Original Article

Intrauterine Insemination and Luteal Support Therapy Outcomes in Unexplained Infertility, Mild and Marked Luteal Defective Infertile Women

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Summary:

Back ground: Inadequate secretory transformation of the endometrium resulting from deficient ovarian progesterone secretion is a cause of infertility and recurrent abortion in luteal phase defects (LPD) women. LPD are diagnosed in 20% of infertile patients and 60% of patients with recurrent abortion and 50% of anovulatory women.

Aim : The objective of the present study was to compare pregnancy outcome following sperm penetration assay (SPA), intrauterine insemination (IUI) and luteal support therapy (LST) in infertile patients with unexplained infertility (UI) mild and marked LPD.

Materials and Methods: Men with normal semen analyses and positive sperm penetration assay scores were included in this Study while those men with abnormal semen and negative SPA score were admitted to 1C SI program in another study. The patients were divided into three groups: first group n= 42 with UI without LPD, second group n= 60 with mild LPD and third group n= 58 with marked LPD. Progesterone (P) concentration was assayed on cycle day 21 and patients showing P concentration of < 3.50 ng/ml were considered to have marked LPD and those with <10 ng/ml were considered to have mild LPD. All patients received clomiphene citrate, human menopausal gonadotropin and human chorionic gonadotropin (HCG) for ovulation induction. The patients received 1500 IU of HCG on cycle day 14, 17, 20 and 23 after IUI. Beta-HCG test was performed two weeks after IUI and when the test was positive, the patients continued to receive the HCG treatment every three days for a period of three months.

Results: There were no significant differences in the SPA and semen analysis parameters between the groups. The Progesterone concentration was significantly different among the groups (18.4, 8.9, and 2.4 in the first and second and third groups ($P<0.05$) respectively on cycle day 21 prior to ovulation induction. Two weeks following IUI, the Progesterone concentration in the marked LPD group was significantly lower compared to mild and unexplained infertility groups (13.5 versus 20.3, and 22.8 ng/ml, $P<0.05$, respectively). The pregnancy rate per cycle was 35.7% in the unexplained infertility group and 40% in the mild LPD group and 31% in the marked LPD group ($P>0.05$).

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Conclusion: In conclusion, the use of IUI and luteal support therapy in the mild, marked LPD infertile patients and unexplained infertility resulted in similar pregnancy rates.

Introduction:

Progesterone is required for preparation of the uterus for embryo implantation. It is well known that any reduction in the concentration of serum progesterone during early stages of pregnancy results in abortion (1). Women with luteal phase defect (LPD) are characterized by abnormal corpus luteum function associated with inadequate progesterone secretion. Multiple factors are responsible for LPD and these factors include reduction in the concentration of FSH in the follicular phase of menstrual cycle, abnormal secretion of LH and abnormal response of endometerium to progesterone. Inadequate secretory transformation of the endometrium resulting from deficient ovarian progesterone secretion is a cause of infertility and recurrent abortion in LPD women and it is diagnosed in 20% of infertile patients and 60% of patients with recurrent abortion and 50% of unovulatory women. It has been estimated that about 50% to 60% of infertile women have some sort of LPD (2).

Ovulation induction by exogenous gonadotropin administration in infertile women during intrauterine insemination and in vitro fertilization and embryo transfer treatment cycles usually results in a temporary LPD. This causes suppression in progesterone secretion, which affects embryo implantation. The increase in the estradiol/progesterone ratio in the stimulated cycles has an inhibitory action on embryo implantation in human and animal studies (3-5). These observations indicate that the application of luteal support therapy in the form of progesterone and/or human chorionic gonadotropin (HCG) may have beneficial effect on embryo implantation and maintenance of pregnancy in the stimulated cycles in infertile female patients and especially those with LPD problem (6-7).

The objective of the study was to evaluate the clinical significance of intrauterine insemination and luteal support therapy in infertile patients with unexplained infertility and luteal phase defect.

MATERIALS AND METHODS

The mean age of the women was 30.4 years with a mean of 6.8 years infertility duration. The mean age of the husbands was 34.7 years and the mean motility of the sperm was 75.4% and mean sperm concentration was 56 million. In order to exclude the males as a variable in the study, sperm hypo-osmotic test (HOST), sperm penetration assay using hamster zona-free oocytes were used to examine the fertilization potential of the sperm. Men with normal HOST and positive sperm penetration scores were admitted to the ovarian hyperstimulation and intrauterine insemination program while those men with abnormal semen parameters, HOST and negative sperm penetration scores were admitted to intracytoplasmic sperm injection program in another study.

The patients were divided into three groups: first group n=42 with unexplained infertility, second group n=60 with mild LPD and third group n=58 with marked LPD. Progesterone concentration was assayed on day 21 of the menstrual cycle and patients showing progesterone concentration of less than 3.5 ng/ml were considered to have a marked LPD and those with less than 10 ng/ml were considered to have a mild LPD.

