THE EFFECT OF LOW-CARBOHYDRATE DIET ON GROWTH HORMONE SECRETION AND VISCERAL FAT IN METABOLIC SYNDROME
Center of Diabetes, Endocrine and Metabolism, Sakura Hospital, Toho University Medical Center, Chiba, Japan

Objective: We have reported that low-carbohydrate in low-calorie diets induced visceral fat reduction accompanied with improvement in glucose and lipid metabolism in type 2 diabetes with obesity, and that growth hormone (GH) has a potent lipolytic effect on triglycerides in visceral adipose tissue. The aim of this study was to investigate the effect of low-carbohydrate diet on GH secretion, visceral fat and metabolic parameters in the patients with metabolic syndrome (Mets) compared with high-carbohydrate diet.

Methods: Thirty Japanese subjects with Mets were randomly assigned to take a low-carbohydrate diet (n=15, 25 kcal/kg/day, protein:carbohydrate:fat = 25:39:35) or a high-carbohydrate diet (n=15, 25 kcal/kg/day, protein:carbohydrate:fat = 26:62:10) for 4 weeks. At week 8 and 4, body weight (BW), body fat distribution and blood sampling were measured. To assess the fat distribution, visceral fat area (VFA) and subcutaneous fat area (SFA) were measured by CT scan.

Results: After 4 weeks of diet, BW, SFA, FBS, TC and LDL-C decreased significantly in both groups. Only in low-carbohydrate diet group, VFA, IRI, TG decreased and GH increased significantly. The decrease in BW, VFA, IRI, TG and the increase in HDL-C, GH, IGF-1 were significantly higher in low-carbohydrate diet group than in high-carbohydrate diet group. The change in GH correlated negatively with change in VFA.

Conclusion: Low-carbohydrate diet induced the visceral fat reduction and the beneficial effect on metabolic parameters in Mets. And the increase in GH secretion might associate with visceral fat reduction in Mets.

IDENTIFY METABOLIC SYNDROME USING C-PEPTIDE & HDL-C LEVELS IN TYPE-2 DIABETES MELLITUS INDIVIDUALS OF SOUTH INDIA
C. N. Manjunath1, S. Sornnava2, S. Banu3, D. N. Setty2, J. Nr3
1Cardiology, Sri Jayadeva Institute of Cardiovascular Sciences and Research, 2Diabetology, Karnataka Institute of Diabetology, 3Biochemistry, Sri Jayadeva Institute of Cardiovascular Sciences and Research, Bangalore, India

Aim: The progress of metabolic syndrome continues with the onset of type-2 diabetes mellitus (T2DM). Can it be monitored for better management? The study aims to identify the role of c-peptide and correlate it with insulin resistance, BMI, beta cell function, insulin sensitivity lipid profile and HbA1c.

Method: 96 Type-2DM individuals from south India. 58.3% males and 41.7% females were selected and fasting blood samples were collected for estimation of fasting C-peptide, FBS, PPBS, HbA1c, lipid profile. Analysis was done using standard Roche systems and reagents. Anthropometric measurements for BMI and HOMA-2 was used to obtain beta cell function, insulin sensitivity and insulin resistance. Statistically ANOVA, P-value, r-value were applied for correlation of c-peptide with parameter of Metabolic Syndrome.

Results: C-peptide showed significant correlation in different quintiles with parameters of metabolic syndrome like BMI & % Beta cell function positively. While insulin sensitivity showed negative significant correlation with c-peptide quintiles. Insulin resistance shows positive correlation till the 4th quintile following which the effect was not seen. C-peptide and HbA1c did not have clear cut relation based on quintiles. Lower HDL-cholesterol was significantly related to the higher C-peptide levels. Similarly triglycerides and C-peptide was positively significantly correlated but no such effect was seen with other parameters of lipid profile.

Conclusion: This study demonstrates that C-peptide, HDL-Cholesterol and triglycerides are useful parameters to identify insulin resistance and monitor progress of metabolic syndrome in type-2DM individuals of south India.

