CLINICAL OUTCOME AND HORMONE PROFILES BEFORE AND AFTER LAPAROSCOPIC ELECTROINCISION OF THE OVARIES IN WOMEN WITH POLYCYSTIC OVARY SYNDROME

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Abstract

The aim of study was to evaluate clinical outcome and hormone profiles of laparoscopic electroincision of the ovaries in women with polycystic ovary syndrome (PCOS) before and after treatment. Forty five clomiphene-citrate resistant women with polycystic ovary syndrome underwent laparoscopic electroincision of the ovaries. Serum levels of follicle stimulating hormone (FSH), luteinizing hormone (LH), testosterone (T), androstenedione, 17 OH progesterone and beta endorphins were recorded before and 24 hours after the treatment. Clinical and reproductive outcome and hormone profiles were analyzed. Patients were observed during 12 months period. Laparoscopic electroincision of the ovaries was successfully performed without complications in all patients. LH/FSH ratio was 1,66 24 hours after treatment. Serum levels of T, androstenedione, 17 OH progesterone, and beta endorphins were significantly reduced 24 hours after laparoscopic electroincision of the ovaries. In follow-up period 87% of patients were recorded to have regular menstrual cycles and 61% pregnancy rate was achieved spontaneously. Laparoscopic electroincision of the ovaries is an effective treatment in clomiphene-citrate resistant women with polycystic ovary syndrome. The high pregnancy rate of the procedure offers a promising management for patients with polycystic ovary syndrome.

KEY WORDS: laparoscopic electroincision of ovary, polycystic ovary syndrome, hormone profiles.

Introduction

In 1935, Stein and Leventhal had first described the polycystic ovary as a complex of symptoms related to anovulation. Polycystic ovary syndrome (PCOS) is a result of functional outfall with unspecific central or local defect.

Clinical and biochemical characteristics of PCOS are not consistent, thus ovarian morphology may vary. Nature of this disorder is still unknown. Is it a transitional or permanent state, it is a question which is hard to answer. The most frequent symptoms that occur in women with PCOS are oligomenorrhea, amenorrhea, hirsutism and adiposity. It is the most common endocrine disorder of reproductive-aged women. PCOS is complex and heterogeneous disorder that presents a challenge for clinicians. The optimal therapeutic approach is unknown because the pathophysiological and molecular basis of the PCOS is not fully understood. There are three hypothesis that give an explanation of clinical and laboratory test results in PCOS (1).

1. **LH hypothesis**: Primary neuroendocrine disorder causes too many pulsation of LH in frequency and amplitude, which results in ovarian hyperandrogenism and anovulation.
2. **Insulin hypothesis**: A single defect in insuline action causes hyperinsulinemia, which results in increased androgen secretion and anovulation.
3. **Ovarian hypothesis**: Primary defect is in the synthesis or the metabolism of sexual steroids, which results in overly increased ovarian androgen secretion and anovulation.

There is a hypothesis that PCOS has a genetic basis, which has not been confirmed yet. Some authors claim that the dominant transmission is related to X- chromosome, while others suggest that PCOS has a more complex hereditary scheme than autosomal dominant, probably connected to X- chromosome, and that polygenic and environmental factors can have significant role (2). In some families there are repeated PCOS cases, which suggests the genetic component of this syndrome. Treatment strategies focus, in PCOS patients, on the reduction of clinical manifestation of hyperandrogenism, restoration of regular menses and achieving pregnancy.

Treatment of hirsutism includes androgen suppressor and peripheral androgen blockers. Combined oral contraceptive pills are the most commonly used androgen suppressor and the treatment of choice for menstrual dysfunction for those who do not desire pregnancy. The first-line treatment for infertility in PCOS is clomiphene citrate. Ovulation induction with gonadotrophins is the standard treatment strategy for women with clomiphen citrate-resistant PCOS. Laparoscopic electrocautery of the ovaries is an alternative treatment modality, leading to a comparable cumulative pregnancy rate (3). Laparoscopic ovarian drilling is an effective treatment in clomiphen citrate-resistant women with PCOS. Androgen levels and luteinizing hormone concentrations showed a statistically significant decrease after the treatment, and improving their clinical and reproductive outcome (4). Laparoscopic ovarian cauterisation increases ovarian sensitivity for gonadotrophine by causing considerable increase in ovulation percentage and pregnancies, with decreased dose of human menopausal gonadotrophine(5). Furthermore, laparoscopic electroincision performed in Gynecology and Obstetrics Hospital in Sarajevo has proved to be an efficient method for inducing spontaneous ovulations in clomiphene citrate resistant patients.

