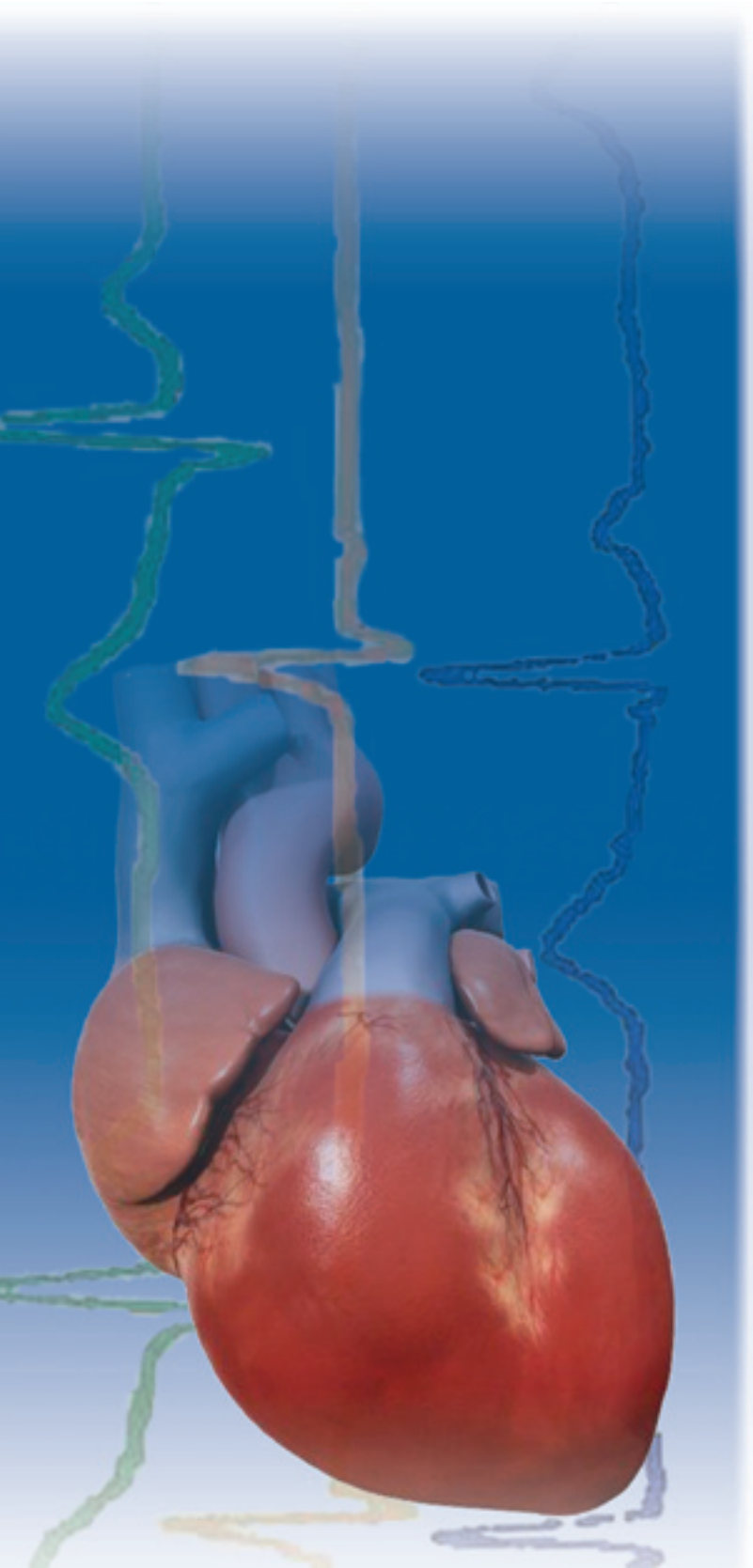
Editorial



La Revista Latinoamericana de Hipertensión (RLH) publica su tercer número del año 2006. Los trabajos que a continuación se mencionan fueron revisados por árbitros expertos en el área de hipertensión arterial, la mayoría fueron presentados en el V Congreso Latinoamericano de Hipertensión, celebrado en el Hotel Maremares, Puerto La Cruz, del 31 de Mayo al 3 de Junio del presente año.

