

## PRETREATMENT WITH C.C. FOR REDUCTION IN H.M.G. REQUIREMENTS

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### SUMMARY

In the present study, clinical and hormonal characteristics of patients in whom lowering of HMG requirements was possible by pre-treating these subjects with 150 mgms/day of C.C. for five days have been studied. It was found that those patients who show a positive withdrawal bleeding with progesterone clinically and in whom the levels of FSH and LH are higher were the right choice for C.C. pretreatment. Such a reduced HMG requirement effectively decreased complication rates like ovarian enlargements and hyperstimulation syndrome besides reducing the cost of therapy.

### INTRODUCTION

Anovulation refractory to induction with clomiphene citrate (C.C.) is treated with Human Menopausal Gonadotrophins (H.M.G.). However, the latter therapy is known to be associated with significantly higher complication rates like ovarian enlargements and hyperstimulation syndrome and multiple pregnancies besides the high cost involved. (Thompson and Hansen, 1970). However, one of the

methods studied for reducing HMG requirements is to pretreat cycles with C.C. Many workers have been working in this field for quite some time (Cox and Cox 1967, Croke et al, 1969, Rabau et al, 1968).

However, what remains to be seemingly less studied are the characteristics of patients in whom such a pretreatment may be effective. March (1984) cited some characteristics of patients in whom success can be achieved by pretreatment with CC. In the present study characteristics of patients in whom pretreatment with CC for reducing HMG

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requirements and thereby reducing complications and cost of therapy are being presented.

**MATERIAL AND METHODS**

This study was carried out in the Dept. of Obst. and Gynec., Medical College and SSG Hospital, Baroda. 14 patients who were distinctly anovulatory on history and failed to ovulate with CC were treated with HMG. CC was administered upto a maximum of 150 mgm daily for 5 days followed by 5000 I.U. of HCG.

Of these 14 patients, 4 had primary amenorrhoea, 7 had secondary amenorrhoea and the remaining 3 had oligomenorrhoea. Progesterone was administered for withdrawal bleed. FSH and LH of all these subjects was measured after they failed to respond to CC. Laparoscopy with chromopertubation was done in all cases to rule out any tuboperitoneal cause. As per the practice in our unit, it was done after ovulation induction with CC failed for 3 cycles, as these cases were distinctly anovulatory on history. Husbands were examined and semen analyses carried out in all these cases results of which were found to be normal.

All these cases were initially treated with HMG administered daily in individualized doses in sequentially increased doses every third day. Ultrasonography for follicular monitoring, BBT chart and vaginal cytology were studied to judge ovulation. This increase in HMG was done till minimum follicular size of 18 mm was achieved after which 5000 I.U. of HCG was administered. Ovulatory responses or otherwise was noted. All of these patients were in subsequent

cycles subjected to a pretreatment of CC for 5 days in a daily dose of 150 mgm. Thereafter, besides BBT and other clinical studies, USG was carried out on the day after completion of CC. HMG was started in sequentially increasing doses every alternate days upto the follicular size of 18 mm was achieved. HCG was administered in a dose of 5000 I.U. and ovulatory response if any, was noted.

The results so obtained were studied in the light of the hormonal characteristics of these subjects and data analysed accordingly.

**RESULTS**

In all, there were 14 patients in whom a comparison of requirement of HMG in a CC pretreated cycle and non-pretreated cycles could be carried out. Their ages were within the range of 22 to 36 yrs. and the duration of infertility varied between 2 and 12 yrs.

As shown in Table I 50% of patients presented with secondary amenorrhoea when progesterone was administered to ellicit a withdrawal bleed. 7 had no bleed. These two constituted distinct

Table I  
Characteristics of Patients

| Menstrual History       | Number | Percentage |
|-------------------------|--------|------------|
| Primary Amenorrhoea     | 04     | 28.57      |
| Secondary Amenorrhoea   | 07     | 50.00      |
| Oligomenorrhoea         | 03     | 21.43      |
| Progesterone withdrawal |        |            |
| +ve                     | 07     | 50.00      |
| -ve                     | 07     | 50.00      |

groups which were studied.

Hormonal estimation of F.S.H. and L.H. were interestingly and a significantly different in both groups as shown in Table II. Those patients who showed a bleed on progesterone had significantly higher levels of FSH and LH vis-a-vis those subjects who did not bleed. Interestingly the HMG requirements were also significantly different in both these groups as shown in Table III.

In low FSH patients. Ovulatory response was achieved with a mean of 15 ampules of HMG per cycle when not pretreated with CC and 16 ampules when

CC pretreatment, the difference not being significantly different. However when HMG requirement before and after CC pretreatment was compared with the group with high levels of FSH and having a +ve withdrawal bleed on administering progesterone a significant difference was found (Table III).

8 patients conceived 11 times during this study. Of these 11 pregnancies, 5 aborted spontaneously, one was a preterm delivery and the remaining 5 reached term. In one primigravida LSCS was required, for breech presentation with a big baby.

As regards the complications, 3 patients requiring higher doses of HMG had ovarian enlargements and one had OHSS of moderate intensity requiring admission to the hospital whereas in the group where HMG requirement could be effectively reduced due to CC pretreatment, one patient had ovarian enlargement and one patient had mild OHSS (Ovarian hyperstimulation Syndrome). However in both the groups one patient had multiple pregnancy in the form of twins.

It is obvious that in some patients who

Table II

Hormonal Levels

F.S.H. Levels :

Withdrawal -ve group : 1.4 to 3.6 MIU/ml

Withdrawal +ve group : 5.5 to 7.0 MIU/ml

LH Levels :

Withdrawal -ve group : 2.0 to 14 MIU/ml

Withdrawal +ve group : 12.0 to 54 MIU/ml

Difference between both groups statistically significant ( $P < 0.01$ )

Table III

HMG Requirements

|                             | HMG + HCG         |             | CC + HMG + HCG    |             |
|-----------------------------|-------------------|-------------|-------------------|-------------|
|                             | No. of Amp. cycle | No. of days | No. of Amp. cycle | No. of days |
| Low FSH (-ve withdrawal)    | 15                | 8.7         | 16                | 9.2         |
| Higher FSH (+ve withdrawal) | 09*               | 7.3         | 04*               | 3.3         |

All values are means

\* Diff. between two groups statistically significant ( $P < 0.01$ )

**Table IV**  
**Obstetric Outcome**

|                                    | Number Percentage |       |
|------------------------------------|-------------------|-------|
| Total cycles treated               | 69                |       |
| Total cycles ovulatory             | 66                | 95.65 |
| Total patients concieved           | 08/14             | 57.1  |
| Total cycles with pregnancy result | 11/66             | 16.67 |
| Spontaneous Abortions              | 05                | 45.45 |
| Preterm labour                     | 01                | 9.09  |
| Full term normal delivery          | 04                | 36.36 |
| L.S.C.S.                           | 01                | 9.09  |

require HMG, a reduction in HMG requirement is possible if CC pretreatment is done. These patients are those in whom progesterone withdrawal bleeding is positive. March (1984) also showed similar results.

Not only the cost which is very important, but also the complication rates could be reduced by decreasing the requirement of HMG by CC pretreatment. This has been clearly found in this study

and is in concurrence with the results of Robertson et al (1976) and Kenman and Jonu (1983).

Thus, by identifying the specific characteristics of patients of anovulation refractory to CC, HMG requirement can be reduced in some of them by a CC pretreatment.

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