RELATIONSHIP BETWEEN N-TERMAL PRO-B-TYPE NATRIURETIC PEPTIDE LEVELS AND METABOLIC SYNDROME
Y. Y. Bao1, L. X. Shang2, N. L. Zhou1, M. R. Hu1
1Department of Endocrinology and Metabolism, 2Department of Sports Medicine, Huashan Hospital, Fudan University, Shanghai, China

Introduction: Previous studies have shown that obese individuals have reduced natriuretic peptide levels. But conflicting data exist on the relation of natriuretic peptide levels to other metabolic risk factors. We investigated the relationship between plasma N-terminal pro-B-type natriuretic peptide levels (NT-proBNP) and metabolic syndrome (Mets), metabolic risk factors in 469 patients free of heart failure.

Material and Methods: 230 diagnosed Mets cases and 239 non-Mets cases were included in this study. Echocardiography examinations were performed and left ventricular mass index was calculated according to Devereux correction formula. NT-proBNP was measured by electrochemiluminescence. The log-transformed NT-proBNP levels were used for abnormal distribution. Multiple linear regression analysis was performed to assess the association between levels of NT-proBNP and metabolic factors. Covariance analysis was used for group comparisons.

Results: Log NT-proBNP levels was independently related with age, gender, body mass index, systolic blood pressure, diastolic blood pressure, fasting blood glucose, triglyceride, high density lipoprotein cholesterol, low density lipoprotein cholesterol, and left ventricular mass index in multiple linear regression analysis (P < 0.05). Adjusted log NT-proBNP levels were lower in persons with Mets compared with those without Mets (P < 0.05). Individuals with hyperlipidemia, elevated body mass index, diastolic blood pressure and fasting plasma glucose had lower levels of log NT-proBNP than those without Mets (P < 0.05).

Conclusions: There is a relationship between metabolic components and lower plasma NT-proBNP concentration. These findings raise the possibility that reduced plasma NT-proBNP levels is a manifestation of Mets, which might possess significant clinical and pathophysiologic implications.

DIAMEL INTERVENTION TRIAL ON METABOLIC SYNDROME: A RANDOMIZED, DOUBLE-BLIND PLACEBO-CONTROLLED STUDY
National Institute of Endocrinology, Havana, Cuba

Aim: To assess whether Diamel (Diuretic supplement containing lettuce and oligoelements) administration could improve any of the clinical and metabolic parameters of metabolic syndrome (MS).

Subjects and Methods: Inclusion criteria: Diagnosis of MS according to WHO, no present or past treatment for elevated blood glucose concentrations and age between 19-70 years. Participants were randomly allocated either oral Diamel or Placebo (together with appropriate diet according to patient’s weight and physical activity) at a dose of two
capsules before the three main meals of each day for one year. All subjects were studied for the presence of *H. pylori* infection, as well as for free cholesterin, creatinine and uric acid (UA) concentrations. Insulin resistance (IR) was assessed by estimating insulin sensitivity index (HOMA-IR). Three indirect indexes used to predict insulin sensitivity (IS) were calculated.

**Results:** MS screening was carried out in 267 overweight/obese subjects. 110 individuals fulfilled MS criteria for eligibility being 100 randomized to treatment. Diabetic administration improved fasting glucose and insulin concentrations, IS, IR, and reduced UA concentrations from month 6 to the end of treatment when compared to Placebo. Diabeto also improved the abdominal perimeter, creatinine and UA after 12 month of treatment in comparison with the beginning of treatment. The BMI, IR and IS where found to be improved in both groups. No adverse effects were reported.

**Conclusions:** Lifestyle modification intervention improves some MS parameters per se; however, long-lasting treatment with Diabeto appears to add additional benefit to the health of persons with MS.