Un tema de importancia fundamental en el área de hipertensión es el Síndrome Metabólico, el cual suele afectar a un gran número de pacientes hipertensos acompañados de sobrepeso, dislipidemia, diabetes mellitus, hiperinsulinemia y resistencia a la insulina. Los autores describen los aspectos patogénicos y terapéuticos de este síndrome lo cual constituye una puesta al día de utilidad para los médicos prácticos que atienden pacientes hipertensos. Un trabajo interesante es el impacto que tiene la creación de una Unidad de Hipertensión Arterial en el área Sur-Oeste de Caracas en la prevalencia de la hipertensión arterial provocando un notable descenso de la prevalencia de 27% a 16% lo cual se explica por varios factores, entre ellos, la educación a la comunidad, el mejor manejo terapéutico, etc. Finalmente se reporta la prevalencia de obesidad en adultos en el Municipio Sucre del Estado Miranda y el uso de productos glicanicos para el tratamiento del sobrepeso y la hipercolesterolemia.

Todos los artículos son de importancia actual tanto en países desarrollados como países en desarrollo.

Manuel Velasco

Rafael Hernández Hernández

Editores en Jefe

Maria José Armas de Hernández

Editor Ejecutivo

Revista Latinoamericana de Hipertensión

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Sociedad Latinoamericana de Hipertensión
Escuela de Medicina José María Vargas, Cátedra de Farmacología, piso 3. Esq. Pirineos. San José.
Caracas-Venezuela.

Comercialización y Producción:
Felipe Alberto Espino
Telefono: 0416-811.6195 / 0414-2189431
e-mail: felipeespino@gmail.com
Diseño de portada y diagramación:
Mayra Gabriela Espino
Telefono: 0412-922.25.68
e-mail: mayraespino@gmail.com

Alcance y Política Editorial

La Revista de la Sociedad Latinoamericana de Hipertensión es una publicación biomédica periódica, arbitrada, de aparición trimestral, destinada a promover la productividad científica de la comunidad nacional e internacional en toda el área del Sistema Cardiovascular; la divulgación de artículos científicos y tecnológicos originales y artículos de revisión por invitación del Comité Editorial.

Está basada en la existencia de un Comité de Redacción, consistente en Editores en Jefe, Editores asociados y Comité Editorial. Los manuscritos que publica pueden ser de autores nacionales o extranjeros, residentes o no en Venezuela, en castellano o en ingles (los resumenes deben ser en ingles y castellano). Los manuscritos deben ser trabajos inéditos.

La Junta Directiva de la Revista no se hace responsable por los conceptos emitidos en los manuscritos. Los autores deben aceptar que sus manuscritos no se hayan sometidos o hayan publicados en otra revista. El manuscrito debe ir acompañado de una carta solicitud firmada por el autor principal y el resto de los autores responsables del mismo.

Forma de Preparación de los Manuscritos

Para la publicación de trabajos científicos en la Revista de la Sociedad Latinoamericana de Hipertensión, los mismos estarán de acuerdo con los requisitos originales para su publicación en Revistas Biomédicas, según el Comité Internacional de Editores de Revistas Biomédicas (Arch. Intern. Med. 2006:126(36):1-47), www.icmje.com. Además, los editores asumen que los autores de los artículos conocen y han aplicado en sus estudios la ética de experimentación (Declaración de Helsinki). A tales efectos, los manuscritos deben seguir las instrucciones siguientes:

1. Mecanografiar original a doble espacio en idioma español, papel bond blanco, 216 x 279 mm (tamaño carta) con márgenes por lo menos de 25 mm, en una sola cara del papel. Usar doble espacio en todo el original. Su longitud no debe exceder las 10 páginas, excluyendo el espacio destinado a figuras y leyendas (4-5) y tablas (4-5).

