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DEFINITION OF EFFICIENCY OF DIFFERENT APPROACHES IN TREATMENT OF INFERTILITY FOR PATIENTS WITH POLYCYSTIC OVARY SYNDROME AND HYPERPROLACTINEMIA

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Abstract. Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women. The clinical manifestation of PCOS varies from a mild menstrual disorder to severe disturbance of reproductive and metabolic functions with severe long-term health consequences. High-frequency of endocrine-metabolic disorder's and anovulatory infertility and also frequent absence of effect from the use of traditional charts of medicament induction of ovulation resulted in the search of alternative ways of proceeding in fecundity. The aim of this study was to evaluate the clinical efficiency of different treatments cancellation and infertility in women with PCOS and hyperprolactinemia. **Materials and methods.** We performed retrospective analysis of 502 consecutive case histories during 5 years of reproductive results of treatment of women is with anovulatory infertility, caused by different factors. Aim of the study was to determine the efficiency of conservative and surgical treatment. **Results.** Differentiated application of conservative medical therapy allows to attain the effect of proceeding in a fertile function in 33, 8% of patients. It is found that surgical induction of ovulation by ovarian laparoscopic partial degradation is an option in the management of female infertility associated with PCOS, especially as a second-line treatment after the failure of

clomiphene citrate treatment, enhancing the efficiency of complex infertility treatment to 40%. It is feasible to develop an algorithm differentiated use of infertility treatments in women with PCOS and hyperprolactinemia.

Keywords: Polycystic ovary syndrome (PCOS); reproductive health; hyperandrogenism; infertility; hyperprolactinemia; hirsutism; menstruation disorders.

Introduction. Demographic potential of Ukrainian population is burdened with considerable extension of female infertility [1]. According to local scientists fertility rate in excess of 10% can be considered as direct reproductive losses that significantly impair the demographic situation of the country. Many of Ukrainian females have anovulatory infertility. It has a tendency to spread in the population, with involvement in the pathogenesis of disorders of ovulation excess synthesis of androgens and prolactin.

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women. The clinical manifestation of PCOS varies from a mild menstrual disorder to severe disturbance of reproductive and metabolic functions [3-5]. Significant progress achieved domestic and foreign scholars and the development of surgical induction of ovulation in PCOS [6, 7].

However, the results of treatment of anovulatory infertility associated with PCOS, indicating that the disease is distinguished not only clinical polymorphism, but also has several pathogenic variants. It is possible that this group of patients, along with there are other endocrine disorders that also affect metabolic processes. Thus, the high incidence of hyperprolactinaemia was found among patients with PCOS deepens dysmetabolic changes in the patient, involving additional mechanisms in the pathogenesis of blocking ovulation [8-10]. This can be explained as the influence of prolactin receptors on ovarian stimulation and compression as β- cells of the pancreas, leading to the development of insulin resistance. So important is the optimization approaches to the treatment of patients with PCOS with regard to the likely role of

hyperprolactinemia. However, to date research on the comparative evaluation of clinical effectiveness (efficiency) of different methods of multivariate stimulate ovulation in anovulatory infertility, occur less frequently.

The aim was to evaluate the clinical efficiency of different treatments cancellation and infertility in women with PCOS and hyperprolactinemia.

Materials and methods. The survey was conducted at the department of invasive methods and diagnostics of university clinic of Odessa National Medical University (Odessa) and multi-field medical center" Avicenna "(Melitopol). The conducted retrospective analysis of reproductive results of treatment of women is with multivariable anovulatory infertility. Retrospective search depth was 5 years. A total analysis includes 502 case histories

During the study of data of medical documentation we paid attention to the next features. PCOS Diagnosed in agreement with criteria of Rotterdam consensus sponsored in part by the European Society for Human Reproduction and Embryology and the American Society for Reproductive Medicine (2003), based on the presence of chronic oligo- or anovulation, clinical and/or biochemical signs of hyperandrogenism, or polycystic ovaries on ultrasound examination [11]. Patients with hyperprolactinemia were conducted double determination of prolactin in serum by enzyme-linked immunosorbent assay (ELISA)to exclude tumours and pituitary hypothalamic syndromes X-ray and/or MRI of the brain were performed.

