaluate the role of pre-operative serum LH in predicting ovulation in PCOS women undergoing ovarian drilling.

PATIENTS AND METHODS

The present cross sectional study enrolled 58 women already diagnosed to have PCOS. The sample was divided into two groups according to serum concentration of LH so that the first group includes 29 women with low serum LH and 29 women with high serum LH. Those women underwent surgical ovarian drilling and were followed up for ovulation. The study was carried out in Al-Diwaniyah Maternity and Children teaching hospital in Al-Diwaniyah province in Iraq and extended from January 2016 through June 2017.

Age; body mass index and serum hormonal studies (FSH, LH and testosterone were estimated for all women participating in the present study. Data were collected and analyzed using Statistical Package for Social Sciences (SPSS version 23). Categorical variables were presented as number and percentage whereas numeric data were presented as mean and standard deviation. Chi-Square test was used to study association between rate of ovulation in PCOS women and grouping according to serum LH concentration, while independent sample t-test was used to study differences in means of numeric variables. P-value for significant level was considered at ≤ 0.05 and for highly significant level at ≤ 0.01.

RESULTS

Current study included 58 women with PCOS who underwent ovarian drilling as a surgical approach to treat the disease, 29 women with low LH serum level (16.69 ±4.72 IU/L) and 29 women with high LH serum level (24.69 ±6.34 IU/L). Mean age of patient within low LH group was 25.97 ±3.87 year and that of women with high LH was 26.34 ±3.22 year and there was no significant difference between the two groups (P=0.686). There was also no significant difference in mean BMI between the two groups, 29.12 ±1.61 and 29.49 ±1.89, respectively (P=0.426). In addition, the difference in mean serum FSH between the two study groups was insignificant, 7.55 ±2.15 IU/L versus 8.31 ±3.32 IU/L (P=0.306). Mean serum testosterone of women with low LH was 81.97 ±12.95 IU/L and those with high LH was 86.55 ±15.82 IU/L; the difference was insignificant (P=0.232). LH / FSH ratio was highly significant higher in the group of high serum LH than group with low serum LH, 3.14 ±0.61 versus 2.31 ±0.66 (P<0.001), as shown in table 1.

Ovulation was reported in 20 out of 29 women in group of high serum LH accounting for 68.9% ovulation rate and in 11 out of 29 women in group of low serum LH accounting for 37.9% ovulation rate. The difference in rate of ovulation was significantly higher in group of high serum LH than that of group with low serum LH (P=0.018), table 2. Odds ratio was estimated and showed that women having PCOS and High serum LH will have a chance of ovulation after ovarian drilling of 3.64 more than that of women with low serum LH (95% CI of 1.23 to 10.78), table 2.

DISCUSSION

The present study showed that outcome of surgical ovarian drilling performed to women with PCOS is significantly more favorable in PCOS women with high LH and that pre-operative serum LH is a good predictor of successful surgical outcome. Prediction of surgical outcome depending on serum LH may be utilized in two ways; firstly women with high serum LH can be assured about the high rate of successful ovulation and secondly women with pre-operative low serum LH can be offered a medical intervention to increase LH level before preceding into surgical ovarian drilling. Hayashi et al., in 2005 (18) estimated pre-operative serum LH in 40 PCOS women undergoing laproscopic ovarian drilling and found that Preoperative serum luteinizing hormone (LH) levels were significantly higher in women who ovulated after LOD than in those who did not ovulate. The findings of the present study agree with the findings of Hayashi et al. (18) Ott et al., in 2009 (19) evaluated the preoperative serum LH concentration in 100 infertile women with clomiphen resistant PCOS undergoing laproscopic ovarian drilling and reported that luteinizing hormone was independent predictor of ovulation (OR 1.58, 95%CI: 1.30-1.92). The present study agreed with Ott et al., in that luteinizing hormone was independent predictor of ovulation in PCOS women; however the Odd ratio was slightly higher (OR = 3.64). Although the role that LH plays in folliculogenesis is still controversial, recent evidence points toward facilitatory actions of LH activity in ovulation induction. Thus, a study (20) compared the response to either highly purified FSH (75 IU FSH/ampoule; group A, 25 subjects) or human menopausal gonadotrophin (75 IU FSH and 75 IU LH/ampoule; group B, 25 subjects) in normoovulatory GnRH agonist-suppressed women, who were candidates for intrauterine insemination. A fixed regimen of two daily ampoules of highly purified FSH or human menopausal gonadotrophin was administered in the initial 14 days of treatment; menotropin dose adjustments were allowed thereafter.

