

IMPROVING PREGNANCY RATES IN PATIENTS WITH CLOMIPHENE FAILURES

PANKAJ DESAI ● MAYA HAZRA

SUMMARY

137 patients treated by induction of ovulation over a period of 8 years are being presented. They were grouped into nine different groups suggested by Chong et al (1987). It was found that those patients who had a normal ovulatory response to CC (0₁ group) as monitored by cervical mucus and BBT, had a highest conception rate with CC than with alternative therapies. Those patients who had anovulatory responses (A₁, A₂ and A₃ groups) with CC had significantly better chances of conception when alternative therapies to CC were used. Thus this grouping system can prove to be useful in improving pregnancy rates in patients who fail to conceive with CC by judiciously and scientifically indicating patients wherein alternative therapies like HMG, HCG etc can be used.

INTRODUCTION

Anovulation - the most common cause for female infertility - is most commonly treated with clomiphene citrate. Successful ovulatory rates upto 95% are reported. But pregnancy rates go only upto a high of about 75% (Murray et al 1971, Lobo R. A. 1982). These group of patients who ovulate but fail to conceive with CC have remained a source of many therapeutic alternatives.

On many occasions these alternatives are

used empirically and with poor patient selection. As a result the success rates with these also remain limited. It was Chong et al (1987) who suggested grouping of these clomiphene ovulators but non pregnant and non ovulators patients into nine different groups based on cervical mucus and BBT studies. Employing therapeutic alternatives with a scientific rationale in these groups, was claimed to give much higher pregnancy rates.

These groups were used in the present study primarily to improve pregnancy rates and also evaluate their efficacy.

Dept. of Obst. & Gynec., Medical College & Hospital,
Baroda.

Accepted for Publication on 26.11.1992.

MATERIAL AND METHODS

The present study was carried out in the Dept. of Obstetrics & Gynaecology, SSG Hospital and Medical College, Baroda. 137 patients whose complete relevant records were available and who were treated with clomiphene citrate (CC) were studied. These patients were from January 1984 to December 1991. CC was given in a dose of 50 mgms/day from 3rd day to 8th day of the cycle (except in PCOD where 25 mgms/day was given in first cycle).

The responses achieved in them were studied by cervical mucus and BBT principally, besides others. Ultrasound follicular monitoring was not available at the institution during most of the study period. Thus for the sake of uniformity, though available for last one to two years, its results have not been included in the present study.

Infertility work up included a diagnostic laparoscopy, semen analysis, sputum for tuberculous bacilli, x-ray chest and a PCT. A timed endometrial biopsy, elaborate hormonal assays, pituitary imaging scans and organism cultures were done in relevant cases. CC was increased whenever required upto a maximum of 150 mgms/day.

Cervical mucus (CM) was checked on day 14 to 16 (periovulatory) for clarity, cellularity, spinnbarkeit and ferning. Whenever CM response was poor for that day, every 48 hours it was repeated till BBT registered a shift. If BBT failed to register a shift CM study was stopped on day 26 awaiting a menstrual period.

BBT was recorded in the standard way by fertility thermometer and graphed on a standard BBT chart.

CC was discontinued after 6 cycles maximally and earliest after 3 cycles in patients with normal ovulatory response, with no pregnancy. They were then grouped as CC failures.

Poor CM was treated with conjugated estrogens 0.625 mgms/day from day 5 to 13. Patients with short luteal phase were treated by an increased dose of CC or by HCG 2000

I.U. on day 4 and 11 after the BBT shift. Patients with only 4 to 6 days of luteal phase (A_1 as per Chong's group) were treated with HCG 5000 I.U. at mid cycle when an excellent CM response was seen. HMG was given as per the standard protocol.

Chi-square test was used as a statistical method.

These patients were grouped in groups forwarded by Chong et al (1987). Their responses to CC and alternative therapy, were also grouped and results crystallised.

RESULTS

137 patients treated with CC were studied. The indications for the use of CC is as shown in Table I.

Table I

Indications for the use of CC

Indication	No. of cases
*Anovulation	41
*Oligo ovulation	61
*Luteal Phase Defect	28
*LUF	07
Total	136

Responses of these patients as regards CM and BBT records were studied. On basis of these responses they were grouped in nine groups as suggested by Chong et al (1987) and shown in Table II.

As shown in table III, 40.4% patients were normal ovulators (O_1) and 21.7% though ovulating had a short luteal phase.

Amongst the anovulators these with monophasic BBT and with good cervical mucus but no bleeding (A_2) exceeded the other groups.