In the course of further analysis on the retrospective phase of the study were identified six groups of patients, depending on the efficiency of conservative or used surgical treatments.

The first group consisted of 21 (10.7 %) women with an initial phase of the hypothalamic-pituitary dysfunction with menstrual disorders and genital infantilism, which became pregnant due to the correction of hormonal relations by therapy on the type of rebound - effect.

Another group included 27 (13.8 %) women with PCOS who become pregnant during treatment with standard ovulation stimulation by the medications include clomiphene citrate (a selective estrogen receptor modulator). One woman had born twins, however one patient (twice) had ectopic pregnancy.

The third group involved of 23 (11.7 %) women with PCOS and adrenal hyperandrogenism, without severe symptoms of hyperprolactinemia who became pregnant by the treatment of derivatives of the corticosteroid hormones cortisol and aldosterone that are produced naturally by the adrenal glands (Dexamethasone). All pregnancies resulted in deliveries in time without conclusions.

The fourth group was composed of 25 (12.8%) patients with PCOS in combination with adrenal hyperandrogenism and symptoms of hyperprolactinemia. They were treated with Dexamethasone and a dopamine agonist ergoline derivative - Bromocriptine, is an in communicating from a minimum dose to maximal or effective (optimize). In all cases, the patient became pregnant within six months of beginning treatment after the renewal of ovulation.

The fifth group contained of 18 (9.2%) women who became pregnant in the ordinary cycle after surgical induction of ovulation by laparoscopic partial ovarian destruction (that was directed at inefficiency by applications of medicine correction).

Determinations of authenticity of differences between the compared groups or subgroups on frequencies of separate clinical indexes or outputs performed by using χ^2 test with Yates correction given for paired comparisons and Bonferoni correction for multiple comparisons to the control group. Statistical study was performed using the programmatic complex Statistica 10.0 (StatSoft Inc., USA) [12].

The results. From the general amount of patients with anovulatory infertility (502 persons) 196 women are selected with verification of PCOS in combined with symptoms of hyperprolactinemia.

In results of research a variant of multifactor anovulatory sterility of met in 39. 0 % of cases, this version exceed the values led by different studies that have been described by other researchers. In assessing the hormonal profile of patients showed that the levels of prolactin are higher than the reference value and averaged 18.8 ± 1.1 ng / ml (Table 1).

According to the data of table, the results of hormonal profile of inspected women indicate a variability of damages of women with PCOS and hyperprolactinemia, and PCOS and hyperandrogenism. Patients had increased fraction of LH / FSH to 2.1 ± 0.1 by increasing LH content (up to 13.2 ± 0.5 IU / l) and decrease in FSH (to (6.5±0.2) mIU/l), hyperandrogenism - androstenedione level - 4.2±0.2 nmol/l, testosterone -2.8±0.2 nmol/l, DHEA -S - 4.0±0.3 nmol/l), progesterone (8.0 ± 0.5 nmol/l) on a background of moderate hypoestrogenic state (45.0 ± 2.2 pg / ml). Representative for all patients where normal levels of AMH (2.7 ± 0.2 ng / ml), indicating a high ovarian reserve.

Request of surgical induction after the previous course of hormonotherapy in 82 (41.8%) of women with sterility was not effective. These women were guided to assisted reproductive technology clinic.

As established in Table 1 the patients of different groups did not differ on age, middle age in groups had laid down 27.8±0.7. The investigation of complaints of patients found that and menstrual disorders prevailed among other conditions, and infertility duration on the average laid down 5.6±0.4 years. In further study the presence of statistically significant differences by the hirsute number, free testosterone index in patients with III and IV groups. Relatively low levels of prolactin (6.9 ± 0.5 ng/ml) were observed in patients with a preliminary phase of the hypothalamic-pituitary dysfunction.

