Using of Bromocriptine Therapy with Clomiphene Citrate in Comparison with the Use of Clomiphene Alone in Polysystic Ovary Disease (PCOD)

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Abstract :

This study was a prospective study which was done in Tikrit Teaching Hospital to compare the use of Bromocriptine with Clomiphine Citrate and Chlomiphine alone in Normoprolactinemic anovulatory women with (PCOD). A total of 44 infertile Normoprolactinemic women, these women were divided into two group, each group of (22) women, the first group was treated with Bromocriptine (2.5) mg twice per day and with Clomiphine Citrate (100) mg per day from second to six day of cycle for three month duration, second group was treated with Clomiphine Citrate also the same dose as mentioned above. After treatment regular mences resumed in 68.2 % for the first group and 50 % for the second group, the pregnancy rate were 40% for the first group and 22.7% for the second group. The final conclusions in this study were that Clomiphine Citrate with Bromocriptine showed higher rate of regular resumption on mences and pregnancy than Clomiphine alone.

Introduction:

Most couples desire pregnancy after marriage, but only 85-90% of them achieve pregnancy within 12-18 months of unprotected intercourse[1]. In other words, 10-15% of couples will remain unsuccessful in their attempts at pregnancy and are those labels as infertile couples[2]. There are numerous causes for infertility, 40% of infertility is due to female infertility [3]. The polycystic ovary syndrome (PCOS) is one of the most common cause of anovulatory infertility[1].

PCOD is an endocrine disease of unknown aetiology, most frequently associated with anovulation. The classification of the disease is based on both clinical and endocrine features with a well known ultrasound ovarian pattern, obesity, hirsutism, oligomenorrhoea, with chronic anovulation and hyperandrogenaemia, are variably associated with abnormal gonadotrophin secretion, an elevated serum concentration of LH, depressed FSH and LH/FSH ratio $\geq 2[4,5,6,7]$.

Clomiphene citrate is the first choice of treatment, but approximately 20% of PCOD patients with failed ovulation despite higher dose of clomiphene citrate, [2]. 30% of patients with PCOD show mild hyperprolactinaemia, [8,9,10,11].

Furthermore, a transient rise in plasma prolactine (PRL) concentration can be observed during the late follicular and luteal phase of both natural and stimulated cycles, [12].

It is known that hypothalamic dopamine is the major inhibitor of PRL secretion in human, [13] and there may be a possible, if controversial role for central dopamenergic mechanisms in release of LH. Several investigators, [14,15] also indicated adopaminergic control on gonadotrophin secretion and suggested that a reduction of dopamine inhibitory effect might cause abnormal PRL and LH release PCOD patients who do not respond to clomiphene citrate require specialist

infertility therapy and in absence of any other infertility factors, one of the available options is addition of bromocriptine to clomphene citrate, [16]. There is many studies explain the use of bromocriptine and clomphene citrate and their effects on ovulation and pregnancy which is corresponding to our ideas in this research and it is not the first time those drags were used.

Subject and Method:

This was a prospective study, a total of 44 infertile PCOD patients were seen in one year (March 2005 -March 2006). All the women fulfilled our criteria for diagnosis of PCOS.

history of anovulatory infertility Α and/or oligomenorrhoea hirsutism, amenorrhoea, or hyperandrogenaemia, elevated LH or an LH/ FSH ratio of ≥ 2 , increased ovarian volume and ≥ 10 follicles of 2-8mm in diameter by U/S examination. Tubal factors were excluded by hysterosalpingography. All the male partners had normal semen quality, according to world health organization (WHO) criteria, [16].

The selected patients had the following :-

2 or more of PCOS sign.

Absence of galactorrhoea.

Normal serum prolactin.

Normal hysterosalpingography.

Normal spermogram.