As shown in Table IV, normal

Table II

Chong's Groups of C. C. Responses

Type	Characteristics
O ₁	Biphasic BBT with atleast 12 days of luteal phase and total length of cycle of 25 days (normal ovulatory response).
O ₂	Similar to O ₁ but with poor cervical mucus (poor ovulatory estrogenic response).
O ₃	Biphasic BBT, luteal phase only persisted for 7 to 11 days (short luteal phase).
A ₁	Luteal phase only persisted for 4 to 6 days (LUF).
A ₂	Monophasic BBT, with good cervical mucus and no bleeding (follicular response only)
A ₃	Monophasic BBT, poor cervical mucus and no bleeding (No response).
M ₁	Cycles last for 23 days (short cycles)
M ₂	BBT starts high (above 98° F) and remains elevated for the duration of the cycle, they all bleed (hyperthermic response).
M ₃	BBT starts high (more than 98° F) drops for a few days and then rises : all bleed (triphasic response)

ovulators (p₁) had the highest chance of conception with CC and amongst their failures the conception with alternative therapy remains low. Amongst ovulators with short luteal phase (O₃) chances of conception with CC or CC + luteal support remained nearly equal - 46.67% versus 55.6% (Statistically insignificant).

On the other hand, all patients presumed

Table III

Patients Distribution as per groups

Group	No. of Patients	%
O ₁	56	40.88
O ₂	17	12.41
O ₃	30	21.90
A ₁	08	5.84
A ₂	12	8.76
A ₃	04	2.92
M ₁	05	3.64
M ₂	02	1.46
M ₃	03	2.19
Total	137	100.00

anovulatory in groups A₁, A₂ & A₃ had a significantly higher conception rates when treated with alternative therapeutics like HMG + HCG. Conception rates in these groups with CC tittered around 30% whereas the same with alternative therapy rose to around 70%.

Patients in the present study in the miscellaneous groups (M₁, M₂ and M₃ of Chong) were too small in number to conclude convincing results.

DISCUSSION

By scientifically grouping patients undergoing ovulation induction and subsequently treating them accordingly is bound to improve the pregnancy rates. Grouping patients according to responses observed has also been tried by Murray et al (1971). But the grouping system used herein by Chong (1987) has been found to be easier and comparatively more pragmatic.

Examining figures across the board 84.6% pregnancy could be achieved in all with CC and alternative therapeutic regimens specified

Table IV

Incidence of Pregnancy in different group

Group	O ₁	O ₂	O ₃	A ₁	A ₂	A ₃	M ₁	M ₂	M ₃	T
CC treated (No.)	56	17	30	08	12	04	05	02	03	137
Pregnancy (No.)	50	02	14	02	04	01	01	00	00	74
%	89.29	11.76	46.67	25	33.3	25	20	—	—	54.02
Alternately treated CC failures (No.)	04	10	09	05	04	03	02	01	04	42
Pregnancy (No.)	02	05	05	03	03	02	01	00	02	23
%	50	50	55.56	60	75	66.67	50	—	50	54.76

in the preceding sections. These are figures for 137 patients in whom totally 701 cycles were analysed over a period of 8 years. However to make these results more subtle and efficacious the grouping system used herein seems to be of distinct help.

In patients who fall in Group O₁ after induction with CC it is nearly useless to give alternate therapy, if they fail to conceive with CC. Her chance of conceiving with CC is in fact highest and thus other regimes may prove empirical. However in group O₂ with poor cervical mucus and a biphasic BBT nearly five times higher conception rates could be achieved by alternate therapy (conjugated estrogen supplementation with CC).

All patients who continued to have anovulatory type of BBT and CM conceived nearly three times more with alternative therapies (like HMG + HCG combinations) as compared to CC.

CONCLUSION

In deciding for the alternative therapies in

"CC failures" it is beneficial to use the grouping system of Chong et al (1987) and thus classifying the responses accordingly. It will prevent the empirical use of alternative therapies which are not only costly but also have side effects. By following this grouping system conception rates following induction of ovulation can be improved much more scientifically and rationally.

ACKNOWLEDGEMENT

We are extremely thankful to the Dean, Medical College, Baroda, the Superintendent, SSG Hospital, Baroda and the Head of the Dept. of Obst. & Gynec. SSG Hospital, Baroda for allowing us to carry out this study.

BIBLIOGRAPHY

1. Chong A. P., Lee J. L., Forte C. C., Tumillo M. E. *Fertil. Steril.* 48 (6) ; 941, 1987.
2. Lobo R. A., Gyster M., March C. M., Goebelsmann U., Mishall D. R. : *Fertil. Steril.* 37 ; 168, 1982.
3. Murray M., Clarke F. J. *Obstet. & Gynec. Brit. C'wealth* 78 ; 1108, 1971.