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ORIGINAL STUDY

TREATMENT OF POLYCYSTIC OVARY SINDROME RETROSPECTIVE STUDY 2004-2010

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ABSTRACT

The aim of the study is the investigation done in the 95 cases of polycystic ovary syndrome, the diagnosis, therapy and posttherapy results. Polycystic ovary syndrome is one of the most frequent endocrine conditions, its frequency is estimated between 1,5 and 20% (the average is 5-8%) in the fertile female population. Polycystic ovary syndrome has a wide etilogical spectrum and multiple clinical symptoms and it is considered an exclusion diagnosis. The importance of polycystic ovary syndrome in the medical practice resultes from the fact that is the most common cause of hirsutism and clinical elements of androgenism and the first cause of infertility thru anovulation and with metabolic consequences (insuline resistance, obesity, lipid profile disorder, second degree diabetes with serious cordio – vascular implications). The study follows the clinical features of the group of patients. The analyzed group consists of 95 patients, studied according to the pathological mechanism, the identification of long-term risk factors, the diagnosis and therapy accurracy. The numerous treatment options must be individualized in relation with patients characteristics. Menstrual cycle regulations thru: usage of oral contraceptives in 54 cases; Ciproteron Acetate in 3 cases; Methformin in 11 cases. Four patients have undergone surgical treatment. The ovulation was stimulated in 10 cases by administrating Clomifen. Using diferent schemes of treatment led to pregnancy in 12 cases, which represents 12,63% of total studied cases. The patients were prescribed treatment according to their options: menstrual cycle regulations; pregnancy. The numerous therapeutical options must be individualised in relation with patients characteristics and preferences.

KEYWORDS*: POS, secondary amenorheea, obesity, methformin*

1. Introduction

Polycystic ovary syndrome is a heterogeneous disorder freaquently characterized by a spectrum of anatomic and hormonal elements which vary in point of intensity and implication [1]. Being of uncertain etiology, it may include genetic aspects, environmental factors, reducing activity process and even hypercaloric diets. The diagnosis criteria are [2,3]

- oligoovulation or anovulation
- clinical or biochimical hyperandrogenism on a long term
-polycystic ultrasound aspect

The signs and symptoms may vary from one patient to another over the years. As a result, women with Polycystical ovary syndrome may address to many medical field like: gynecology, internal medcine, endocrinology or dermatology [4]. The particular secretion of gonadotropins: high LH (Luteinizing Hormone) and low FSH (Follicule Stimulating Hormone) are due to the increased GnRH(Gonadotropin Realising Hormone) pulsation freaquency. The increase of GnRH pulsations may be assigned to the opioide hypothalamic inhibition through the chronic lack of progesterone. The increase of GnRH pulsations generates raise in amplitude and LH secretion frequency, in connection with the high levels of estrogens. [5, 6].

2. Material and methods

This study analyses 95 patients diagnosed with Polycystic ovary syndrome in the Ambulatory of the Obstetrics- Gynecology Hospial Galati.

The group of 95 patients was selected from 4833 patients who came to „Buna Vestire" Hospital Galati.

The analysed patients come from: Urban 68, Rural 26

The analysed patients are assigned on age groups:(figure 1, table I)

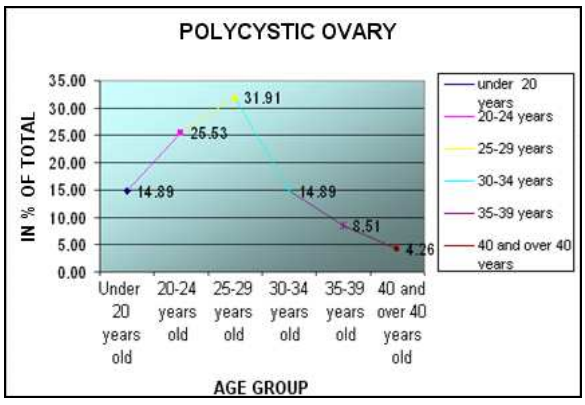

Figure 1. *Polycystic ovary*

Table I. *Polycystic ovary*

Under 20 years old	20-24 years old	25-29 years old	30-34 years old	35-39 years old	40 and over 40 years old
14,89%	25,53 %	31,91%	14, 89%	8,51%	4,26%

Polycystic ovary syndrome (PCOS), being heterogenous, presents different clinical snd biological symptom combinations (7). Many of these symptoms occur immediately after menstruation.(8) At menopause many of them improve.