In this study the treatment protocol was planned in two groups, second group include 22 patients treated with clomiphene citrate alone in dose 100 mg per day from second to sixth day of cycle, and first group 22 patients treated with clomiphene citrate 100 mg per day from second to sixth day of the cycle and bromocriptine 2.5 mg twice daily for (3) months duration, only 2 patients were dropped out from this group due to personal reasons.

								daily		phar-	
Table (1): Method of Work									macy		
				Mode of	Sourse						Hospi-
Group	No.	Type of Drag	Dose	administer-	of						tal or
_				ation	Drag	2 nd	22	Clomiphen	100	11	exter-
		Clominhon	100		Hospi-	group	22	citrate	mg/day	orally	nal
1 st group	22	citrate +	mg/day+ 2.5 mg orally	orally	tal or	lor					phar-
				exter-						macy	
		Bornioeriptine	twice		nal	total	44				

Results:

The age of patients in first group ranged from 16 to 38 years with a mean 26.9 years. The age of patients in second group ranged from 18 to 35 years with a mean 22.0 years .

The duration of infertility in first group was from 1 to 11 years with a mean 6.2 years and in second group was from (1-18) years with a mean 4.5 years.

The irregularity of menses in first group was 65% and in second group was 63.3% before treatment as in following table:

 Table (*): Distribution of regularity of menses in 2 groups before treatment

Type of	Clomiphene +	Clomiphene	Total	
menses	Bromocriptine	alone		
Regular	No.%	No.%	No.%	
8	7 (35%)	8 (36.4%)	15 (35.7%)	
Irregular	13 (65%)	14 (63.6%)	27 (64.3%)	
Total	20 (100%)	22 (100%)	42 (100%)	

after treatment there was significant effect on regularity of menses in first group, 68.2% had regular menses and in second group 50% had regular menses as in following table:

Table (**v**): Regularity of menses in patients with previously irregular menses in 2 groups after treatment

	Clomiphene + Bromocriptine	Clomiphene alone	Total
Regular menses	No.%	No.%	No.%
Yes	9 (68.2%)	7 (50%)	16 (59.3%)
No	4 (31.8%)	7 (50%)	11 (40%)
Total	13 (100%)	14 (100%)	27 (100%)

The pregnancy rate was significantly different, in the first group it was 40 % and in second group 22.7 % as in following table :

 Table (4): Pregnancy rate in two groups

Dragmanar	Clomiphene +	Clomiphene	Total
Pregnancy	Bromocriptine	alone	Total
	No.%	No.%	No.%
Yes	8 (40%)	5 (22.7%)	13 (31%)
No	12 (60%)	17 (77.3%)	29 (69%)
Total	20 (100%0	22 (100%)	42 (100%)

Table (4) shows the pregnancy rates in two groups based on infertility type.

Table (5): Pregnancy rate in two groups based	lon
Infertility type	

intertainty type						
Туре	Dreg	Clomiphene +	Clomiphen	Total		
of	nonov	Bromocriptin	e	Totai		
infertility	nancy	e	alone			
		No.%	No.%	No.%		
Primary	Yes	7 (43.8%)	4 (17.6%)	10 (30.3%)		
	No	9 (56.3%)	14 (82.4%)	23 (69.7%)		
	Total	16 (100%)	17 (100%)	33		
Secondar	Total	10 (10070)	17 (10070)	(100%)		
У	Yes	1 (25%)	2 (40%)	3 (33.3%)		
	No	3 (75%)	3 (60%)	6 (66.7%)		
	Total	4 (100%)	5 (100%)	9 (100%)		
A	A 1 4 11 (5) 1					

And table (5) shows pregnancy rates in two groups based on age.

