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Original Research

Evaluating clinical role of oral natural or synthetic progesterone during stimulated IUI cycles for unexplained infertility

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ABSTRACT:

Background: Primary infertility is defined as the inability to conceive after a year of unprotected intercourse, and secondary infertility is defined as not becoming pregnant after a prior pregnancy.The present study was conducted to evaluate clinical role of oral natural or synthetic progesterone during stimulated IUI cycles for unexplained infertility. **Materials & Methods:** 84 women with unexplained infertility were recruited. Patients with baseline Serum (Sr). progesterone records who received Oral Natural Micronized Progesterone Sustained Release (Oral NMP SR) (Group I) or Dydrogesterone following CC/HMG induction protocol and human Chorionic Gonadotropin (HCG) Inj., (Group II) were further analysed following Luteal Phase Support (LPS) with oral natural or synthetic progesterone. Serum Progesterone levels in both groups were assessed. **Results:** The mean weight was 29.3 kgs in group I and 30.1 kgs in group II. Menses duration was 28.4 days in group I and 29.4 days in group II. The difference was non- significant (P> 0.05). In group I, mean serum level at baseline was 5.4 and at mid luteal level was 31.2. The percentage change was 85%. Patients achieving mid-luteal sr. prog level (≥14 ng/ml) were 80%. In group II, it was 0.31 at baseline and 20.5 at mid luteal level. The percentage change was 98%. Patients achieving mid-luteal sr. prog level (≥14 ng/ml) were 83%. The difference was significant (P< 0.05). **Conclusion:** Oral NMP SR clinical supplementation offers dosing convenience with few adverse effects, implies therapeutic compliance, and offers an alternative approach to traditional formulations.

Keywords: infertility, luteal, progesterone

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INTRODUCTION

Primary infertility is defined as the inability to conceive after a year of unprotected intercourse, and secondary infertility is defined as not becoming pregnant after a prior pregnancy.[1] The WHO estimates that between 3.9% and 16.8% of Indians are primary infertile. According to the National Family Health Survey (NFHS)-II, 3.8% of women in the 40–44 age range are childless.[2] Higher education, marriage age >25, delaying childbearing for ≥1 year, obesity, polycystic ovarian syndrome, irregular menstrual patterns, endometriosis, STDs, and menarche age >14 years are all significant risk factors. With a prevalence rate of roughly 10%, unexplained infertility continues to be a prevalent category among the several types of infertility. Idiopathic infertility, also name for unexplained infertility, is the inability of a couple to conceive for which there is no known cause.[3,4]

Pituitary and/or follicular malfunction, gamete dysfunction, and changes in endometrial function are common reasons. An altered luteal phase, which is seen in roughly 30% of women with infertility that cannot be explained, could also be the cause. This could manifest as a shorter luteal phase or a lower peak serum progesterone level.[5] Unknown infertility is frequently treated using intrauterine insemination (IUI). In order to improve embryo implantation and sustain pregnancy, HCG trigger is administered after the clomiphene citrate/HMG induction stimulation regimen, followed by IUI and progesterone supplementation throughout the luteal phase.[6] The present study was conducted to evaluate clinical role of oral natural or synthetic progesterone during stimulated IUI cycles for unexplained infertility.

MATERIALS & METHODS

The study was carried out on 84 women with unexplained infertility. All gave their written consent to participate in the study.

Data such as name, age, etc. was recorded. Patients underwent IUI procedure for unexplained infertility. Patients with baseline Serum (Sr). progesterone records who received Oral Natural Micronized Progesterone Sustained Release (Oral NMP SR) (Group I) or Dydrogesterone following CC/HMG induction protocol and human Chorionic Gonadotropin(HCG) Inj., (Group II) were further analysed following Luteal Phase Support(LPS) with oral natural or synthetic progesterone. Serum Progesterone levels in both groups were assessed. Results thus obtained were subjected to statistical analysis. P value < 0.05 was considered significant.

RESULTS

Table I Baseline demographics

Parameters	Group I	Group II	P value
Weight (Kgs)	29.3	30.1	0.75
Menses duration (days)	28.4	29.4	0.81

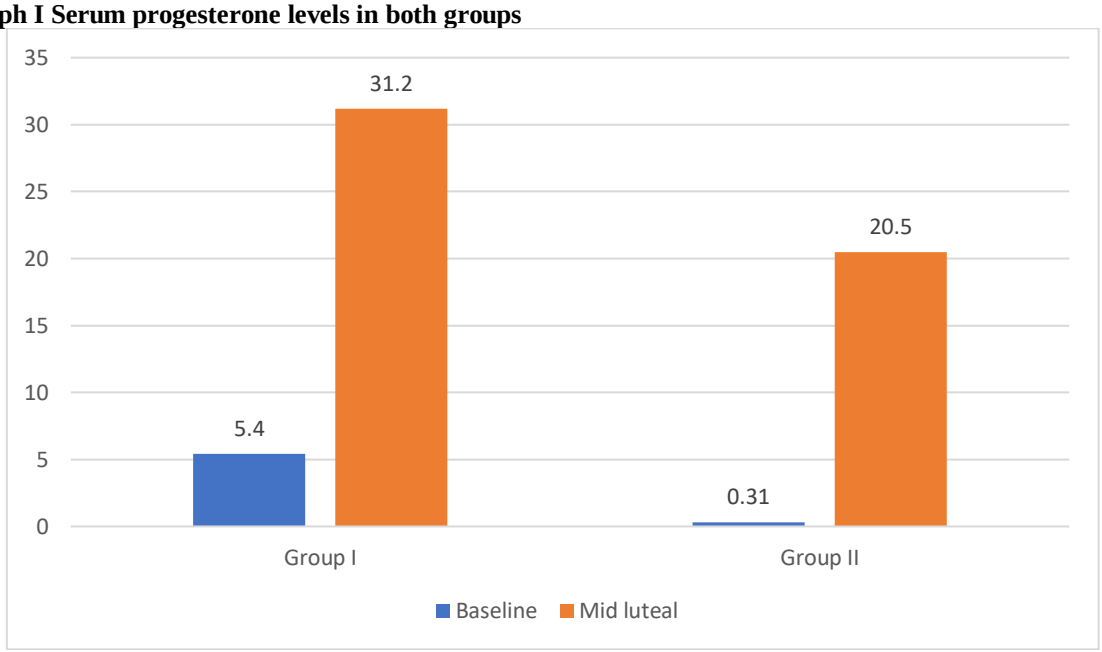
Table I shows that mean weight was 29.3 kgs in group I and 30.1 kgs in group II. Menses duration was 28.4 days in group I and 29.4 days in group II. The difference was non- significant (P> 0.05).