**CLINIC-ENDOSCOPIC AND ANATOMICAL PECULARITIES OF GASTROESOPHAGEAL REFLUX DISEASE IN PATIENTS WITH ABDOMINAL OBESITY**

A.A. Churikova1, L. Zvenigorodskaya2, N. Samsonova3, E. Bondarenko4, S. Khorosaka1

1Metabolic Syndrome, 2Central Scientific Research Institute of Gastroenterology, Moscow, Russia

**Purpose of the study:** To examine clinic, endoscopic, anatomical peculiarities of gastroesophageal reflux disease (GERD) in patients with abdominal obesity.

**Materials and Methods:** examination has been carried out on 75 patients with GERD and obesity (main group) and 56 with GERD without obesity (control group). The following activities were performed: collection of complaints, daily pH-metering, esophagogastroduodenoscopy, histologic examination of biopsy samples taken from mucous coat of the lower third of the esophagus.

**Results acquired:** For patients with obesity the dyspeptic symptoms are prevailing: belching with air and/or consumed food (44%), bitter taste in mouth (36%), nausea (24%), while a chief complaint of those suffering from GERD without obesity is epigastric burning (68%) (P < 0.05). Composite De Meester score was lower for patients of the main group (58.6 ± 2.3) compared to those of the control one (91.2 ± 8.5) (P < 0.05). At esophagogastroduodenoscopy reflux esophagitis was found in patients of the main group in 53.3% cases and in 35.7% cases in the control group. Anatomical symptoms revealed in patients with obesity: absence of the intercellular spaces expansion (64%), increase of stratified squamous epithelium basal layer thickness (58%) and presence of inflammatory infiltration in lamina propia of esophageus epithelium (49%).

**Conclusions:** The peculiarities of GERD in patients with obesity are: prevailing of dyspeptic symptoms and absence of epigastric burning, motor-evacuation abnormalities and typical morphological signs.

**FAT OVERLOAD INFLUENCES LIPOGENIC FACTORS IN THE METABOLIC SYNDROME**

M. Clemente-Postigo1, F.J. Tinahones2, F. Cardona3

1Laboratorio de Investigación Biomédica. HUVV (Fundación IMABIS), 2Laboratorio de Investigación Biomédica. HUVV (Fundación IMABIS): CIBER Fisiopatología de la Obesidad y la Nutrición, Málaga, Spain

**Introduction:** Several epidemiologic studies have related lipids increase in postprandial state to individual risk for the cardiovascular disease development, possibly due to the increased plasma triglycerides and fatty acids levels through enzymes of fatty acid metabolism as FASN, FATP or SCD1. SREBP1, LXRA and RXRA transcription factors are well known to be involved in fatty acid metabolism. It is well known that the interaction between nutrition and human genome determines gene expression and the metabolic response.

**Aims:** It is well established in experimental models but not in vivo that nutrients interact with transcription factors. Thus the aim of this study was to evaluate fat overload influence on gene expression of lipogenic regulators in peripheral blood mononuclear cells (PBMC) of patients with metabolic syndrome (MS).

**Methods:** Twenty-one MS patients were included. Patients underwent a 60g fat overload with a commercial preparation (Supracle®). At baseline and after fat overload anthropometrical and biochemical variables as well as gene expression of Epigenic factors were studied.

**Results:** The fat overload led to an increased SREBP1, RXRA and LXRA expression in PBMC, and it was associated with FASN expression. Besides, triglyceride levels, at baseline and postprandially, correlated with FASN expression. In addition, there was a positive correlation of SREBP1 with RXRA, and LXRA with plasma lipid peroxide levels in both baseline and fat overload state.

**Conclusions:** Fat overload lead to an increase of lipogenesis regulators in PBMC in patients with MS. Thus, it is possible to use this model to study lipid metabolism response in vivo.