Table (6): Pregnancy rate based on age in two groups

			U	
Age	Pregnancy	Clomiphene + Bromocriptine	Clomiphene only	Total
	Yes	3 (50%)	3 (21.4%)	6 (30%)
≤ 23	No	3 (50%)	11 (78%)	14 (70%)
	Total	6 (100%)	14 (100%)	20 (100%)
> 23	Yes	5 (35.7%)	2 (25%)	7 (31.8%)
	No	9 (64.3%)	6 (75%)	15 (68.2%)
	Total	14 (100%)	8 (100%)	22 (100%)

The pregnancy rate in two groups based on the duration of infertility as shown in following table:

Fable (7):]	Pregnancy	rate based	on the	duration	of infertility	
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Duration of infertility	Pregnancy	Clomiphene +Bromocriptine	Clomiphene only	Total
< 3 ur	Yes	1 (16.7%)	3 (20%)	4 (19%)
\geq 5 yr.	No	5 (83.3%)	12 (80%)	17 (81%)
	Total	6 (100%)	15 (100%)	21 (100%)
> 3 yr.	Yes	7 (50%)	2 (28.6%)	9
	No	7 (50%)	5 (71.4%)	12
	Total	14 (100%)	7(100%)	21

Discussion:

PCOD is a common disorder with biochemical and hormonal variation and dysfunction even in the presence of normal range of hormones [17].

Several investigators have support the idea that mild transient hyperprolactinemia and PCOS syndrome are not distinct entity [9, 10, 11, 15].

A mild dopamine deficiency could cause an increase of both PRL and LH in patient with PCO, and the inhibitory effect of hypothalamic dopamine and dopamine agonists on PRL is well documented. Clinical experience suggested that successful induction of ovulatory achievement of pregnancy with bromocriptine can occur in absence of galactorrhoea and with normal prolactine level [18, 19, 20, 21].

The mechanism of bromocriptine action, may be a follicular responsiveness either due to normalized elevated nocturnal serum prolactin level or suppression of LH, [3].

In this study 68 % of the first group patients after treatment had regular menses (due to induction of ovulation) and pregnancy in 40 % of patients was achieved.

Although the mechanism is not clear, many authors [14,22,23,24,25] have demonstrated on inhibitory role of dopamine and its agonists, on LH secretion and androgen concentration both in normal and hyper PRL women. According to its capacity to reduce LH secretion, dopamine agonists were proposed as a useful tool in the

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management of PCOS [11, 14]. Clomiphine citrate and Bromocrotine both can be used as a drags for induction ovulation. Both Bromocirtine and Clomiphine citrate combination for induve ovulation is better than Bromocriptine or Clomiphine alone.

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استعمال عقار البروموكربتين مع الكلوميفين مع استعمال الكلوميفين بمفرده

لمرض تكيس المبايض المتعدد

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الملخص:

ان هذه الدراسة تعتبر دراسة متقدمة تم إجراءها في مستشفى تكريت التعليمي للمقارنة بين النساء اللواتي يعانين من تكيس المبايض المتعدد واللواتي يستخدمن برومو كرينين وكلوموفين ستريت وأولئك اللواتي يعانين من نفس المرض ويستخدمن كلوموفين فقط. إن العدد الكلي أربع وأربعون امرأة عقيمة مع مستوى برولاكتين طبيعي قسمن إلى مجموعتين، تحتوي كل مجموعة على ائتين وعشرين مريضة، تم علاج المجموعة الأولى ببرموكريتين بجرعة (٢٠٥) ائتين ونصف ملغ مرتين في اليوم وكلوميفين ستريت (١٠٠) مائة ملغ في اليوم من اليوم الثاني إلى اليوم السادس من الدورة الثين ونصف ملغ مرتين في اليوم وكلوميفين ستريت (١٠٠) مائة ملغ في اليوم من اليوم الثاني إلى اليوم السادس من الدورة عولجت المجموعة الثانية بكلوميفين ستريت بنفس الجرعة كما ذكر في أعلاه. بعد العلاج استعيدت الدورة الشهرية المبيعية في ٦٨,٢ % في المجموعة الأولى و ٥٠ % ف المجموعة الثانية. أما معدل الحمل فكان ٤٠ % للمجموعة الأولى و ٢٢,٢ % للمجموعة الثانية.

الاستنتاج النهائي في هذه الدراسة هو أن استخدام البرموكريتين والكلوميفين اظهر نسبة عالية في استعادة الدورة الشهرية الطبيعية ونسبة الحمل أكثر من الكلوميفين وحده.