Table 1: Characteristics of the study sample

Characteristics	Group (low LH) n = 29	Group (high LH) n = 29	P
Age (years)	25.97 ±3.87	26.34 ±3.22	0.686
BMI (kg/m^2)	29.12 ±1.61	29.49 ±1.89	0.426
LH (IU/L)	16.69 ±4.72	24.69 ±6.34	<0.001*
FSH (IU/L)	7.55 ±2.15	8.31 ±3.32	0.306
Testosterone (IU/L)	81.97 ±12.95	86.55 ±15.82	0.232
LH / FSH ratio	2.31 ±0.66	3.14 ±0.61	<0.001*

*Highly significant at P<0.01.

Table 2: Association between rate of ovulation and LH hormone level

Response	Group (low LH) n = 29	Group (high LH) n = 29	χ^2	P	OR	95% CI	
						Lower	Upper
Ovulation	11 (37.9)	20 (68.9)	5.613	0.018	3.64	1.23	10.78
No ovulation	18 (62.1)	9 (31.1)					
Total	29 (100.0)	29 (100.0)					

OR: Odds ratio; CI: confidence interval

Treatment was monitored with daily blood samples for the measurement of LH, FSH, 17beta-estradiol E(2), progesterone, testosterone, hCG, inhibin A, and inhibin B, and transvaginal pelvic ultrasound was performed at two-day intervals. Although preovulatory E(2) levels were similar, both the duration of treatment (16.1±0.8 vs. 12.6±0.5 days; $P<0.005$) and the per cycle menotropin dose (33.6±2.4 vs. 23.6±1.1 ampoules; $P<0.005$) were lower in group B. The study concluded that ovulation induction with LH activity-containing menotropins is associated with shorter treatment duration, lower menotropin consumption, and reduced development of small ovarian follicles. These features can be exploited to develop regimens that optimize treatment outcome, lower costs, and reduce occurrence of complications such as multiple gestation and ovarian hyperstimulation (21).

CONCLUSION

Pre-operative serum LH is a reliable predictor for ovulation in PCOS women undergoing ovarian drilling.

REFERENCES

1 Johansson J, Stener-Victorin E. Polycystic Ovary Syndrome: Effect and Mechanisms of Acupuncture for Ovulation Induction. *Evidence-based Complementary and Alternative Medicine : eCAM*. 2013;2013:762615.

2 Yildiz BO, Bozdag G, Yapici Z, Esinler I, Yarali H. Prevalence, phenotype and cardiometabolic risk of polycystic ovary syndrome under different diagnostic criteria. *Human Reproduction*. 2012;27:3067–3073.

3 March WA, Moore VM, Willson KJ, Phillips DIW, Norman RJ, Davies MJ. The prevalence of polycystic ovary syndrome in a community sample assessed under contrasting diagnostic criteria. *Human Reproduction*. 2010;25(2):544–551.

4 Sir-Petermann T, Codner E, Pérez V, et al. Metabolic and reproductive features before and during puberty in daughters of women with polycystic ovary syndrome. *The Journal of Clinical Endocrinology and Metabolism*. 2009;94(6):1923–1930.