**EFFECT OF APOCIII S37I POLYMORPHISM IN POSTPRANDIAL RESPONSE TO A FAT OVERLOAD IN METABOLIC SYNDROME PATIENTS**

M. Clemente-Postigo1, F.J. Tinahones2, F. Cardona3

1Laboratorio de Investigación Biomédica. HUVV (Fundación IMABIS), 2Servicio de Endocrinología y Nutrición, HUVV; CIBER Fisiopatología de la Obesidad y la Nutrición., 3Laboratorio de Investigación Biomédica. HUVV (Fundación IMABIS), CIBER Fisiopatología de la Obesidad y Nutrición, Málaga, Spain

**Objectives:** Apolipoprotein CIII (APOCIII) is a major component of triglyceride rich lipoproteins (TRLs). It has been shown its implication in TRLs catabolism and the S37I polymorphism has been associated with hypertriglyceridemia in patients with different pathologies and in healthy subjects. The aim of this study was to analyze the possible association between the minor S2 allele and the postprandial response of plasma triglyceride levels in metabolic syndrome (MS) patients.

**Methods:** We selected 73 patients with MS and 21 healthy subjects that didn't show MS characteristics. The participants underwent a 60g fat overload with a commercial preparation and it was measured their fasting and postprandial lipid profile. The APOCIII S37I polymorphism was genotyped.

**Results:** We found significant differences in fasting triglyceride (P = 0.048), 3h triglyceride (P = 0.002) and 4th triglyceride (P = 0.002) levels in patients with S22S genotype respect S1S1 and S1S2 patients. The triglyceride increase respect baseline was also higher in S22S homozygous patients at 4h than in the others MS patients (P = 0.001) pointing out that all S22S MS patients had a triglyceride increase higher than 150mg/dl at 4h (P = 0.028). In addition, S22S patients had incremented postprandial chylomicron-triglyceride levels (P = 0.006) respect the other genotypes. Controls didn't show significant variations in triglycerides levels respect genotype and other lipids parameters were not affected by the APOC3 genotype.

**Conclusion:** Homozygosity for the minor allele of the APOC3 S37I polymorphism was associated to a worse postprandial response in MS patients but not in healthy controls.
between groups T and S (S > T) while detraining reestablish the size as in sedentary rats (T = 73.6 ± 1.31; D = 62.52 ± 2.354; S = 80.68 ± 1.565 mm, P = 0.05 T vs. D and S). During lipogenesis, T showed the lowest, S the intermediate and D the greatest capacity: in absence of insulin (INS) (T = 194 ± 23.56; D = 268.1 ± 29.04; S = 241.6 ± 29.54); in presence of insulin (INS +) (T = 304.6 ± 32.33; D = 451.5 ± 39.05; S = 371.1 ± 36.66 P < 0.05 T vs. D). In incorporation into the FA moiety: INS (T = 449.7 ± 4.83; D = 654.3 ± 6.10; S = 555.3 ± 3.70 P < 0.05 T vs. D; INS + (T = 57.33 ± 4.13; D = 79.06 ± 6.93; S = 64.97 ± 5.85 P < 0.05 T vs. D) (values in nmol/mmol cells).

Conclusion: Cessation of exercise training for 8 weeks increased lipogenic capacity of PE fat pad, especially when insulin-stimulated

POLYCYSTIC OVARY SYNDROME AND -108C>T PON1 POLYMORPHISM

P. Ferk1, N. Teran2, B. Leskošek2, K. Geršak2

1Department of Pharmacochemistry and Experimental Toxicology, Faculty of Medicine, University of Maribor, Maribor, 2Institute of Medical Genetics, Department of Obstetrics and Gynecology, University Medical Centre Ljubljana, 3Institute for Biostatistics and Medical Informatics, Faculty of Medicine, Ljubljana, Slovenia

Introduction: Insulin resistance and increased oxidative stress are frequent features of polycystic ovary syndrome (PCOS). Activity of serum paraoxonase 1 (PON1), an antioxidant enzyme, was reported to be reduced in insulin-resistant disorders. The -108C>T PON1 polymorphism was shown to highly influence PON1 gene's transcriptional activity. -108T allele probably predispose to lower serum PON1 levels and consequently to increased oxidative stress.