Material and Methods

45 patients underwent this study in the Gynecology and Obstetrics Hospital in Sarajevo in the past 3 years and had been treated for sterility in which both the clinical and laboratory tests results indicated to PCOS. The patients have had a menstrual cycle disorder (oligomenorrhea, amenorrhea secundaria), meaning the cycles were anovulatory and they had visible hirsutism, while some of the patients had serious adiposity. Ultrasound findings were characteristic for polycystic ovaries. Laboratory test results of hormonal status before laparoscopy have showed increased LH/FSH ratio which was higher than 2. There was also an increase in testosterone, androstenedione and 17OH progesterone serum levels. All patients had been previously treated with clomiphene citrate, and the treatment was unsuccessful as they were clomiphene citrate resistant.

The patient age group was between 21 and 36.

The day before laparoscopic electroincision the levels of LH, FSH, testosterone, androstenedione, 17 OH progesterone and beta endorphin had been determined. We performed laparoscopic electroincision of the ovaries with characteristics of PCOS (figure 1). The cut on each ovary was 2,5 - 3 cm in length and 4-5 mm deep (Figure 2). The patients had normal findings of uterine tubes and the uterus. We determined the level of hormones in serum 24 hours after the treatment by performing a classic radioimmunollogy method.

FIGURE 1. Laparoscopy demonstrates the ovaries in women with polycystic ovary syndrome

FIGURE 2. Laparoscopic electroincision of ovary

Statistical analysis

Values of serum hormonal levels before and after the laparoscopic electroincision were set in a table and statistically tested by the method of T test. For each group of values of hormone levels, there was an average value (x), a variable and a standard deviation (SD), and there were common values for standard deviation and variable. Value T was determined by putting the SD and the variable together. The level of significance P is calculated from the calculated T in the tables. If P>0,05 than there is no significant difference, but if P<0,05, than there is a significant difference between the values of hormone levels before and after the treatment.

Results

Laparoscopic electroincision has been completed in all patients without any complications. Analyzing the values of hormones we confirmed that there was a significant difference of values before and after the treatment (table). The average value of LH levels in treated patients was 16,35 IU/L (SD=10,32) before the treatment, and 9,26 IU/L (SD=5,95) 24 hours after the treatment. The difference between levels of LH in serum before and 24 hours after the treatment is significant (P<0,05). The average value of FSH levels in all treated patients was 5,46 IU/L (SD=2,55) before the treatment, and 5,55 IU/L (SD=3,23) 24 hours after the treatment. The difference between levels of FSH in serum before and 24 hours after the treatment is not significant (P>0,05). The ratio of average values of LH/FSH serum level before the intervention was 2,99 and 24 hours after the treatment it had decreased to 1,66. The average value of testosterone levels in treated patients was 5,0 nmol/L (SD=1,66) before the treatmant, and 3,05 nmol/L (SD=1,09) 24 hours after the treatment. The difference between levels of testosterone in serum before and 24 hours after the treatment is significant (P<0,05). The average value of androstenedione level in treated patients was 18,73 nmol/L (SD=7,5) before the treatment, and 11,51 nmol/L (SD=6,77) 24 hours after the treatment. The difference between levels of androstenedione in serum before and 24 hours after the treatment is significant. The average value of 17OH progesterone levels in treated patients was 7,52 nmol/L (SD=2,05) before the treatment, and 5,79 nmol/L (SD=2,5) 24 hours after the treatment. The difference between levels of 17OH progesterone in serum before and 24 hours after the treatment is significant (P<0,05). The average value of beta endorphin levels in treated patients was 20,34 pg/ml (SD=11,88) before the treatment, and 12,49 pg/ml (SD=4,08) 24 hours after the treatment. The difference between levels of beta endorphin in serum before and 24 hours after the treatment is significant (P<0,05). In the month following the laparoscopic electroincision,

Table Hormones level and beta endorphin average values before and after electroincision polycystic ovaries

	Before electroincision ovaries	24h after electroincision ovaries	
LH (IU/L)	16,35 (SD=10,32)	9,26 (SD=5,95)	P<0,05
FSH(IU/L)	5,46 (SD=2,55)	5,55 (SD=3,23)	P>0,05
T(nmol/L)	5,0 (SD=1,66)	3,05 (SD=1,09)	P<0,05
Androstenedion (nmol/L)	18,73 (SD=7,5)	3,05 (SD=1,09)	P<0,05
17OH progesteron (nmol/L)	7,52 (SD=2,05)	5,79 (SD=2,5)	P<0,05
Beta endorphin pg/ml	20,34 (SD=11,88)	12,49 (SD=4,08)	P<0,05

P< 0,05 - significant difference
P> 0,05 - non-significant difference

40 patients (87,5%) had their menses and their cycle have become regular and ovulatory, which we have confirmed by measuring the basal temperature and following the development of follicles with ultrasound. In the following period of 6 months 28 patients (61%) achieved pregnancy.