Table 1

Clinical physiognomies of patients

Indices	I group (n=21)	II group (n=27)	III group (n=23)	IV group (n=25)	V group (n=18)
Age, year	27.0±0.4	30.0±0.5	30.1±0.4	26.2±0.3	30.0±0.4
BMI, kg/m²	22.3±0.4	24.9±0.4	24.6±0.3	20.3±0.4	22.3±0.4
Hirsute number, scores	6.9±0.1	8.7±0.4	9.9±0.2*	7.3±0.2	8.9±0.1*
FSH, mIU/l	9.8±1.5	4.2±0.2	7.1±0.4	11.3±0.3	9.8±1.5
LH, mIU/l	11.8±1.3	12.1±0.3	10.0±0.6	14.0±0.4	14.8±1.3
LH/FSH	1.2±0.3	3.3±0.5	1.7±0.2	1.4±0.1	1.2±0.3
Estradiol, pmol/l	68.2±5.6	45.0±2.2	50.1±7.0	57.9±4.5	68.2±5.6
Progesterone, nmol/l	1.6±0.1	1.2±0.2	2.0±0.2	1.9±0.2	1.6±0.1
17-OH progesterone, nmol/l	1.2±0.2	0.8±0.5	1.9±0.2	1.1±0.1	1.2±0.2
DHEAS, mcmol/l	3.4±0.3	4.0±0.3	4.9±0.2	4.8±0.3	4.4±0.3
Prolactin, ng/ml	6.9±0.5	11.3±0.4	16.4±0.5	34.2±1.2 *	16.9±0.5
TTH, mMI/l	1.8±0.2	1.9±0.2	2.6±0.2*	1.5±0.3	2.8±0.2*
T4, pmol/l	4.2±0.2	4.0±0.3	4.4±0.3	4.3±0.2	4.2±0.2
Androstenedione, nmol/l	4.2±0.2	4.0±0.2	4.8±0.4	3.8±0.2	4.2±0.2
AMH, ng/ml	2.7±0.2	3.1±0.3	3.0±0.3	2.4±0.3	2.7±0.2

The highest levels of 17 -OH progesterone (1.9 ± 0.2 nmol/l) were observed in patients of group III. However, the content of DHEAS was highest in patients with III and IV groups (up to 4.9 ± 0.2 mmol / l).

Therefore, differentiated pathogenic treatment of multivariable anovulatory infertility with application of antiandrogenic therapy by Dexamethasone for adrenal genesis hyperandrogenism and Bromocriptine at hyperprolactinemia of non-cancerous growth genesis proceeds in the broken mechanisms of ovulation promotes efficiency of application of Clomiphene and leads to pregnancy in 33.8% of patients.

Our results are higher on efficiency, which over of other scientists in the undifferentiated treatment of anovulatory infertility, which testifies to the efficiency of the applied drug schemes.

With the uselessness of this treatment tactics and preservation of polycystic ovaries we recommend a surgical induction of ovulation by laparoscopic partial ovarian destruction, because such method improves the efficiency of complex infertility treatment to 40%.

Conclusions.

1. Multifactorial infertility as a combination of hyperprolactinemia and PCOS occurs in every third women with impaired fertility function.
2. Differentiated application of conservative medical therapy allows to attain the effect of proceeding in a fertile function in 33, 8% of patients.
3. It is concluded that surgical induction of ovulation by ovarian laparoscopic partial degradation is an option in the management of female infertility associated with PCOS, especially as a second-line treatment after the failure of clomiphene citrate treatment, enhancing the efficiency of complex infertility treatment to 40%.
4. It is feasible to develop an algorithm differentiated use of infertility treatments in women with PCOS and hyperprolactinemia.

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