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# INTRA UTERINE INSEMINATION OUTCOME FOLLOWING THE DRILLING OF POLYCYSTIC OVARIAN SYNDROME OF INFERTILE WOMEN

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## ABSTRACT

**Background:** Polycystic ovarian syndrome (PCOS) is one of world wild problem, affecting women during their reproductive age. The PCO and PCOS in Iraqi women are found as the first common cause of infertility with negative response to medical treatment .One of the second line of treatment is Laparoscopic ovarian drilling (LOD) that used to induce ovulation in women with PCOS. **Objective:** The objective of the present study is to investigate the effect of PCO drilling on pregnancy rate following intrauterine insemination (IUI). **Patients, materials and methods:** Fifty couples were involved in current study during the period from September 2013 to July 2014. Laparoscopic ovarian drilling was done for the spouses after confirming diagnosis of PCOS by laparoscopy .The women were inseminated either through intrauterine insemination or natural intercourse into two groups depending on the results of husband semen analysis. **Results:** There was a significant ($P<0.01$) decrease in LH ,testosterone and prolactin hormones with elevation in progesterone level following the LOD operation compared to before the drilling of PCOS women. The pregnancy rate following IUI was 8% and after natural intercourse was 20%.and total pregnancy rate was 14%. **Conclusions:** This study concluded that LOD must be recommended as line treatment option for treatment resistance of PCOS women. The drilling is effective to turn back a normal levels of reproductive hormones and ovulation with successful pregnancy . Therefore LOD considered the ultimate clinical endpoints for studies on female infertility treatment.

**KEYWORDS:** Laparoscope ovarian drilling, IUI, PCOS.

## INTRODUCTION

Polycystic ovarian syndrome is the most common reproductive endocrinopathy affecting 6 to 12% of women during their reproductive age.[1-2] It is also the major cause of anovulatory infertility.[3] The first-line treatment of anovulatory infertility in PCOS patients is clomiphene citrate.[3-4] Disorders in inducing ovulation and anovulation are well recognized in women with PCOS.

Ovarian wedge resection was the first established treatment for anovulatory PCOS patients[5] but was predominately abandoned because of the risk of postsurgical adhesion formation, which changed endocrinological (or hormonal) subfertility to mechanical subfertility as a result of scarring.[6-7] Then it was replaced by medical ovulation induction with clomiphene citrate and gonadotropins.[8]

Ovulation induction with clomiphene is not always successful, with almost 20% of women described as 'clomiphene-resistant'[9],those can be managed with gonadotropins but often have an increased of follicles and are insecure to the risks of ovarian hyperstimulation syndrome (OHSS) and multiple pregnancies. Although effective, gonadotrophins are an expensive, time-consuming and inconvenient form of treatment requiring intensive monitoring.

An alternative to medical ovulation induction is surgical therapy using laparoscopic techniques known as laparoscopic ovarian 'drilling' (LOD). This was first described by Gjonnaess in 1984.[10] The technique can be done on an outpatient basis with less trauma and fewer postoperative adhesions than with ovarian wedge resection.

After LOD ,Success rates for future ovulation range about from 53% to 92%.[11] More specifically, approximately 80% of patients who underwent ovarian drilling starting ovulation, while nearly 50% were able to become pregnant. Patients who are not responding that is to say ovulating after an ovarian drilling procedure have been shown, in many cases, to be more responsive to clomiphene citrate, even if they were previously immune to the drug.[12]

Multiple pregnancy rates are considerably decreased in those women who conceive following laparoscopic drilling.[13] The PCO and PCOS in Iraqi women are found as the first common

cause of infertility with negative response to medical treatment.[14] Therefore, the objective of the present study is to find the effect of PCO drilling on pregnancy rate following intrauterine insemination.

## MATERIALS AND METHODS

Fifty couples were attendance at the Higher Institute of Infertility Diagnosis and Assisted Reproductive Technologies – Al-Nahrain University, during the period from September 2013 to November 2014. The couples were subjected to complete physical examination both systemic and local of Female and Male Infertility Clinics. Laparoscopic ovarian drilling was done for patients after confirming diagnosis of PCOS by laparoscopy. After waiting the spontaneous ovulation for about 4 months which is the average expected time to resume ovulation after LOD[15], in those who were not responder after that time, medical ovulation induction done by different drugs and doses according to patient age, weight, and ovarian response by ultrasound follow up. After achieving ovulation whether it is spontaneous or induced, either IUI was done to evaluate its effect on pregnancy rate in patients with PCOS who underwent LOD, or the couple guided for natural intercourse depending on the normal criteria of semen analysis.

