

The Relation between the Dose of Clomid and the Response of Ovaries to Induced Mature Follicle in Women at Al-Nassiyra- City

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Abstract

The study included (80) women in different ages divided them equally into four groups, who seek to become pregnant and they were not poly cystic and not received clomiphene citrate table since one year ago at least, these women were given clomid in different doses from 2nd day of cycle for 5 days and then measure the diameter of largest Graafian follicle at day (13) of cycle by doing ultra sound, and the result showed that the dose of 50 mg/3 times daily is the Most effective dose. The aim of study is to reach the significant dose of clomiphene to establish mature follicle (18-20 mm).

Key words: clomide, response of ovaries.

Introduction

Clomiphene citrate was first synthesized in 1956 and introduced for clinical trial use in 1960. It was first used successfully to induced ovulation in 1961 and continues to be the most commonly used drug for this purpose, as well as in the empirical treatment of unexplained infertility (Litc,1992) (Rossing1994) and it is ineffective in inducing ovulation in patients with hypogonadism who desire pregnancy because such patients are hypoestrogenism(Adashi,1986)(Keith Edmonds,1997).

Clomiphene citrate is an orally active synthetic non-steroidal compound with oestrogenic as well as anti-oestrogenic properties, which has traditionally been the treatment of choice in woman with an ovulatory cycle. (LedaM, ASHmonga, BeckJI, 2005) It displaces oestrogen from its receptors in the hypothalamic – pituitary axis, reduces the negative feedback effect of oestrogen and encourage GnRH secretion (AshMonga, DavidM, SteinerAZ2005).

The tablet of clomid is 50 mg only, advice the client to take medication at the same time every day to maintains drug levels and if there is missing dose advise to take as soon as possible (BeckJI, 2005) From side effects of clomid are due to anti-oestrogenic effect include thickening of cervical mucus and hot flushes in 10% of woman (AshMonga, jAMESr,LedaM,EdenJA1989, VanCampenhout), Other side effect include abdominal distention 2%, abdominal pain, nausea, vomiting, headache, breast tenderness, and reversible hair loss (JonathanS, VanCampenhout)

Clomid has amydratic action that can result in blurred vision and scotomas in 1.5% of woman (BeckJI2005) These changes are reversible –significant ovarian enlargement occurs in 5%, if client has ovarian cysts, clomiphene may enlarged them, but ovarian hyper stimulation syndrome (OHSS) is rare

1%(koustaE1997,AdashiEY1994) the multiple pregnancy rate associated with clomiphene is 7-10%,so should only be used when ultra sound is available in order to minimize this side effect (AshMonga, James, KoustaE 1997, BalenAH1994, ADASHIey, 1994) , there is relative link between ovarian cancer and woman receiving more than(12)consecutive cycles of clomiphene, so should be limited use for less than six cycles(Rossing1994,Adashi1994)

Assessment of clomiphene therapy

It should be determined whether the client has preexisting conditions for which clomiphene would be contraindicated ,such as abnormal and undiagnosed vaginal bleeding, endometriosis, fibroid tumors, mental depression, active hepatic dysfunction(or history of it),or thrombophlebitis^(Beckji2005)

Method and materials

Clomiphene citrate which is used in the study is citrate de clomiphene (50mg) manufactured by patheon france S.A. which date of issue is November 2004.

From 15th of December in 2012 to 15th of April in 2013 we deal with (80)female ,they are different in ages ,parity and period of infertility, and divided them for 4 groups, then start with clomiphene therapy from 2nd day of cycle for 5 days ,but in different doses and then measure the diameter of the largest graafian follicle in day(13) of cycle by doing ultra sound(by the same device).

These 4 group include:

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- A. 20 female take 100 mg in 2 divided dose .
 - B. 20 female take 150 mg in 3 divided doses.
 - C. 20 female take 200 mg in 2 divided doses.
 - D. 20 female not taking clomiphene citrate at all.

But the patient must not take clomiphene at least for one year ago, and not complain from poly cystic ovarian syndrome.

Results

By doing the ultra sound for all female at the 13th day from the first day of menstrual cycle we found the best dose of clomiphene which be used with group B ,because it give about 80 % positive result(introduce mature follicle, while group A and C give same result 65 %,and group D give only 55 % ,as shown in (table 1) and (diagram 1).

Also in relation to ages we can see the good response for all groups in different doses are female ages between 25-34 years old ,while in age between 35-44 years old is poorly response in 4 groups as shown in (table 2).

Also we found the possibility of developing ovarian cyst as side effect is common with both group A and C, from other side these 2 groups give a chance to developed more than one mature follicle as shown in (table 3).

Table 1: Positive result for all groups.