Aim: In the present case-control study, we investigated a possible association of the -108C>T PON1 polymorphism with the presence of PCOS in Slovene population.

Patients and Methods: For 118 patients with PCOS and 108 controls volunteered with proven fertility, BMI and HOMA index were calculated, serum fasting insulin and serum fasting glucose concentrations were measured and genomic DNA from peripheral blood leukocytes was genotyped using PCR-RFLP.

Results: Our PCOS patients had significantly higher BMI compared to controls. All women had normal serum fasting glucose and insulin concentrations. Serum fasting glucose levels did not differ significantly between PCOS patients and controls, while serum fasting insulin concentrations and HOMA index were significantly higher in PCOS group. Despite an excess of -108T alleles and -108T:T genotypes in PCOS patients, differences in the allele and genotype distributions between PCOS group and controls did not reach statistical significance.

Conclusion: No significant association between the -108C>T PON1 polymorphism and PCOS was observed in Slovene population. Other factors influencing serum PON1 activity in PCOS patients should be considered.

EFFECT OF SPIRONOLACTONE AND METFORMIN COMBINATION ON CLINICAL, BIOCHEMICAL AND HORMONAL ASPECTS OF WOMEN WITH POLYCYSTIC OVARY SYNDROME: SIX MONTH OPEN LABELED STUDY

M.A. Ganje, M. Ashraf, G. Khurana, M.L. Sobla Nilar

Departments of Obstetrics and Gynecology, Govt. Medical College, Clinical Biochemistry, University of Kashmir, Biostatistics, Radio Diagnosis and Endocrinology, Sher-i-Kashmir Institute of Medical Sciences, Srinagar, India

Objective: The aim was to see if combination of spironolactone and metformin improves the efficacy over either drug alone.

Methods: We compared the efficacy of spironolactone (n = 49; 50 mg/day), metformin (n = 56; 1000 mg/day) with their combination (n = 62; 50 mg and 1000 mg). A total of 179 adolescent and young women with polycystic ovary syndrome (PCOS) were enrolled and the effect was on menstrual cyclicity, hirsutism, BMI, LH, RF, hormonal levels, glycemia and insulin sensitivity at baseline, 3rd, and 6th month of treatment evaluated in 167 women.

Results: Mean age of subjects was 22.42 ± 5.27, 23.57 ± 5.23 and 23.56 ± 5.27 years in metformin, spironolactone and combination. Mean BMI of subjects was 26.8 ± 4.0 Kg/m² and was comparable in three groups at baseline. Number of menstrual cycles in the metformin, spironolactone and combination increased from 5.59 ± 1.96, 6.45 ± 2.63, and 6.13 ± 2.54 at baseline to 8.8 ± 2.35, 9.4 ± 2.45 and 9.3 ± 3.0 at 3rd month and to 10.02 ± 1.60, 10.39 ± 2.84 and 10.3 ± 3.20 / year at 6th month (P = 0.02), respectively. Hirsutism score decreased from 13.27 ± 2.74, 13.65 ± 2.72 and 14.11 ± 3.05 at baseline to 10.84 ± 2.42, 10.27 ± 2.50 and 10.29 ± 2.29 at 3rd month, 9.67 ± 2.19, 9.56 ± 2.29 and 8.39 ± 2.29 at 6th month respectively. All the three groups showed improvement in glucose tolerance and insulin sensitivity, though the effect of the combination was better than metformin which in turn was superior to spironolactone.

Conclusion: We conclude that although, both these drugs are effective in the management of PCOS, the combination at these doses seems superior in terms of clinical benefits as well as prevalence of adverse effects.

DIAMEL THERAPY IN POLYCYSTIC OVARY SYNDROME REDUCES HYPERINSULINEMIA, INSULIN RESISTANCE AND HYPERANDROGENEMIA

J.A. Hernández-Yero1, F. Santana Pérez2, G. Ovies Carballo2, E. Cabrera Rode3

1Asistencia Médica, 2Investigaciones, 3Inmunología, Instituto Nacional de Endocrinología, La Habana, Cuba

Background: The Diamel is a nutritional supplement constituted by vitamins, oligoelements, amino acids, lettuce extract and bilberry extract activated by multivitamins and mult минералов. The laboratory, Madrid, Spain, with favorable influence on the insulin resistance.