2. Cada uno de los componentes del original deberán comenzar en página aparte, en la secuencia siguiente:
a. Página del título.
b. Resumen y palabras claves.
c. Texto.
d. Agradecimientos.
e. Referencias.
f. Tablas: cada una de las tablas en páginas apartes, completas, con título y llamadas al pie de la tabla.
g. Para la leyenda de las ilustraciones: use una hoja de papel distinta para comenzar cada sección. Enumere las páginas correlativamente empezando por el título. El número de la página deberá colocarse en el ángulo superior izquierdo de la misma.

3. La página del título deberá contener:
3.1. Título del artículo, conciso pero informativo.
a. Corto encabezamiento de página, no mayor de cuarenta caracteres (contando letras y espacios) como pie de página, en la página del título con su respectiva identificación.
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4. La segunda página contiene un resumen en español y su versión en inglés, cada uno de los cuales tendrá un máximo de 150 palabras. En ambos textos se condensan: propósitos de la investigación, estudio, método empleado, resultados (datos específicos, significados estadísticos si fuese posible) y conclusiones. Favor hacer énfasis en los aspectos nuevos e importantes del estudio o de las observaciones. Inmediatamente después del resumen, proporcionar o identificar como tales: 3-10 palabras claves o frases cortas que ayuden a los indexadores en la construcción de índices cruzados de su artículo y que puedan publicarse con el resumen, utilice los términos del encabezamiento temático (Medical Subject Heading) del Index Medicus, cuando sea posible.

5. En cuanto al texto, generalmente debe dividirse en: introducción, materiales y métodos, resultados y discusión.
6. Agradecimientos, sólo a las personas que han hecho contribuciones reales al estudio.
7. Las referencias bibliográficas serán individualizadas por números arábicos, ordenados según su aparición en el texto. La lista de referencias bibliográficas llevarán por título "Referencias Bibliográficas" y su ordenamiento será según su orden de aparición en el texto.
Las citas de los trabajos consultados seguirán los requisitos de uniformidad para manuscritos presentados a revistas Biomédicas, versión publicada en: Ann lntern Med. 2006; 126(36): 1-47, www.icmje.com. No se aceptarán trabajos que no se ajusten a las normas.
8. Tablas: En hoja aparte cada tabla, mecanografiada a doble espacio; no presentar tablas fotográficas; enumere las tablas correlativamente y proporcione un título breve para cada una; dé a cada columna un encabezamiento corto o abreviado; coloque material explicativo en notas al pie de la tabla y no en el encabezamiento; explique en notas al pie de la tabla las abreviaturas no estandarizadas usadas en cada tabla; identifique claramente las medidas estadísticas de las variables tales como desviación estándar y error estándar de la medida; no use líneas horizontales ni verticales: citar cada tabla en orden correlativo dentro del texto; citar la fuente de información al pie de la tabla si ésta no es original.
9. Ilustraciones: Deben ser de buena calidad; entregarlas separadas; las fotos, en papel brillante con fondo blanco, generalmente 9 x 12 cm. Las fotografías de especímenes anatómicos, o las de lesiones o de personas, deberán tener suficiente nitidez como para identificar claramente todos los detalles importantes. En caso de tratarse de fotos en colores, los gastos de su impresión correrán a cargo del autor(s) del trabajo. Lo mismo sucederá con las figuras que superen el número de cuatro.
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15. Todos los aspectos no previstos por el presente reglamento serán resueltos por el Comité Editorial de la Revista.