The female patients were received ovulation induction in form the of human menopausal gonadotropin and human chorionic gonadotropin treatments.

Ultrasound examination and estradiol assay were performed on cycle day 10 and 12.

Intrauterine insemination was carried out when at least two mature follicles size > 18mm observed by vaginal sonography and estradiol concentrations were 250-300 pg/ml per follicle and endometrial thickness was 10 mm.

The patients received 1500 IU of human chorionic gonadotropin (HCG) on cycle day 14, 17, 20 and 23 after intrauterine insemination (IUI). Beta-HCG test was performed two weeks after IUI and when the test was positive, the patients continued to receive the HCG treatment every 72 hours for a period of three months. The data were

presented as mean +/- standard error of the mean. One way analysis of variance was used for statistical analysis of the data and a P value < 0.05 was considered statistically significant (P < 0.05).

RESULTS

There were no significant differences in the sperm penetration scores, HOST and sperm motility index in the unexplained infertility, mild and marked luteal phase defect infertile patients (Figure 1 -5 and Table 1 -2). The progesterone concentration was significantly different among the unexplained infertility, mild and marked LPD groups (18.4, 8.9, and 2.4, respectively, P <0.05) on cycle *day 21* prior to ovulation induction and intrauterine insemination (Figure 6).

The progesterone concentration following ovulation induction and intrauterine insemination was significantly lower in the marked LPD group versus mild LPD and unexplained infertility groups (Figure 7, P < 0.05).

The pregnancy rate per cycle was 35.7% in the unexplained infertility group, 40% in the mild LPD group and 31% in the marked LPD group (Figure 8 and Table 3.).

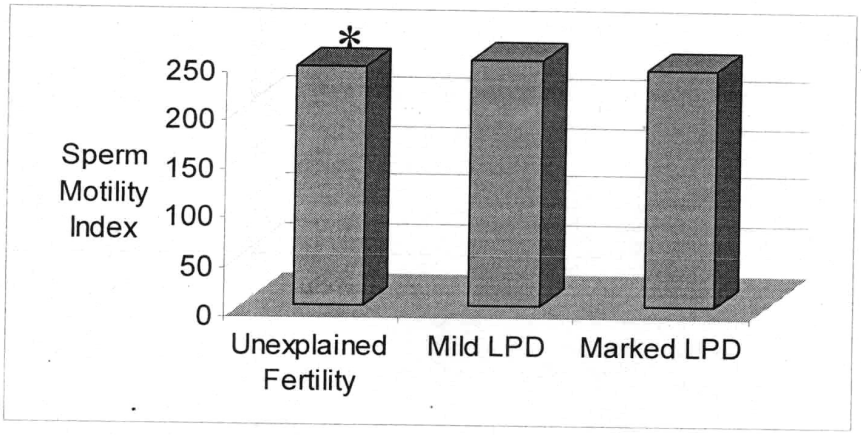

Figure 1. Sperm Motility Index in Unexplained Infertility, Mild and Marked Luteal Phase Defect Infertile Groups.
*P>0.05

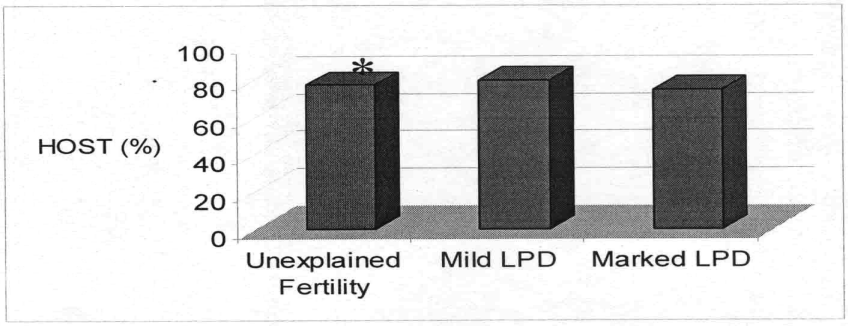

Figure 2. HOST Percentages in Unexplained Mild and Marked Infertile Groups.
*P>0.05

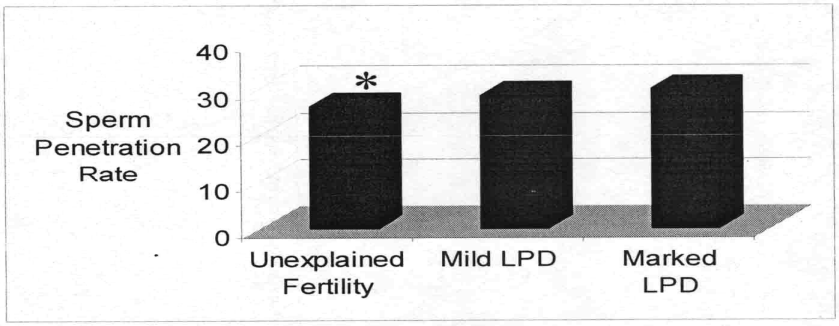

Figure 3. Sperm Penetration Rate in Unexplained Mild and Marked Infertile Groups.