5 Azziz R, Carmina E, Dewailly D, et al. Position statement: criteria for defining polycystic ovary syndrome as a predominantly hyperandrogenic syndrome: an androgen excess society guideline. *The Journal of Clinical Endocrinology and Metabolism*. 2006;91(11):4237–4245.

6 Stener-Victorin E, Holm G, Labrie F, Nilsson L, Janson PO, Ohlsson C. Are there any sensitive and specific sex steroid markers for polycystic ovary syndrome? *The Journal of Clinical Endocrinology and Metabolism*. 2010;95(2):810–819.

7 Nisenblat V, Norman RJ. Androgens and polycystic ovary syndrome. *Current Opinion in Endocrinology, Diabetes and Obesity*. 2009;16(3):224–231.

8 Hogg K, Young JM, Oliver EM, Souza CJ, McNeilly AS, Duncan WC. Enhanced thecal androgen production is prenatally programmed in an ovine model of polycystic ovary syndrome. *Endocrinology*. 2012;153(1):450–461

9 Sir-Petermann T, Maliqueo M, Angel B, Lara HE, Përez-Bravo F, Recabarren SE. Maternal serum androgens in pregnant women with polycystic ovarian syndrome: possible implications in prenatal androgenization. *Human Reproduction*. 2002;17(10):2573–2579.

10 Barry JA, Kay AR, Navaratnarajah R, et al. Umbilical vein testosterone in female infants born to mothers with polycystic ovary syndrome is elevated to male levels. *Journal of Obstetrics and Gynaecology*. 2010;30(5):444–446.

11 Witchel SF. Puberty and polycystic ovary syndrome. *Molecular and Cellular Endocrinology*. 2006;254-255:146–153.

12 van Houten EL, Kramer P, McLuskey A, et al. Reproductive and metabolic phenotype of a mouse model of PCOS. *Endocrinology*. 2012;153:2861–2869.

13 Patel K, Coffler MS, Dahan MH, Malcom PJ, Deutsch R, Chang RJ. Relationship of GnRH-stimulated LH release to episodic LH secretion and baseline endocrine-metabolic measures in women with polycystic ovary syndrome. *Clinical Endocrinology*. 2004;60(1):67–74.

14. Jonard S, Dewailly D. The follicular excess in polycystic ovaries, due to intra-ovarian hyperandrogenism, may be the main culprit for the follicular arrest. *Human Reproduction Update*. 2004;10(2):107–117.

15 Magoffin DA. Ovarian theca cell. *International Journal of Biochemistry & Cell Biology*. 2005;37(7):1344–1349.

16 Badawy A, Elnashar A. Treatment options for polycystic ovary syndrome. *International Journal of Women's Health*. 2011;3:25-35.

17 Young JM, McNeilly AS. Inhibin removes the inhibitory effects of activin on steroid enzyme expression and androgen production by normal ovarian thecal cells. *Journal of Molecular Endocrinology*. 2012;48(1):49-60.

18 Hayashi H, Ezaki K, Endo H, Urashima M. Preoperative luteinizing hormone levels predict the ovulatory response to laparoscopic ovarian drilling in patients with clomiphene citrate-resistant polycystic ovary syndrome. *Gyn Endocrinol*. 2005;21:307–311.

19 Ott J, Wirth S, Nouri K, et al. Luteinizing hormone and androstendione are independent predictors of ovulation after laparoscopic ovarian drilling: a retrospective cohort study. *Reproductive Biology and Endocrinology : RB&E*. 2009;7:153.

20 Filicori M, Cognigni GE, Taraborrelli S, Spettoli D, Ciampaglia W, Tabarelli De Fatis C, et al. Luteinzing hormone activity in menotropins optimizes folliculogenesis and treatment in controlled ovarian stimulation. *J Clin Endocr Metab*. 2001;86:337–43.

21 Kumar P, Sait SF. Luteinizing hormone and its dilemma in ovulation induction. *Journal of Human Reproductive Sciences*. 2011;4(1):2-7.