The group of 95 patients presnted:

- irregular menstruation- 86 cases/ (76,7%)
- infertility- 74 cases/ (66%)
-hirsutism- 25 cases/ (22,3%)
- hyperandrogenism- 20 cases/ (17,8%)
- obesity - 20 cases/ (17,8%)
- acne, seborrhea- 36 cases/ (32,1%)

Chronic amenorrhea, oligoamenorrhea and prologed bleeding are specific to this disease. Menstruation that lasts more than 35 days is anovulatory in 50-90% of cases. Women with PCOS frequently suffer from hirsutism, acne and seborrhea. In the diagram below are repersented the FSH and LH value frequency for the patients with amenorrhea.(figures 2, 3) The values are assigned almost normal for these two hormones with a small deviation towards the low values.

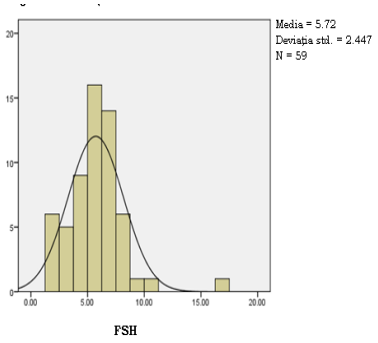

Figure 2. *FSH value frequency*

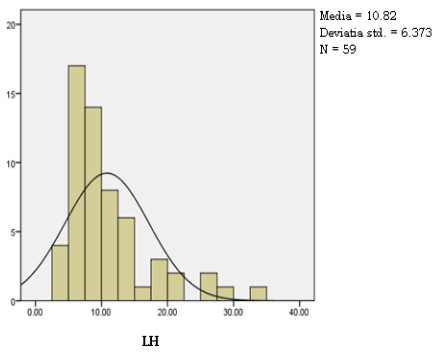

Figure 3. *LH value frequency*

Comparing the insulin, LH and FSH level, the LH/ FSH report and BMI (obesity) in case of women with normal or high level of gonadotropins is shown in the table below.(table II)

Table II. *LH/FSH report*

Parameter	PCOS with LH/FSH>2	PCOS with LH/FSH<2
LHmU/ml	13,7	10,1
LH/FSH	24	45
BMI (obesity)	25,8	19,7

Determining LH/FSH abnormal report in case of women with PCOS still remains an important problem.

Table III. *LH/FSH report*

Parameter	PCOS with LH/FSH>2	PCOS with LH/FSH<2
Obesity	9	27
Testosterone	11	53
LHmU/ml	13,7	10,1
FSH	4,9	4,4
LH/FSH	24	45

In this study 45 cases were diagnosed with hyperandrogenism. Insulin resitance is associate with androgenic (abdominal) type of obesity. [7-9]. Most of the patients with high cholesterol levels have BMI>25. In the late 1980s the LH/FSH report was considered a real standard for the PCOS diagnosis. In this study the high report of the gonadotropins was found in 47,87% of the patients. The level of the free testosterone is not related to the LH and insulin value.(table III)

Insulin resistance

Blood sugar level that was determined to the group of 95 patients showed the following values.(10)

-71 patients with normal blood sugar, representing 75,53%

-23 patients with high blood sugar, representing 24, 46%

The frequency blood sugar levels shows that this factor is assigned almost following the normal law, around the average of 92,04% and with a standard error of 10, 171.(figure 4)

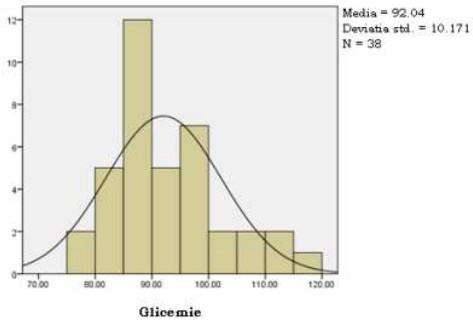

Figure 4. *Blood sugar frequency*

Blood sugar level was dermined and in case of 23 patients who had the value between 105-120 mg/ml, the oral Glucose Tolerance Test (TTGO) was performed. Insulin resistance was associated with obesity.(table IV)

The tables below show the frequency of TTGO:

Table IV. *TTTGO*

TTGO			
	Frequency	**Percent**	**Total percent**
YES	23	20,5%	20,5%
NO	89	79,5%	100%
TOTAL	112	100%	

Patients with PCOS were investigate for dyslipidemia to measure the total cholesterol (LDL, HDL), triglycerides. (table V) Gynecological

ultrasonography is the real standard in the morphological diagnosis of polycystic ovary (figures 5).