Aims: To assess the effect of Diamel on the insulin resistance and sexual hormones in women with polycystic ovary syndrome(PCOS).

Methods: Women with PCOS(n = 37) took part in a six-month double-blind placebo-controlled study and were randomized to placebo(n = 19) or Diamel(n = 18), with ages between 18 to 35 years and HOMA-IR index ≥2.6. The women were distributed in two groups: one that took Diamel or placebo(2 capsules before the breakfast, lunch and food). Were followed during 6 months with clinical and biochemical evaluation by fasting plasma glucose, fasting plasma insulin, HOMA-IR, HOMA-B and Raynau indexes, gonadotropins, testosterone and lipids.

Results: The clinical characteristics in both groups were similar with overweight or obesity and menstrual irregularity, and the basal values in gonadotropins and testosterone, without significant differences. The HOMA-IR Index diminished in significant form in the group with Diamel and 37.5% of women of that group reached regular menstrual cycles for a 18.5% in the patients with placebo. The LH levels diminished in the group with Diamel and the values of testosterone presented a tendency to the diminution like average in this group.

Conclusions: The Diamel diminished the insulin resistance in women with PCOS, improvement in the levels of LH and testosterone. This nutritional supplement can represent a new therapeutic alternative in the treatment of these patients.

© 2011 Rujin Hospital, Shanghai Jiaotong University School of Medicine and Blackwell Publishing Asia Pty Ltd 254
ABSTRACT
The polycystic ovary syndrome (PCOS) is the main cause of anovulatory sterility. Its prevalence is almost 7%. PCOS does have not a constant hormonal profile, which is why using approaches such as the Rotterdam criteria is necessary to diagnose it. The proven effect of insulin on the ovary modified the concept of the specificity in insulin’s action on certain tissues: resistance to insulin’s action results in the compensatory hyperinsulinism that tries to stimulate all the tissues, but also worsens ovarian steroidogenesis. There are drugs known as “insulin sensitizers” that are used to treat certain forms of diabetes mellitus which include metformin and thiazolidinediones (rosiglitazone and pioglitazone). Recently a compound that is composed of amino acids and trace elements (Diamel) has been used to neutralize the free radicals in the cell and restore the intracellular signals of the insulin. The long term effect however, might not correct the polycystic ovary syndrome as insulin resistance is associated to a higher risk of increased glucose intolerance, diabetes, dyslipidemia, atherosclerosis and vascular disease. Therefore, preventive measures that are currently available should used. Key words: polycystic ovary syndrome, insulin resistance, insulin sensitizers
Medical Research Unit on Endocrine Diseases, Specialities Hospital, National Medical Centre Siglo XXI, Mexican Social Security Institute, Mexico, Federal District
Correspondence: mhernandezvalencia@prodigy.net.mx
Received: June, 2010. Accepted: October, 2010.

This article should be quoted as: Hernández-Valencia M, Hernández-Rosas M, Zárate A. Treating insulin resistance in the polycystic ovary syndrome. Ginecol Obstet Mex 2010; 78(11):612-616.

www.nietoeditores.com.mx
The polycystic ovary syndrome is the most common endocrine disorder during a woman's reproductive cycle. Its prevalence is 4 to 7%, with extreme reports of up to 32%, depending on the population under study; it is therefore the main cause of anovulatory sterility. The way patients suffering from polycystic ovary syndrome are treated is constantly changing due to progress in therapeutic, metabolic research and that done on infertility.