Metabolic syndrome; treatment of hypertensive patients with this syndrome

Zafar H. Israili[1], Badiâa Lyoussi[2], Rafael Hernández-Hernández[3], and Manuel Velasco[4]

[1]Department of Medicine, Emory University School of Medicine, Atlanta, Georgia, USA
[2]UFR Physiology – Pharmacology, Laboratory of Animal Physiology, Department of Biology, Faculty of Sciences Dhar El Mehraz, Fez, Morocco.
[3]Clinical Pharmacology Unit and Hypertension Clinic, School of Medicine, Universidad Centroccidental "Lisandro Alvarado". Barquisimeto, Estado Lara, Venezuela
[4]Department of Pharmacology, "JM Vargas" Medical School, Central University of Venezuela, Caracas, Venezuela

Address correspondence to:
Dr. Zafar H. Israili
Department of Medicine
Emory University School of Medicine
69 Jesse Hill Jr. Drive, Atlanta, Georgia, USA
Phone: 678-480-5860
Fax: 404-522-3799
E-mail: zisrail@emory.edu

Introduction

Hypertension is no longer viewed as a case of isolated high blood pressure (BP) in a patient, but rather a complex pathology with associated risk factors and co-morbidities. More than 80% of individuals with stage I or greater hypertension (as defined by the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; JNC- 7)[1] have additional co-morbidities, which increase the risk of cardiovascular (CV) complications. At least 20% of hypertensive patients have at least three of the following comorbidities and/or CV risk factors: obesity, glucose intolerance, hyperinsulinemia, low levels of high-density-lipoprotein (HDL)-cholesterol, elevated low density lipoprotein (LDL)-cholesterol and triglyceride levels, left ventricular (LV) hypertrophy, and tobacco use.[2] When some of these individual CV risk factors cluster in an individual, the person is said to have metabolic syndrome (see below). Hypertension is the key component of the metabolic syndrome. Therefore, the aim of treatment of hypertension in a patient is not only to control high blood pressure (BP) but also to reduce the associated CV risk factors and treat other co-morbidities. Treatment of several of these risk factors simultaneously results in improvement in CV outcomes in individuals with established hypertension. This review discusses the metabolic syndrome and some of the options available in treating hypertensive patients with this syndrome.

Metabolic syndrome

Metabolic syndrome (also called syndrome X, syndrome X plus, metabolic syndrome X, dysmetabolic syndrome, dysmetabolic syndrome X, multiple metabolic syndrome, plurimetabolic syndrome, deadly quartet, and Reaven's syndrome) is a constellation or clustering of metabolic abnormalities present in one person, which are thought to result (Figure 1) from a primary disorder of insulin resistance, hence it is also called the insulin resistance syndrome. When present as a group in one person, the multiple metabolic disorders promote atherosclerosis and increase the risk for CV disease (Figure 2) and premature death – therefore, the metabolic syndrome is also called cardiometabolic-, cardiovascular dysmetabolic-,metabolic cardiovascular-, or atherothrombogenic syndrome[3,4].

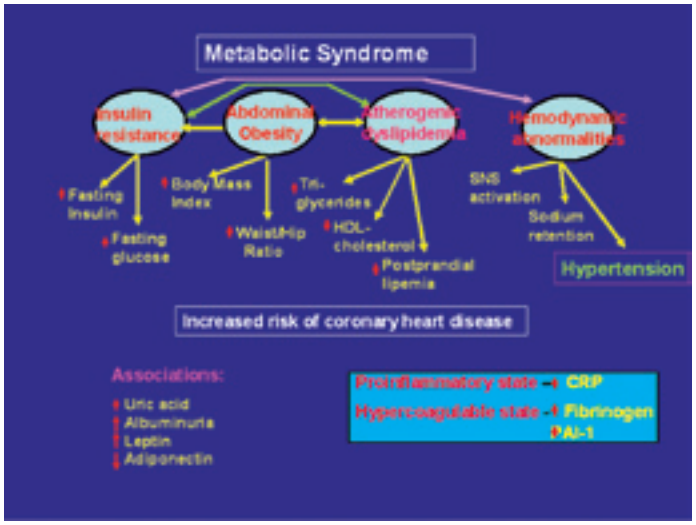

Figure 1. The components of the metabolic syndrome and their effects on various risk factors