Table V. *Obesity*

Obesity			
	Frequency	**Percent**	**Total percent**
YES	89	79,5%	79,5%
NO	23	20,5%	100%
TOTAL	112	100%	

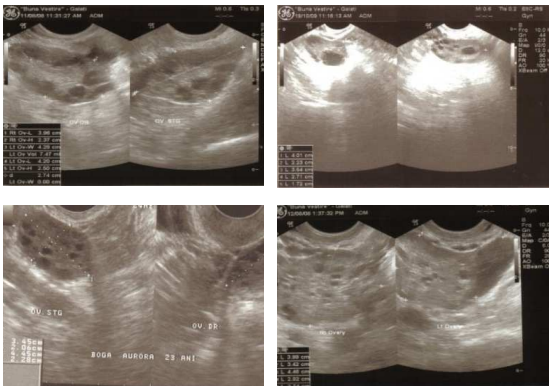

Figure 5. *Polycystic ovary*

Herapy aims are focused on two aspects: symptoms improving: irregular menstruation, acne and hirsutism, and preventing or minimizing long-term complications which may occur, HTA, diabetes, hyperlipemia, cardio-vascular complications.[10-12]

As the polycystic ovary disease is physiological by nature, the treatment must be applied for a long-term (table VI). The patients have been informed and advised on the importance of a close follow-up. The first measures to be taken are diet and hygene. These measures are considered important for overweight female patients as it may cause a decrease in insulin resistance. The study on the alotted group proved that 23 female patients(8%) had obesity problems [13,14]. These patients have been monitored in order to reduce the calory ratio by decreasing the lipid uptake followed by an increase in fiber uptake [15,16]. The demonstrated effects are a decrease in hyper insulinism and hyper androgenism. [17-19]. Another suggested method was that of increasing the physical activity which leads to an improvement in the peripherical use of glucose and also in insulin resistance.

3. Results and discussions

A female patient lost 17 kg after the diet and hygene treatment had been applied while also increasing her physical activity. This led to resuming both menstrual cycles and ovulation. The pregnancy climaxed into a 37 week vaginal delivery.

The treatment of hyperandrogeny symptoms

This treatment must associate both mechanical means and hormonal treatments. Out of the total number of patients diagnosed with polycystic ovary disease, the following showed symptoms of hyper androgeny:

- hirsutism 27 (9%)
- acne 37 (12%)
- seborrhea 38 (13%)

The mechanical means such as electric epilation were used with 10 of the patients. Mijloacele mecanice cum ar fi: epilarea electrică au fost folosite la 10 dintre paciente. If physical and paraclinical tests led to the diagnosis of POS, the selected treatment implies the interruption of hypothalamic-hypophysis axis by an estro-progestative relation. In addition, an increase in SHNG may be observed which may lead to a decrease in free testosterone or the active form of androgens.

Diane 35 represents the selective treatment for women with POS and acne. The effects of oral drospinerone contraceptives were fast: the improvement in clinical hyperandrogenism symptoms have also been demonstrated by the development of biochemical markers: the value of of total plasmatic testosterone dropped significantly. Reevaluation by

means of an ecograph proved a decrease in size and improvement in nature in 50% of all cases.

54 patients have been treated, this representing 57,45%. The treatment has been well tolerated, side effects being rare: mastodynias, cephapalgia and mood disorder that dissipated after the first three stages of treatment.

It was noticed a slight tendency to gain weight, caused especially by food irregularities.

A number of 5 cases representing 5,31% have been treated with cyproteron acetate , an anti androgene and also an effective progestative in the treatment of hirsutism cases. Clinically, it is used periodically alongside ethinylestradiol in order to prevent dismenorrhea when the administration of cyproterone is stopped. Oral contraceptives are usually associated with this treatment.

The treated patients did not want to get pregnant. All treated patients improved their menstrual cycles that become regular.

