

## The Pregnancy Rates with Intrauterine Insemination (IUI) in Superovulated Cycles employing different protocols (Clomiphen Citrate (CC), Human Menopausal Gonadotropin (HMG) and HMG+CC) and in Natural Ovulatory Cycle

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### Introduction

Achieving maximum pregnancy rate when ovarian stimulation is combined with intrauterine insemination (IUI), is a valuable method of infertility treatment.<sup>1,2</sup> Use of ovarian stimulation in IUI increases the number of oocytes available for fertilization which could possibly correct unpredicted ovulatory dysfunction.<sup>3</sup> The monthly fecundity rate can be improved by active management with super ovulation and IUI.<sup>4</sup> In polycystic ovarian syndrome(PCOS) patients represent one of the most challenging subpopulation to treat safely and successfully using superovulated cycles and IUI.<sup>5</sup> In a multicenter prospective study, the combination of superovulated cycles with gonadotropins and IUI had proved superior to IUI alone.<sup>6</sup> It has been shown that IUI without associated superovulation has little value in treatment of male infertility.<sup>4</sup> In a randomized trial, superovulation and IUI resulted a 3-fold greater pregnancy rate compared with IUI alone.<sup>7</sup> Poor results were reported when IUI was performed in natural cycles, not only for male factor subinfertility but also for unexplained and cervical factor subinfertility.<sup>8,9</sup> The aim of our work is to study the effects of different protocols of induction ovulation in IUI cycle on infertile couples.

### Subjects and Methods

In a retrospective blind study, 441 consecutive cycles of IUI was performed on 209 infertile couples categorized as having unexplained infertility, male factor, endometriosis, tubal disease, hostile mucus, ovulatory dysfunction and multifactorial infertility. The study was done at Birmingham Women's Hospital in the Academic department, assistant conception unit (ACU) from January 1995 to June 1996.

IUI was performed either in natural ovulatory cycle

or with induced ovulatory cycles by using clomiphen citrate (CC), human menopausal gonadotrophin (HMG) and HMG+CC which was chosen by the technician according to patients's condition; CC treatment was used in anovulatory cycles, male factor, hostile mucus and unexplained infertility, HMG+CC treatment were used in endometriosis, multifactorial and ovulatory dysfunction, HMG treatment was used in CC failure and poor responders.

In our department the natural cycle with IUI programme mainly is used for sperm stored patients and male factor infertility.

In the CC protocol, after scanning on day 2, 50 or 100mg CC was orally administrated from day 2-6 of treatment cycle. The most common side effects were weight gain, hot flushes, headaches and mood swings, but they

Table. Pregnancy occurrence employing different ovulation induction protocols.

Protocol	Number of patients	Number of cycles	Number of pregnancies	Pregnancy per cycle	Pregnancy per patient
Natural	8	37	1	2%	12%
Clomiphene	27	41	2	4%	7%
Clomiphene + HMG	129	285	21	7%	16%
HMG	35	89	8	9%	23%

CC+HMG+IUI, 9 pregnancies occurred (preg. rate 7% per cycle, 16% per patient).

In 35 patients who received 80 cycles of HMG+IUI 8 pregnancies occurred (preg. rate 9% per cycle, 23% per patient). The results are illustrated in Table.

### Discussion

Methods chosen for ovulation induction have been a critical bearing on the success of IUI and poor results have been obtained in natural cycles.<sup>8,9</sup> In our study the natural cycle with IUI programme mainly used for sperm stored patients, had a pregnancy rate of 20% per cycle.

In a randomized trial, comparing superovulated cycle and IUI with timed intercourse in women with unexplained infertility has determined that the pregnancy rate is higher with superovulated cycle and IUI (20% versus 11.4%).<sup>7</sup> Ovarian stimulation by using CC+HCG+IUI in couples with oligo-

ovulation, unexplained infertility and male factor can improve the result of pregnancy.<sup>10</sup> The results with this regime in one study were 14.2% pregnancy per cycle in oligo-ovulation, 3.9% pregnancy per cycle in male infertility and 16.3% pregnancy per cycle in unexplained infertility.<sup>11-13</sup> In another study the pregnancy rate in CC+IUI cycle was 4% per cycle.<sup>14</sup> The result in our study with CC+HCG+IUI was 4% per cycle.

Using the HMG for ovarian stimulation has resulted in much higher monthly fecundability compared with CC.<sup>15</sup> The uncertainty regarding the efficacy of adding IUI to clomiphene influences the researcher to proceed from clomiphene treatment to the combination of gonadotropins and IUI, with an expectation of achieving a pregnancy rate of 15% per cycle.<sup>4</sup> In a meta-analysis of methods used to treat unexplained infertility, pregnancy rate with IUI alone was (3.8%), clomiphene and IUI (8.3%) and gonadotropins and IUI (17.1%).<sup>16,17</sup> Combined therapy of controlled superovulation with HMG+IUI has been introduced as an effective method of treating infertile couples with patent fallopian tubes when more traditional therapy has failed.<sup>18,19</sup> Endometriosis associated infertility can be successfully treated with controlled ovarian stimulation (COS) with HMG and IUI. The pregnancy rate in superovulated group was significantly higher than untreated group (11% versus 2%).<sup>20,21</sup> The pregnancy rate of HMG+IUI in our study was 9% per cycle. Combination of both CC and HMG with IUI have been used to minimize the cost and side effects than with HMG alone. This method may decrease the amount of HMG required by approximately 50% and also decreases risk of multiple pregnancies and hyper stimulation syndrome which can be expected.<sup>4</sup> In our study the result of pregnancy with CC+HMG employing IUI was 7% per cycle.

## Conclusion

We found that the pregnancy rate is higher with combination of HMG ovulation and IUI than natural cycle+IUI, CC ovulation+IUI and CC+HMG ovulation+IUI. The result also shows HMG+IUI to be a viable treatment option in patients with infertility refractory to other treatment.

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## **Abstract**

**Objective:** To compare the result of IUI in infertile couples with different protocols of induction ovulation.

**Methods:** In a retrospective study, 209 infertile couples with different diagnosis (unexplained, male factor, endometriosis, tubal disease, ovulatory dysfunction and multifactorial infertility) were subjected to different protocol of induction

ovulation: 50-100 mg CC in day 2-6, 50 mg CC in day 2-6 + 2 amp HMG in day 5, 7, 9, 11, and 2 amp HMG per day. Natural ovulatory cycle + IUI was used for sperm stored patients. 441 consecutive cycles of IUI was performed 36-40 hours after HCG injection. The data were analysed with student T-test and Mann-Whitney test. The significance was defined as  $P < 0.005$ .

**Results:** Thirty one pregnancies (7% per cycle, 15% per patient) occurred. One pregnancy occurred (pregnancy per cycle was 2% and per patient was 12%) in 8 patients undergoing 37 cycles of IUI with natural ovulation. The result with CC in 27 patients undergoing 41 cycles IUI was 2 pregnancies (4% per cycle, 7% per patient). In 129 patients receiving 283 cycles of IUI with CC+HMG 21 pregnancies occurred (7% per cycle, 16% per patient). In 35 patients receiving 80 cycles of IUI with HMG 8 pregnancies occurred (9% per cycle, 23% per patient).

**Conclusion:** The method chosen for ovulation induction had a critical bearing on the success of IUI. The result of IUI will be better by using induction ovulation compared to natural ovulatory cycle. In our programme the combined use of HMG+IUI yielded a higher rate of pregnancy rate compared with CC+IUI, CC+HMG+IUI and natural ovulatory cycle+IUI (*JPMA* 54:503;2004).