Discussion

Therapy of PCOS aimed at causing ovulation, reduction of clinical manifestation of hyperandrogenism, restoration of regular menstrual cycle and achieving pregnancy. By applying our method of therapy, the laparoscopic electroincision of polycystic ovary, and analyzing the hormonal changes, the clinical and reproductive outcome after the treatment, we achieved the results similar to those of many different authors. The decrease of LH in serum levels to normal levels after the treatment applying the laparoscopic ovarian drilling has become confirmed by other authors (4,6,7). It is assumed that the laparoscopic electroincision reduces an "inhibitor" in the polycystic ovary and it starts the recruitment of cohort follicles. One of them separates from the rest as a leader and this induces ovulation. Values of FSH levels 24 hours after the treatment were slightly increased, but that was not significant. Other authors have also reported that the values of FSH levels in serum after the laparoscopic cauterisation had less dramatic changes, even slightly increased values. Al-Ojami reports that the levels of FSH in serum after the laparoscopic ovarian drilling were significantly increased. This shows that FSH is responsible for recruitment of follicles for the next maturation (8). Based on given results, where the LH serum levels were decreased and levels of FSH remained unchanged or even slightly increased, the ratio of LH/FSH became decreased. We can conclude: what is the leading force for the regulation and development of follicles that leads to ovulation. It is assumed that the laparoscopic electroincision of polycystic ovaries causes functional changes in deeper structures of ovarian cortex, probably by decreasing the inhibin 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 the hypothalamic-hipophyseous basis independently from their aromatization in estrogens, so that they change the response of gonadotrophins in women. Most probably, the relatively high level of LH which stimulates theca insterstitial 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 is a negative influence on the development of follicles because of the defect in aromatization. This initially starts the atresion of follicles, which results in greater production of androgen, and this produces even stronger and wider atresion in the ovary, where the production of androgen is more dominant than the production of estrogen. Our results clearly suggest that the patients with PCOS had very high levels of androgens in serum before the laparoscopic electroincision, and that those values had decreased to normal levels after the treatment. Although the problem in the polycystic ovary syndrome is in the aromatization of androgens, there is probably a factor, which "allows" the androgenes to pass into the circulation, even though their level is lower than in the mature follicle. In mature follicle, there are probably some "carriers" androgens that do not allow their movement to the periphery. Our study showed significant decrease of testosterone, androstenedione and 17OH progesterone levels 24 hours after the laparoscopic electroincision. Androgen levels showed a statistically significant decrease after laparoscopic ovarian drilling (4,6,7). Testosterone and free androgen index decreased significantly after laparoscopic ovarian drilling and remain low during the medium and long-term follow-up periods (9). Testosterone serum levels showed a statistically significant reduction after laparoscopic ovarian drilling (10). The decrease of the level of androgens is very rapid after the laparoscopic electroincision and it occurs before the decrease of other hormones. Mechanism responsible for inducing the development of follicles after the laparoscopic electroincision is probably intraovarian and in some way connected to the levels of androgenes (testosterone and androstenedione). What is factor which, by decreasing the level of androgens, activates the correct development of follicles and re-establishes normal ratio of levels of gonadotrophins and estrogen in the circulation? We can assume that by electroincision of the polycystic ovary we reduce the increased level of inhibin. In the atretic follicle, the androstenedione mostly turns into testosterone, and testosterone turns into dihidrotestosterone. It is thought that if there is an atresion and an increase of androgens it affects the concentration of androgens in plasma. 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 of

plasma androgens inhibits the gonadotrophin secretion, which shows that androgens affect centers in the hypothalamus. What is the role of beta endorphin and how it effects the central neural system and the periphery is not completely clear yet. Our results show that levels of beta endorphin in serum of our patients were within the normal range, but 24 hours after the treatment there has been a significant decrease of these values. Pituitary secretion of immunoreactive beta endorphin is normal in patients with polycystic ovary syndrome (11). A weak association was found between beta endorphin and luteinizing hormone in peripheral plasma, but plasma beta endorphin concentrations correlate more with body mass index in patients with polycystic ovary syndrome (12). After laparoscopic electroincision the ovaries in patients with PCOS in 87,5% cases there ware a re-establishment of ovulatory cycle and 61% achieved pregnancy. Rate of ovulation was 83,5% and pregnancy rate was 59,8% in patient with laparoscopic ovarian drilling (13). Cleemen showed that pregnancy rate was 61% among women with PCOS who had laparoscopic ovarian drilling (14). We consider that in those patients who had laparoscopic electroincision of the ovaries that did not induce ovulation, there has been a developed disease PCOS, in those ovaries there is a very small healthy "potential" needed for the normal development of follicles. Laparoscopic electroincision of ovary is effective during the induction of ovulation and increases the pregnancy rate in cases of polycystic ovary syndrome resistant to clomiphene citrate.

Conclusion

Laparoscopic electroincision of the ovaries is an effective treatment in clomifen-citrate resistant women with polycystic ovary syndrome. With this therapeutic method we succeeded to restore normal ovulatory cycles in 87% patients and 61% achieved pregnancy.

It could be concluded from the above mentioned that with laparoscopic electroincision of the ovaries menstrual cycle can be restored in many patients with polycystic ovaries syndrome. The high pregnancy rate of the procedure offers a promising management for patients with polycystic ovary syndrome, and that this procedure can be accepted as method of choice.

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