

Research Report

The Role of Dominant Follicular Diameter and LH in Predicting Ovulation in Cycle with Clomiphene Citrate

Peran Diameter Folikel Dominan dan Kadar LH dalam Meramalkan Kejadian Ovulasi pada Siklus yang Mendapat Kломifen Sitrat

Budi Wiweko, Andon Hestiantoro, Kanadi Sumapraja, Muharam Natadisastra, Afifah Khairani

Division of Imunoendocrinology
Department of Obstetrics and Gynecology
Medical Faculty of Indonesia University/
Dr. Cipto Mangunkusumo Hospital
Jakarta

Abstract

Objective: To improve diagnostic method to predict ovulation in cycle with clomiphene citrate.

Method: This diagnostic research was done in RSUPN Dr. Cipto Mangunkusumo between January 2011 - October 2011 with 31 women who taking CC 50 mg/day and 30 women with normal cycle.

Result: Affecting with ovulation in the two groups, it was found that in groups with CC, the follicle diameter is 24.33 ± 3.87 mm with LH 14.21 ± 7.95 IU/l, meanwhile in normal group, follicular diameter is 17.62 ± 3.45 mm with LH 14.42 ± 5.91 IU/l. Cut-off point for follicular diameter simultaneously with ovulation determined by ROC curve was found in 24.33mm (AUC 0.67, sensitivity 0.64, specificity 0.56), meanwhile the cut-off for LH is 14.40 IU/l (AUC 0.61, sensitivity 0.57, specificity 0.43).

Conclusion: In group with CC, ovulation occurred in bigger follicular diameter than normal cycle, while LH does not different significantly.

[Indones J Obstet Gynecol 2011; 35-3: 128-9]

Keywords: clomiphene citrate, follicular diameter, luteinizing hormone

Abstrak

Tujuan: Mengembangkan metoda diagnostik untuk meramalkan kejadian ovulasi pada siklus yang mendapat kломifen sitrat.

Metode: Penelitian dengan desain diagnostik ini dilakukan di RSUPN Dr. Cipto Mangunkusumo selama 10 bulan antara Januari 2011 - Oktober 2011 dengan jumlah sampel 31 orang untuk kelompok yang mendapat KS dan 30 untuk kelompok siklus normal.

Hasil: Menilai keberhasilan ovulasi pada dua kelompok, pada kelompok yang mendapat KS didapatkan rerata diameter folikel $24,33 \pm 3,87$ mm dengan kadar LH $14,21 \pm 7,95$ IU/l dan pada kelompok dengan siklus haid normal didapat rerata diameter folikel $17,62 \pm 3,45$ mm dengan kadar LH $14,42 \pm 5,91$ IU/l. Dengan ROC curve didapat titik potong diameter folikel dominan dengan keberhasilan induksi ovulasi pada diameter folikel 24,33 mm (AUC 0,67; sensitivitas 0,64; spesifisitas 0,56), sedangkan titik potong kadar LH dengan keberhasilan ovulasi didapat 14,40 IU/l (AUC 0,61; sensitivitas 0,57; spesifisitas 0,43).

Kesimpulan: Pada kelompok KS ovulasi terjadi pada diameter folikel dominan yang lebih besar dibanding kelompok siklus normal, sedangkan kadar LH saat ovulasi pada kedua kelompok tidak berbeda bermakna.

[Maj Obstet Ginekol Indones 2011; 35-3: 128-9]

Kata kunci: kломifen sitrat, diameter folikel, LH

Correspondence: Budi Wiweko, Department of Obstetrics and Gynecology, Dr. Cipto Mangunkusumo Hospital, East Jakarta.
Telephone: 021-3928620, Email: wiwekobudi@yahoo.co.id

INTRODUCTION

About 15% (1 of 6) reproductive couples suffered from infertility.^{1,2} In women, the main root of this problem is ovulation dysfunction, in which 40% of cases was found because of this.³ Clomiphene citrate (CC) is a one of the choices to overcome infertility in women with ovulation dysfunction.⁴⁻⁷ CC can bind to estrogen receptor in hypothalamic-pituitary to prevent estrogen negative reaction into hypothalamic.⁸ This caused an increase in FSH (Follicle Stimulating Hormone) secretion done by pituitary which forced follicular growth. Non-estrogen effect from CC will prevent positive estrogen feed back to LH. Premature LH surge does not occur while CC maintain follicular growth.⁹ Finally, LH surging in cycle with CC was found in bigger follicular diameter than normal cycle.

METHOD

Research was done in RSUPN Dr. Cipto Mangun-

kusumo Hospital within 10 months period between January 2011 - October 2011 composed by 31 women who got CC (age 25 - 41 years old, BMI 19.88 - 34.76 kg/m²) and 30 for normal cycle (age 24 - 42 years old, IMT 20.54 - 28.12 kg/m²). Data was analyzed using SPSS 18.00.

RESULT

In CC group, it was found that CC is affecting follicular growth, indicating a significant difference in follicular development which measured periodically. In CC group, mean of follicular diameter in 14th, 15th and 16th day of menstrual cycle are 16.76 ± 4.79 mm, 20.27 ± 3.25 mm, and 24.41 ± 3.65 mm with $p = 0.006$ (Table 1), while in normal cycle is in 10th, 11th, and 12th day of menstrual cycle are 13.68 ± 2.82 mm, 16.26 ± 5.08 mm, and 17.46 ± 5.24 mm with $p = 0.020$ (Table 2).