### Female investigation

Complete hormonal study was done for all females included in this study to diagnose the PCO women and exclude anovulated one. These hormones include FSH, LH, and prolactine on day 2-3 of the cycle (CD2) and progesterone at (CD21). Medical history and a pelvic exam was performed to diagnosing PCOS. However, other tests was done to confirm the diagnosis, such as: Blood tests that reveal the levels of certain hormones in the blood, such as FSH, LH, estrogen (estradiol), and androgens (testosterone and DHEAS).[16] Next step is doing ultrasonography which is a scan that uses high frequency sound waves to identify the many small cysts in the ovaries.[16] Thus, the women were considered with PCO when number of follicles more than 10 follicles (2±8 mm diameter), ovarian volume >12 cm3 and bright echogenic stroma.[12]

All operations of LOD were performed by a designated team, which comprised two surgeons in Al- Karakh maternity Hospital – Baghdad. Following ovarian drilling, women were asked to keep a record of their menstrual cycle. If the patient started a menstrual period within 6 weeks of the surgery, a blood sample was taken on day 2 of that cycle for measurement of serum concentrations of LH, FSH, testosterone Another blood sample was taken on day 21-

22 of the same cycle for measurement of serum concentration of progesterone. Ovulation was diagnosed when the progesterone level was ≥30 nmol/l. If spontaneous menstruation did not occur, a random blood sample was taken to measure all the above hormones at 6 weeks following surgery. If the patient did not ovulate as evidenced by the low progesterone levels or lack of menstruation after 4 months, CC or gonadotrophins (Gn) treatment was started. If ovulation was achieved either spontaneously or with the help of CC or Gn, patients were followed-up until they achieved ovulation then IUI, or natural intercourse was done.

**Statistical analysis:** The data of present study were expressed as mean ± SE using SPSS V21 windows 7 and using Excel program 2010 for figures .Depending on the nature of data Students t-Test was used to compare between the results .Chi square was used for diagnostic the significance of pregnancy . P value considered significant when reach < 0.05 and highly significant when reach <0.001.[17]

## RESULTS

In table 1, regarding hormonal changes there was a non significant (P>0.05) decrease in FSH hormone following the laparoscopic ovarian drilling (LOD) operation compared to before the drilling of PCOS women .However both values were in normal limits. There was a significant (P<0.01) decrease in LH hormone following the LOD operation compared to before the drilling of PCOS women. As shown in table 1 also a significant (P<0.01) reduction in prolactin hormone following the LOD operation was observed compared to before the drilling of PCOS women. There was a significant (P<0.01) decrease in testosterone hormone following the drilling operation compared to before the drilling of PCOS women. There was a significant (P<0.01) decrease in progesterone hormone following the drilling operation compared to before the drilling of PCOS women.

**Table -1: Hormonal profile before and after drilling of women with PCOS at follicular phase (normal level) and progesterone at luteal phase (day 21)**

| Hormone Profile | Before Drilling | After Drilling | Normal range | P value |
|---|---|---|---|---|
| FSH | 5.552±0.170 | 4.70±0.128 | 3.5-12.4 µIU /ml | P>0.05 |
| LH | 9.587±0.250 | 7.86±0.185 | (2 - 8) µIU /ml | P<0.01 |
| Prolactin | 15.746±1.359 | 13.153±0.952 | 5-35ng/ml | P<0.01 |
| Testosterone | 0.920±0.041 | 0.741±0.029 | 0.1-0.9 ng/ml | P<0.01 |
| Progesterone | 1.659±0.609 | 13.597±0.632 | 1.5-20.0 ng/ml | P<0.01 |

Table -2: revealed that in patients undergo LOD the pregnancy rate (PR) after natural intercourse was 20% (5 out of 25) and the PR following IUI was 8% (2out of 8) with no significant differences between the type of insemination even the PR in natural intercourse was higher.