Groups	Positive result as number	Positive result as %
	13 from 20	65%
B	16 from 20	80%
C	13 from 20	65%
D	11 from 20	55%

Positive=mature follicle ,its size 18-20 mm

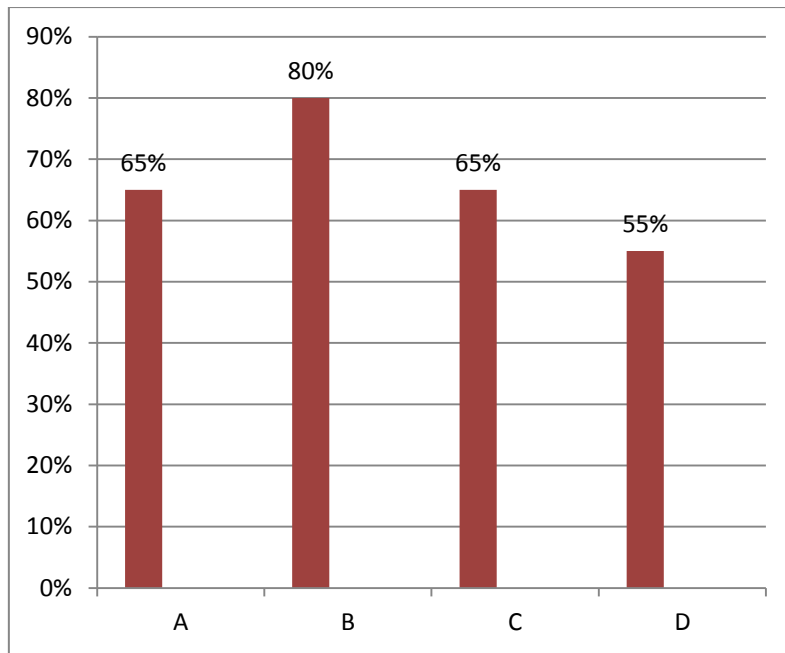


Fig 1: positive result of all groups as percentage.

Table 2: Relation between age and positive result for all groups.

Age in years	A	B	C	D
15-24	38.5%	25%	23%	55%
25-34	38.5%	75%	31%	27%
35-44	23%	-----	46%	18%

Table 3: Cases of developed ovarian cyst as side effect of clomid and cases of developed more than one mature follicle for all groups.

Group	Cases of ovarian cyst	Cases of multiple follicle
A	2 case	3 case
B	-----	-----
C	1 case	1 case
D	-----	-----

Discussion

Previously the starting dose of clomid is 50 mg and if no response to ovulation we can increase dose gradually ,but from 1983 this idea is different when Yee and Vargyas say in their review(1986:142)the most widely used regimen in normally ovulatory woman undergoing on IVF treatment cycle is 100 mg or 150 mg /daily ,they list studies by Quilgley et al(1988).Marss et al(1983),an Australian study by Lopata (1983), and their own work here 150 mg /day have been used on one group of woman ,in an attempt to compare the success rate with those receiving 100 mg /day.

In this study we try to compare the response of ovary to different doses of clomid, and that is clear from the result in tables when we double the dose of clomid from 50 mg every 12 hours to 100 mg every 12 hours the result is the same which is 13 cases response to induced mature follicle ,and not doubling or increase the response ,while when divided the 150 mg all the day (every 8 hours)the no. of ladies whose response will increase to16 cases.

In relation to the age as shown in(table 2) in group D the chance to ovulated mature follicle will decline with the age as normal changes of natural hormone ,but when induced ovulation by clomid the picture is different .in group A there is no clear relation to the age, while in group B the best period to respond to drug is from 24-34 years old,reversly the old age women are good response when given drug as 100 mg every 12 hours. If mother seek multiple pregnancy, advice to take 50mg every 12 hours, and no or little chance with group B and C, as mention from important side effect of clomid is developing ovarian cyst which occur with group A and C only.

Conclusion

1.The study reveal that, the most effective dose of clomid which be used is 50 mg every 8 hours from 2nd day of cycle for 5 days, specially with age group between25-34 years old.

2. In spite of lowchance to induced more than one mature follicle with this regime, the chance to develop ovarian cyst as side effect is low also.

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العلاقة بين جرعة الكلوميدي ومدى استجابة المبايض لإنتاج بيضة ناضجة عند النساء في مدينة الناصرية

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الخلاصة

تضمنت الدراسة على 80 سيدة ومن مختلف الأعمار وقد تم تقسيمهم إلى أربع مجاميع وأعطى العلاج لكل مجموعة بجرعة مختلفة (عدا المجموعة الأخيرة) ولخمس أيام فقط ابتداء من ثاني يوم للدورة الشهرية وبعد ذلك وفي اليوم الثالث عشر للدورة تم قياس حجم البويضات الناتجة الموجات فوق الصوتية لمعرفة أي الجرعة هي الأكثر فعالية بشرط أن لا تكون السيدة مصابة بمتلازمة تكيس المبايض ولم تأخذ الكلوميدي لمدة سنة على الأقل وحسب النتائج تبين أن أفضل جرعة هي 50 ملغم كل 8 ساعات يوميا.