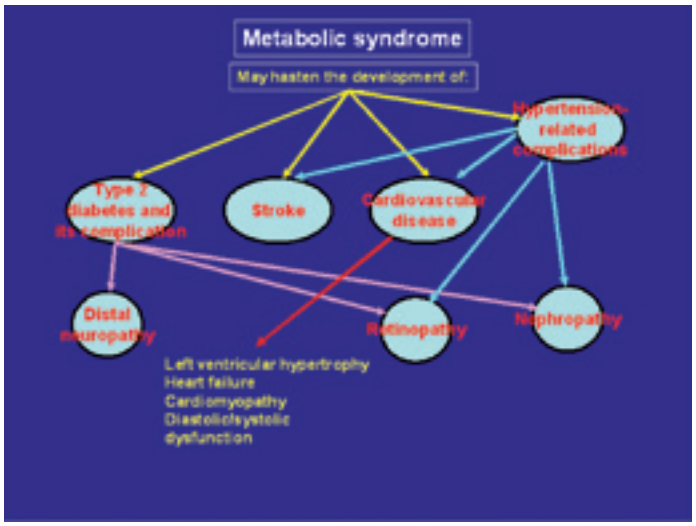

Figure 2. Adverse effects of the metabolic syndrome

Definitions of the metabolic syndrome

Several separate working definitions of metabolic syndrome have been proposed,5-8 which differ in criteria and cutoff points:

(1) World Health Organization[9];

(2) Third Report of the National Cholesterol Education Program (NCEP): Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults; The Adult Treatment Panel III (NCEP/ATP III)[10];

(3) European Group for the Study of Insulin Resistance (EGIR) [5,11];

(4) International Diabetic Federation[12,13];

(5) American College of Endocrinology, American Association of Clinical Endocrinologists[14,15];

(6) Chinese Diabetes Society[5,16,17].

The most widely used diagnostic criteria of the metabolic syndrome are according to NCEP/ATP III and WHO, while the EGIR and the new IDF definitions are also used by many investigators (Table 1).

However, the multiple definitions of the metabolic syndrome cause confusion particularly when comparing data from different studies. To remove some of the confusion, the International Diabetes Federation has proposed a unifying definition of the metabolic syndrome (Table 1), which is somewhat an amalgam of the three major definitions (WHO, EGIR, NCEP/ATP III), but it does not include insulin resistance in the criteria[121](http://www.idf.org/webdata/docs/ accessed August 2005; http://www.medscape.com/viewarticle/504382, accessed August 2005).

Table 1 Definitions of the Metabolic Syndrome

The NCEP Adult Treatment Panel III (NCEP/ATP III): any 3 or more of the following criteria:
1) Waist circumference >102 cm in men and > 88 cm in women; 2) triglycerides ≥1.7 mmol/L; 3) BP ≥ 130/85 mmHg; 4) HDL cholesterol <1.0 mmol/L in men and <1.3 mmol/L in women; 5) Fasting glucose ≥ 6.1 mmol/L (110 mg/dL), later modified to ≥ 5.6 mmol/L (100 mg/dL)
World Health Organization (WHO):
Diabetes, impaired fasting glucose, impaired glucose tolerance, or insulin resistance (assessed by clamp studies) and at least two of the following criteria: 1) Waist-to-hip ratio >0.90 in men or >0.85 in women; BMI > 30 kg/m2 2) Triglycerides ≥1.7 mmol/L (150 mg/dL) or HDL-cholesterol <0.9 mmol/L (35 mg/dL) in men and <1.0 mmol/L (39 mg/dL) in women; 3) BP ≥140/90 mmHg; 4) Urinary albumin excretion rate >20 µg/min or albumin-to-creatinine ratio ≥ 30 mg/g
European Group for the Study of Insulin Resistance (EGIR):
1) Waist circumference >102 cm in men and > 88 cm in women; 2) Fasting glucose ≥ mg/dL, 3) BP ≥ 130/85 mm Hg or medication, 4) HDL-cholesterol: < 40 mg/dL (men), < 50 mg/dL (women), 5) triglycerides: ≥ 150 mg/dL
International Diabetes Federation (IDF):
Central obesity, defined as waist ≥ 94 cm for males and ≥ 80 cm for females in Europids, and ethnic-specific in Chinese (waist ≥ 90 cm for males and ≥ 80 cm for females, Japanese waist ≥ 94 cm for males and ≥ 80 cm for females and South Asians waist ≥ 94 cm for males and ≥ 80 cm for females; together with 2 of the following: a) Triglycerides ≥ 1.7 mmol/L (150 mg/dL) b) HDL-cholesterol, defined as <1.04 mmol/L (40 mg/dL) in males and <1.29 mmol/L (50 mg/dL) in females c) BP ≥130/85 mm Hg; and d) Fasting hyperglycemia (impaired fasting glucose), defined as glucose ≥5.6 mmol/L (100 mg/dL) or previous diagnosis of diabetes or impaired glucose tolerance