Table 1. Difference in mean of follicular diameter and LH in CC group on 12th, 13th, and 14th day of menstrual cycle.

	Day 14			Day 15			Day 16			p
	Mean	SD	CI	Mean	SD	CI	Mean	SD	CI	
Fol. diameter	16.76	4.79	14.1 - 19.4	20.27	3.25	17.5 - 22.9	24.41	3.65	21.7 - 27.0	0.0006
LH	11.80	8.81	-10.2 - 33.8	11.92	4.7	-5.9 - 22.8	12.01	8.10	-9.2 - 31.2	0.370

Table 2. Difference in mean of follicular diameter and LH in normal cycle group on 10th, 11th, and 12th day of menstrual cycle.

	Day 10			Day 11			Day 12			p
	Mean	SD	CI	Mean	SD	CI	Mean	SD	CI	
Fol. diameter	13.68	2.82	10.17 - 17.1	16.26	5.08	9.9 - 22.5	17.46	5.24	10.9 - 23.9	0.020
LH	14.37	12.95	-6.2 - 34.9	16.05	15.36	-8.4 - 40.5	16.90	14.40	-6.14 - 39.94	0.779

Concerning ovulation, these two groups has a significant difference in follicular diameter. In CC group, ovulation happened at follicular diameter 24.33 ± 3.87 mm with LH 14.42 ± 5.91 IU/l (Table 3), whereas in normal cycle, ovulation happened in follicular diameter 17.62 ± 3.45 mm and LH 14.42 ± 5.91 IU/l.

Table 3. Mean of follicular diameter and LH in CC group when ovulation happened

	Mean	SD	P	Range	CI 95%
LH	14.21	7.95	0.91	8.3 - 20.2	0.39 - 29.10
Fol diameter	24.33	3.87	0.45	18.5 - 31.0	21.35 - 37.30

From ROC curve, it was found cut-off follicular diameter when ovulation happened is 24.33 mm with AUC 0.658, sensitivity 0.64 and specificity 0.56, while cut-off LH when ovulation happened is 14.40 IU/l with AUC 0.653, sensitivity 0.57 and specificity 0.43.

ANALYSIS

From this research, we found out that there is a significant difference in follicular diameter in predicting ovulation between group with CC and normal cycle group. Cut-off follicular diameter when ovulation happened is 24.33 mm. This result is in accordance with the literature review which stated that it was happened at 25 mm. LH which measured periodically between two groups were not significantly different, this result stands in contrast to Padma Rekha research which said that there is a significant difference between these two groups. A possible explanation underlining the difference may be caused by sample age distribution, Padma Rekha's research sample were 30 ovulatory women with age below 39 years old, while in this research samples was between 24 - 42 years old which some of them are oligovulatory. In these two groups, it was found out that LH is surging, on the contrary in Kato Ladies Tokyo clinic, there was no LH surge in CC group. This may due to the different day in measuring. In this research, we measured until the 16th day of menstrual cycle, while in Kato

Ladies Tokyo clinic only measured until 14 days of menstrual cycle. Another reasons may be caused by the variety of race between Asian and mongoloid and other factors that has yet to be found.

CONCLUSION

In group with CC ovulation occurred in bigger follicular diameter than normal cycle, but LH in the two groups were not significantly different.

REFERENCES

- Chavarro JE, Rich-Edwards JW, Rosner BA, Willett WC. Use of multivitamins, intake of B vitamins and risk of ovulatory infertility. *Fertility and Sterility*. 2008; 89(3): 668-76
- Benyamini Y, Gozlan M, Kokia E. Variability in the difficulties experienced by women undergoing infertility treatments. *Fertility and Sterility*. [doi: DOI: 10.1016/j.fertnstert.2004.10.014]. 2005; 83(2): 275-83
- Speroff L GR, Kase NG. *Clinical gynecologic endocrinology and fertility*. 6th ed. Mitchell C RR, Stewart J, RD M editors. Baltimore: William and Wilkins, 1994
- Baruah J, Roy KK, Rahman SM, Kumar S, Sharma JB, Karmakar D. Endometrial effects of letrozole and clomiphene citrate in women with polycystic ovary syndrome using spiral artery Doppler. *Arch Gynecol Obstet*. 2009; 279(3): 311-4
- Ahmed B, Ibrahim AA, Mohamed A. Clomiphene citrate or anastrozole for ovulation induction in women with polycystic ovary syndrome? A prospective controlled trial. *Fertility and Sterility*. 2009; 92: 860-3
- Padma RJ, Rajendra SP. Comparison of endocrine and ultrasound profiles during ovulation induction with clomiphene citrate and letrozole in ovulatory volunteer women. *Fertility and Sterility*. 2010; 93: 174-83
- Chaube SK, Prasad PV, Thakur SC, Shrivastav TG. Estradiol protects clomiphene citrate-induced apoptosis in ovarian follicular cells and ovulated cumulus-oocyte complexes. *Fertility and Sterility*. [doi: DOI: 10.1016/j.fertnstert.2005.03.073]. 2005; 84 (Supp. 2): 1163-72
- Clark JH, Markaverich BM. The agonistic-antagonistic properties of clomiphene: A review. *Pharmacology and Therapeutics*. [doi: DOI: 10.1016/0163-7258(81)90055-3]. 1981; 15(3): 467-519
- Hesham AI, Hamdy A, Waleed EK, Adel N, Eman EK, Ahmed MAS. The effectiveness of clomiphene citrate in LH surge suppression in women undergoing IUI: a randomized controlled trial. *Fertility and Sterility*. 2010