The polycystic ovary syndrome does have not a constant hormonal profile. Measuring circulating hormones using the existing analytical methods gives extremely varied results, which in many cases are difficult to interpret; that is why certain approaches have been used to diagnose it. The National Institutes of Health of the United States consider the polycystic ovary syndrome to be chronic anovulation that, according to clinical and biochemical evidence and after excluding other ailments, is associated with an excess of androgens. At the consensus meeting held in Rotterdam, the polycystic ovary syndrome was defined as "a concurrent set of symptoms, signs and biochemical features that can occur in various combinations". It can exist without hyperandrogenism. (Table 1)

Endocrinial changes

The characteristic changes of the polycystic ovary syndrome affect the endocrine system, which results in hyperandrogenism and, in turn, it affects a woman's appearance. Knowledge about the effect of insulin on the ovary changed the concept of the specificity in insulin's action on certain tissues (liver, skeletal muscles and fatty tissue) and also the evidence proving that there are extragonadal factors involved in ovarian functions. When there is resistance to the action of insulin in various tissues, compensatory hyperinsulinemia occurs to try and stimulate these tissues, but then later, it worsens the ovarian steroidogenesis disorder due to the over stimulated ovarian receptors; this is what triggers off the series of metabolic changes of the polycystic ovary syndrome. This disorder is due to the fact that the somatomedin IGF-1 (the insulin-like growth factor type I) vigorously stimulates the cytochrome enzyme P450c-17 in the ovary. That is why the circulating insulin can join the IGF-I receptor and transmit the biological message to increase the production of androgens in the ovarian follicles. Moreover, as IGF-I and FSH share common signalling pathways, not enough of the latter is produced, which then limits the production of estradiol and the follicles don't mature. Consequently, FSH is suppressed and this significantly increases the LH and diverts the metabolic pathway towards the androgens.
Table 1. Diagnostic criteria of the polycystic ovary syndrome

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic anovulation</td>
<td>Oligoovulation or anovulation or both</td>
<td>Ovarian dysfunction (oligo-anovulation or polycystic ovaries or both)</td>
</tr>
<tr>
<td>Clinical or biochemical excess of androgens</td>
<td>Clinical or biochemical signs of hyperandrogenism</td>
<td>Hyperandrogenism (clinical or biochemical)</td>
</tr>
<tr>
<td>Ruling out other disorders</td>
<td>Polycystic ovaries (Positive with two criteria)</td>
<td>Ruling out related disorders</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Existence of the syndrome without evidence of hyperandrogenism existing</td>
</tr>
</tbody>
</table>


In some cases of insulin resistance, various genes associated with the steroidogenesis enzymes are altered, such as the gene of the steroid synthesis CYP 11 alpha-hydroxylase and the genetic defects that increase the serine phosphorylation activity. In turn, this increases the activity of 17, 20 lyases and, consequently, triggers off hyperandrogenism and hyperinsulinemia. This genetic defect in the post-receptor can also cause an abnormality in the insulin receptor’s serine phosphorylation, with a decrease in the intracellular signalling, which could explain the resistance to the action of the insulin.

Determining insulin resistance

Insulin resistance should only be considered as a concept, as there is no laboratory proof that could be clinically used to identify insulin resistance among the population in general. There are tests, such as the euglycemic clamp and the glucose tolerance test that are used to calculate the glycemic index. However this is only useful for research and its clinical use is limited; moreover, there isn't a standard technique for the insulin tests. Another observation made from some of the studies is that more than half of the patients suffering from the polycystic ovary syndrome, obese or slim, suffer from insulin resistance and that's why the prevalence is found to be between 50% and 75%. Nevertheless, the ratio of this finding depends on the screening test used. For the time being, it has been suggested that insulin resistance might be the future cause of type 2 diabetes, which has its own implications.
Treatment

The treatment for patients suffering from the polycystic ovary syndrome is basically symptomatic. The reason why the patient consults the doctor must be accurately established, what the menstrual disorders could be, infertility, hyperandrogenism, obesity and metabolic alterations that give a different response to the different forms of treatment should also be determined. Existing health care focuses on treating the condition of insulin resistance, because when it is corrected a large part of the ovarian functions are restored.