The treatment of progestative deficiency applied to 10 patients consisted of Duphastone 20 mg beginning from the sixteenth day of the menstrual cycle until the twenty fifth in association with clomiphene citrate, maximum dosage of 150mg per day from the third day of the menstrual cycle until the seventh.

Improving luteal deficiency

The chronic anovulation leads to superfluous secretion of estrogens devoided of luteal phase. When estrogen secretion is not counterbalanced by a progesteron secretion, there is the risk of endometrial hyperplasia and thus endometrial cancer.

A number of 15 cases, that is 15,95% of oligomenorrhea without hyperandrogeny have been treated for 10 days a month with a derivate of natural progesterone. Duphastone 20 mg form the sixteenth day of the menstrual cycle up to the twenty fifth. The level of progesterone has been determined with these patients since the twenty first or twenty second day of the menstrual cycle.

Clomiphene citrate represents the first choice in treating BOP. These are tablets of 50 mg.(20). It functions as an estrogen at the level of hypothalamus and hypophysis and may induce the secretion of FSH. This increase in the estrogen level allows for the recruitement of a high number of folicules. The therapeutic schemata resides in administering 50-100mg a day for 5 days; from th third day of the menstrual cycle up to the seventh.

An ultrasound monitoring is required beginning with the tenth and the twelfth day of the menstrual cycle in order to highlight the folicules. This therapeutic schemata has been used with 10 patients that is 11,11%. The dosage of clomiphene citrate has been adapted to the ovary response, the maximum dosage being of 150mg per day.

After this therapeutic schemata has been applied, 5 pregnancies have been obtained out of which one has stopped developing at 7-8 weeks. A case presented a syndrome of slight ovarian overstimulation that was though spontaneously remitted as the treatment was well tolerated.

The treatment of metabolically dysfunction

The metformin – is an oral antidiabetic pertaining to the class of brigandines; it leads to a decrease in the glucose produced by the liver and also to an improvement of insulin-sensitivity followed by weight loss [21].

Several studies emphasize its effectiveness in resuming ovulation. The positive effect of metformin demonstrates the role of hyperinsulinism over hyperandrogeny in POS [22]. The effectiveness of the metformin treatment resides in inducing ovulation in POS patients imune to clomiphenecitrate treatment. A number of 11 patients, that is, 11,70% have been treated with metformin, the dosage being of 1500mg a day.[23,24]

The treatment of metabolical disfunction

The follow-up treatement with metformin 1500mg per day led to 4 pregnancies.

Surgical treatment

The surgical technique used nowadays is the ovarian drilling [25]. Also called ovarian multiperforation resides in performing 6 up to 12 perforations in the ovarian area by means of either electric or laser power [26,27]

More recently, other laparoscopic techniques have been introduced among which CO2, Argon and ND ZAG laser therapy and also ovarian criotherapy.

Surgical treatement- ovarian drilling has been performed on 4 of the patients representing 4,25%. 2 of the patients got pregnant.The follow-up treatement according to patients’ options implied 12 pregnancies (12,632%), out of the total of 95 patients.

Table VI. *Treatment schemata suggested for POS:*

	Anovulation Infertility	Hirsutism (Alopecia)	Menstrual imbalance	Obesity
Change in lifestyle				
Obesity surgery				
Metformin				
Tiazolidine				
Surgical treatment				
Analogous to GnRH				
C O				
Dexametazone steroids				
Progestative				
Statine				
Letrozol				
Clomiphene				
Gonadothropine				
IUD				
Uterine surgery				
Eflornithine HCL cream				
Spironolactone				
Flutamid				
Finasteride				
Mechanical/ Laser therapy				

4. Conclusions

54 patients with oligo amenorrhea have been treated with oral contraceptives. Cyprotherone acetate has been used in the treatement of 3 cases. The treatement with metformin has been used with 11 patients.The clomiphene stimulation of the ovulation has been used with 10 patients. Surgical treatement, ovarian drilling has been used with 4 patients. BOP determines important clinical consequences: irregularities of the menstrual cycle up to amenorrhea, infertility, diabetes, hirsutism, endometrial cancer and cardiovascular disease. Anamnesis, physical examination and hormonal dosage allow for a diagnosis and ethiopathogenic treatment. Several therapeutic options must be personalized according to the preferences and peculiarities of the patients.

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