Table II Serum progesterone levels in both groups

Group	Baseline	Mid luteal	% change	pts achieving mid-luteal sr. prog level (≥14 ng/ml)
Group I	5.4	31.2	85%	80%
Group II	0.31	20.5	98%	83%

Table II, graph I shows that in group I, mean serum level at baseline was 5.4 and at mid luteal level was 31.2. The percentage change was 85%. Patients achieving mid-luteal sr. prog level (≥14 ng/ml) were 80%. In group II, it was 0.31 at baseline and 20.5 at mid luteal level. The percentage change was 98%. Patients achieving mid-luteal sr. prog level (≥14 ng/ml) were 83%.The difference was significant (P< 0.05).

Graph I Serum progesterone levels in both groups



DISCUSSION

The slow, sustained release kinetics of progesterone by SR formulation minimizes immediate drug loading or exposure for any dose related side effects including drowsiness due to the active metabolite Allopregnanolone.[7,8] Oral NMP SR used worldwide since 1986 has been recently introduced in India for management of Luteal Phase Defect (LPD) and as Luteal Phase Support (LPS) during Assisted Reproductive Techniques (ART). Critical factors responsible for success of IUI include age, history of reproductive milestones, type of Controlled Ovarian Hyperstimulation (COH) or stimulation protocol used without underplaying the benefits of luteal phase support with progesterone supplementation.[9,10]The present study was conducted to evaluate clinical role of oral natural or synthetic progesterone during stimulated IUI cycles for unexplained infertility.

We found that the mean weight was 29.3 kgs in group I and 30.1 kgs in group II. Menses duration was 28.4 days in group I and 29.4 days in group II. Malhotra J et al[11]evaluated the clinical role of progesterone supplement as luteal phase support for women with unexplained infertility following stimulation protocol with Clomiphene Citrate (CC)/ Human Menopausal Gonadotropin (HMG). 120

patient records were retrieved especially for subjects undergoing IUI procedure for Unexplained infertility. Patients with baseline Serum (Sr). progesterone records who received Oral Natural Micronized Progesterone Sustained Release (Oral NMP SR) (N=45) or Dydrogesterone (n=33) following CC/HMG induction protocol and human Chorionic Gonadotropin(HCG) Inj., were further analysed following Luteal Phase Support(LPS) with oral natural or synthetic progesterone. Baseline demographics showed 78 patients with mean age, weight and cycle duration of 29.5 yrs, 57.3 kg & 28.6 days respectively. Progesterone was supplemented as Oral NMP SR 200/300 mg OD or Dydrogesterone 10 mg bid in 22, 23 and 33 patients respectively. In all cases ovulation was triggered with HCG inj., followed by IUI within the next 48 hours while baseline sr. progesterone levels were being assessed. Medicines and Healthcare Products Regulatory Agency (MHRA) UK recommended therapeutic compliance to suggest sr. progesterone levels of ≥14ng/ml were recorded as Mid-luteal levels in all of these patients. This therapeutic compliance was noted in 82.2% & 78.8% of the patients treated with oral NMP SR or Dydrogesterone respectively. Pregnancy was observed amongst 5 and 10 patients treated with oral NMP SR and Dydrogesterone respectively at the end of 'First' IUI cycle. Both the groups were well tolerated with drowsiness documented in three cases for Oral NMP SR.

We found that in group I, mean serum level at baseline was 5.4 and at mid luteal level was 31.2. The percentage change was 85%. Patients achieving mid-luteal sr. prog level (≥14 ng/ml) were 80%. In group II, it was 0.31 at baseline and 20.5 at mid luteal level. The percentage change was 98%. Patients achieving mid-luteal sr. prog level (≥14 ng/ml) were 83%. Arici et al[12]tested the hypothesis that in couples undergoing IUI, actively managed cycles using clomiphene citrate (CC) stimulation, ultrasound monitoring, and hCG timing will result in increased pregnancy rate (PR) per cycle compared with unstimulated urinary LH-timed cycles.Fifty-six couples with unexplained infertility (n = 26) or male factor infertility (n = 30) participated in the study.Twenty-nine couples completed the study and the analysis of 95 cycles revealed that among the male factor infertility group, one pregnancy occurred during the 26 cycles of each treatment group (PR per cycle of 3.9% for both treatment groups). In contrast, among the unexplained infertility group, there was a marked difference in the effect of treatments. During treatment A only one pregnancy occurred in 20 cycles (PR of 5% per cycle) whereas during treatment B, six pregnancies occurred in 23 cycles (PR of 26.1% per cycle).

The shortcoming of the study is small sample size.

CONCLUSION

Authors found that oral NMP SR clinical supplementation offers dosing convenience with few adverse effects, implies therapeutic compliance, and offers an alternative approach to traditional formulations.

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