Drug treatment

Insulin resistance and hyperinsulinemia are of interest due to their involvement in pathophysiology and in the symptoms (hyperandrogenism and obesity). Consequently a lot of research has been carried out to determine how useful the “insulin sensitizers”, that are recommended to treat certain types of diabetes mellitus actually, are (Table 2). The main test is that carried out with a biguanide (metformin) and thiazolidinediones (rosiglitazone and pioglitazone), which can decrease obesity and restore menstruation, even ovulation. The dose of metformin is between 500 and 1,000 mg a day. It is taken orally, with meals, to cut down on unpleasant effects such as: dry mouth, nausea, general discomfort and a feeling of weakness.

Treatment for hyperinsulinemia and insulin resistance can partially reduce hyperandrogenism, although this would not apply the other way round. This means to say that correcting hyperandrogenism does not eliminate insulin resistance. The metformin decreases the concentrations of insulin, testosterone, estradiol and glucose but it increases the SHBG, which is considered to be beneficial.

Some observations show that these drugs increase the effectiveness of the ovulation inducers (clomiphene). Studies have also been carried out to find out about the preventive effect of diabetes mellitus when insulin resistance is corrected in women with the polycystic ovary syndrome. An oral glucose tolerance test should be carried out on obese women, as there is more risk of diabetes and the appropriate diagnosis is essential, especially when there is a family history of diabetes.

Recently, a compound made up of amino acids and trace elements (DiaMel) was used. During tests and in vivo it stimulated the pancreatic metabolism and reduced the insulin resistance evaluated by means of the HOMA method. The mechanism of action involves certain molecules from the compound that stimulate the production of insulin (carnitine and ornithine). It reduces the amount of glucose absorbed in the intestine (glycine, sodium methylparaben, fumaric acid, pridoxal), neutralizes the free radicals in the cell due to the
antioxidant effect (Zinc, C, B, calcium, folic acid) and restores insulin's intracellular signals, so the most is made of the insulin. The lipid concentration in the blood (arginine) is also seen to drop, which helps to reduce insulin resistance. These beneficial changes have been observed in a significant number of patients with insulin resistance when they are treated with a dose of 660 mg every 12 hours. On the whole, clinical effectiveness has been proved in preliminary observations of patients suffering from the polycystic ovary syndrome and insulin resistance.

Table 2. Stratified analysis of the drug response in the polycystic ovary syndrome

<table>
<thead>
<tr>
<th>Variable</th>
<th>Clomifene</th>
<th>Metformin</th>
<th>Thiazolidinediones</th>
<th>Diamel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin resistance</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Menstrual changes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperandrogenism</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obesity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anovulation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Return of cysts</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pregnancy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


CONCLUSIONS

Nowadays, the polycystic ovary syndrome is considered to be a state of ovarian hyperactivity that upsets the steroidogenesis which then leads to an excess production of androgens; this might be caused by certain altered genes and environmental factors. The components and the intensity of the medical condition, just like its progress, are variable; therefore it is a good idea to carry out an extensive diagnosis in order to correct the disorder properly. The treatment must be personalised, in particular when it is given to correct the metabolic part. Firstly, the reason why the patient has come to see the doctor must be taken into consideration. At the moment, there are many therapeutic options available to treat ovarian cysts; nevertheless, the results
aren't very consistent in the majority of cases. A pre-established standard is needed to set up which patients must be treated and if the treatment does indeed depend on the type of ovarian cyst. Patients have to be informed of the long term effects of not correcting the polycystic ovary syndrome. The fact that insulin resistance is associated with a greater risk of glucose intolerance, diabetes, dyslipidemia, atherosclerosis, vascular disease and the obstructive sleep dysnea should be emphasized. Preventive measures including changing the patient's life style, low fat, high fibre diet, regular exercise of at least 15 minutes a day and reduce their weight by 5% should also be recommended; this has proven to be enough to restore ovulation.