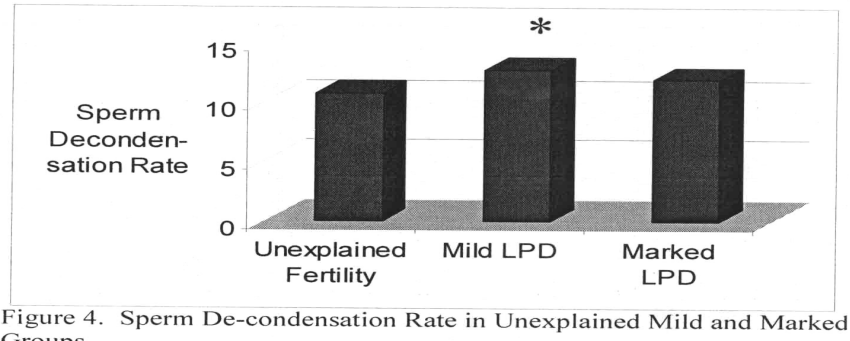

Figure 4. Sperm De-condensation Rate in Unexplained Mild and Marked Infertile Groups.
*P>0.05

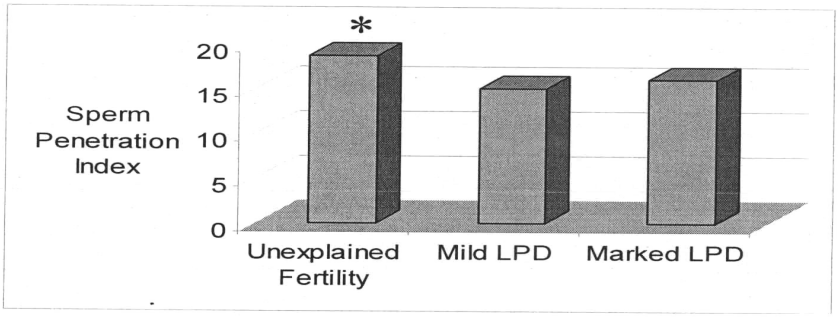

Figure 5. Sperm Penetration Index in Unexplained Mild and Marked Infertile Groups.
*P>0.05

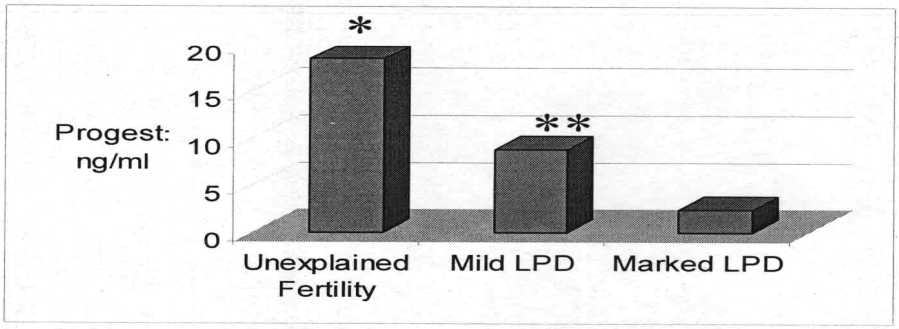

Figure 6. Progesterone Concentration in the Blood of Unexplained Mild and Marked Infertile Women on Cycle Day 21 Prior to Ovulation Induction and IUI.
* P<0.01 Significantly different from other groups.
** P<0.05 Significantly different from Marked LPD group.

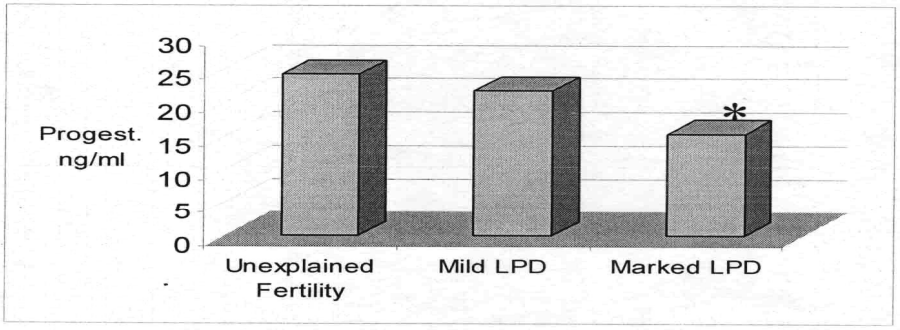

Figure 7. Progesterone Concentration in Unexplained Infertility and Mild and Marked Luteal Phase Defect in Infertile Women Treated with IUI and Luteal Support Therapy.
* P<0.05 Significantly different from other groups.