**Table 2: Result of pregnancy following IUI and natural intercourse after drilling of PCOS women**

| Type of insemination | Number of pregnant women | Pregnancy rate % |
|---|---|---|
| Number of patients | 50 | - |
| Pregnancy natural intercourse | 5/25 | 20.0 |
| pregnancy after IUI | 2/25 | 8.0 |
| Total | 7/50 | 14.0 |

***P>0.05***

## DISCUSSION

In the present study, laparoscopic ovarian drilling (LOD) has been used to induce ovulation in women with PCOS. It also corrects the endocrine abnormalities associated with the syndrome. The study found immediate endocrine responses to LOD which were similar to those founded by previous study, indicating that the effects are similar.[18] Before drilling, the reproductive hormones were negatively effects the status of PCOS spouses leading to anovulatory infertility .It has been found that LH and prolactin levels were significantly higher in PCOS patients (Rotterdam ESHRE/ASRMSresponsored, 2004). After LOD, the main hormonal changes noticed through rapid and persistent fall of testosterone during the first menstruation[19-20] with a transient decrease of gonadotrophins (LH and FSH). The serum concentrations of LH and T in women who underwent LOD were significantly lowered compared to before drilling. This study confirm the previously reports of endocrine changes that occurs shortly after LOD, including lowering of the LH: FSH ratio and the serum concentrations of LH and androgens.[21-23] However the decrease in prolactine hormone reported in this work was controversial to the study of[12] who recorded anhyperprolactinemia following LOD. Although, it has been shown that serum testosterone concentrations decreased after LOD and remained low for up to 6 years[24], this study cannot confirm these long-term endocrine changes produced by ovarian drilling because of the short- term period of the study which was approximately for one year. The mechanism of positive effects of LOD on reproductive hormones is assumed that LOD reduces an “inhibitor” in the PCOS and it starts the recruitment of cohort follicles. One of them separates from the rest as a leader and

this induces ovulation. In this study, the values of FSH levels in serum after the laparoscopic drilling had less dramatic changes, even slightly decreased values. This shows that FSH is responsible for recruitment of follicles for the next maturation. Based on given results, where the LH serum levels were decreased and levels of FSH remained unchanged or even slightly decreased, the ratio of LH/FSH became decreased. This finding may be resulted from the effect of LOD that done on PCO causes functional changes in deeper structures of ovarian cortex, probably by decreasing the inhibin hormone in them. It is considered that the decreased level of LH lessens stromal androgens production, and together with increased level of hormones which stimulate the follicle, it causes the development of the follicle and induces ovulation. Also, there is an evident connection between androgens and the LH serum levels in hyper-androgenic women. Nevertheless, it is not clear if androgens act directly on thehypothalamic-hipophyseous basis independently from their aromatization in estrogens,therefore they change the response of gonadotrophins in women. Most probably, the relatively high level of LH which stimulates theca interstitial cells to the secretion of androgens, and relatively low level of FSH which does not induce successful aromatization, can lead to greater production of androgens and lesser production of estrogens. There was a negative influence on the development of follicles because of the defect in aromatization. This initially starts the atresia of follicles, which results in greater production of androgen, and this produces even stronger and wider atresia in the ovary, where the production of androgen is more dominant than the production of estrogen. This results found that the patients with PCOS had high levels of testosterone in serum before LOD, and those values had decreased to normal levels after the treatment. It is assumed that the increased intraovarian production of androgens of polycystic ovary increases the level of androgens in plasma. That leads to different ratios of LH/FSH. Greater concentration plasma androgens inhibits the gonadotrophin secretion, which shows that androgens affect centers in the hypothalamus. The advantage of LOD can be summarized that after the spouse have had laparoscopic ovarian drilling, she will likely go home the same day, and can resume her regular activities within one day. The risks from this procedure include infections from the incision, bleeding from the incision, pain after the procedure, problems caused by anesthesia, adhesions or scarring inside the body or internal bleeding, although serious complications are rare.[25] If have explored many other options for PCOS, with little or no success, the ovarian drilling may be a treatment for giving a cumulative conception rate of 54% 12 months after surgery.[26] In another study, they found that pregnancy rate in the laparoscopic group was 45% during three months after ovarian drilling.[27]

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