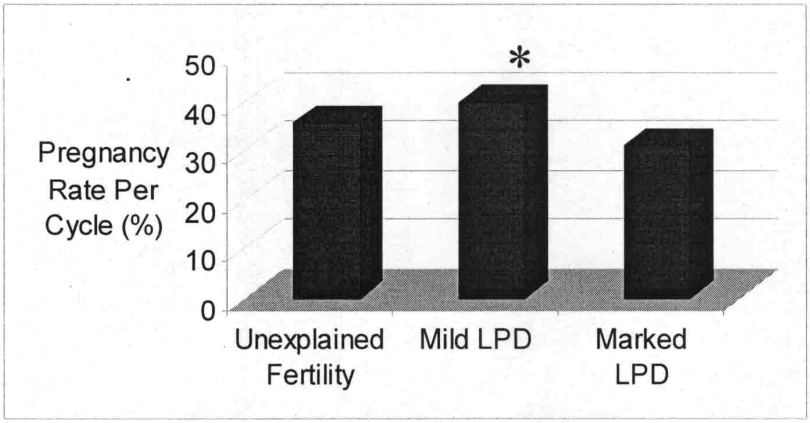

Figure 8. Pregnancy Rate Per Cycle in Unexplained Infertility and Mild and Marked Luteal Phase Defect in Infertile Women Treated with SPA, IUI and Luteal Support Therapy.
* P>0.05

Table 1. Sperm penetration assay data in the unexplained infertility (UI), mild luteal phase defect (MLPD) and marked luteal phase defective groups.

Groups*	UI	Mild LPD	Marked LPD
Sperm penetration rate	22.5%	24.4%	25.2
Sperm decond. Rate	10.9	12.5	11.2
Sperm penetration index	16.4	14.1	15.3

*P> 0.05

Table 2. Sperm motility index (SMI) and sperm hypo-osmotic swelling test (HOST) outcomes in the unexplained infertility (UI), mild luteal phase defect (MLPD) and marked LPD groups.

Groups*	UI	Mild LPD	Marked LPD
Sperm motility index	230	240	236
HOST	70%	75%	73%

*P> 0.05

*P>0.05

Table 3. Pregnancy outcome progesterone (P4) concentration (ng/ml) following ovulation induction (OI) and intrauterine insemination (IUI) and luteal support therapy in infertile women with unexplained infertility and mild and marked luteal defectives.

Groups	UI	Mild LPD	Marked LPD
P4 Cone. Prior OI & IUI	18.4*	8.9**	2.4
P4 Cone. After OI & IUI	22.8	20.3	13.5***
Pregnancy rate/cycle****	35%	40%	31%

***P <0.01 significantly different from corresponding groups**
**** P < 0.05 significantly different from marked LPD group**
***** p <0.01 significantly different from corresponding groups**
******P>0.05**

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Discussion:

The sperm penetration assay including sperm penetration rate, sperm penetration index and sperm de-condensation rate had a similar score in the unexplained infertility, mild luteal defective and marked luteal defective groups. The differences in the sperm penetration assay among the studied groups were not significant (P>0.05). The sperm motility index is the product of percentage of sperm motility X sperm active grade while sperm hypo-osmotic test measures sperm plasma membrane integrity and it is an important score for sperm viability. Both assays are used to measure sperm function tests. The differences in the sperm motility index and sperm hypo-osmotic test scores are not significant different between the studied groups. These observations in sperm function tests are an indication that the male factor in the present study has no significant effect on the outcomes of intrauterine insemination and luteal support therapies. For the above reasons, male factor is not considered as a variable in the present study (8-9). The progesterone concentration significantly improved after ovarian stimulation with gonadotropins compared to its concentration prior to ovulation induction and intrauterine insemination. This improvement in progesterone concentration is due to positive action of the luteal support therapy which results in the stimulation of the corpus luteum to secrete more progesterone to support embryo implantation (10-12). The intrauterine insemination and luteal support therapy outcomes in term of pregnancy rate per cycle were similar in the mild and marked luteal phase defect group sand they were not significantly different from the unexplained infertility group. This may be due to the fact that the early HCG supplementation following intrauterine insemination results in decreased uterine contractions due to stimulation of progesterone secretion from the corpus luteum and also may have caused normal physiological synchronized endometrial transformation (6, 7, and 13). The male factor effect as a variable in the experiment was excluded as mentioned earlier and the unexplained infertility group was considered as a control group which indicates that the treatment was effective in improving pregnancy rates in the mild and marked LPD groups since their values were not significantly different from the score of unexplained infertility group.

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