Components of the metabolic syndrome

The major components of the metabolic syndrome are obesity, glucose intolerance, insulin resistance, low levels of HDL-cholesterol, elevated LDL-cholesterol and triglyceride levels, and elevated BP (Table 1). Hyperuricemia and hyperleptinemia have also been proposed as components of the metabolic syndrome[18-20]. In addition, the metabolic syndrome has been associated with the following:

a) Prothrombotic state (high fibrinogen, decreased fibrinogen activator and/or plasminogen activator inhibitor-1 in blood)[21,22]; b) Proinflammatory state (elevated high-sensitivity C-reactive protein, pro-inflammatory cytokines and adhesion molecules in the blood)[23-27]; c) increased intima-media thickness[21,28,29]; d) decreased adiponectin levels[24,30]; e) low serum magnesium[31]; f) high levels of uric acid[32]; g) high serum ferritin and iron overload[33]; h) polycystic ovary syndrome[34]; i) sleep apnea[35]; j) increased brachial-ankle pulse wave velocity[36]; k) higher values for homeostasis model assessment of insulin resistance (HOMA-IR)[37]; l) low levels of androgens (testosterone and dehydroepiandrosterone) and sex-hormone binding globulin[37,38].

Prevalence of the metabolic syndrome

Metabolic syndrome is becoming increasingly common[18,39,42], with a prevalence of 10% to 30% of the adult population in industrialized countries, depending on the definition used (Table 2)[17,40,43,62]. It is estimated that 47 million Americans have metabolic syndrome; about 40% of adults age 50 or older have the metabolic syndrome[40,61,63,64]. The prevalence rate increases with age, degree of obesity (body mass index), level of hyperglycemia, and the presence of hypertension[65]; the prevalence of the syndrome among diabetics is quite high (70%-90%)[57,66]. Using the WHO definition, the prevalence of the metabolic syndrome in a Swedish population was higher in subjects with a defect in glucose disposition than in normoglycemic individuals, and highest in diabetics (Figure 3): 10% of women and 15% of men with normoglycemia, 42% of women & 64% of men with impaired fasting glucose/impaired glucose tolerance, and 78% of women and 84% of men with type 2 diabetes[57]. Ethnic differences have been reported in the prevalence of the metabolic syndrome (Figure 4)[40,62,66]. In some studies, the prevalence of the metabolic syndrome was higher in females than in males[17,50,53,54,58,66,67]. while in others, males had a higher prevalence than females[46,47,57,60,62]; in some studies no gender difference was noted[49]. However, it may be realized that the prevalence of the metabolic syndrome and its components are dependent on the definition used for the different components.

Table 2. Prevalence of metabolic syndrome in certain populations

Population	Prevalence	Reference
Arab-Americans1	23.0%	43
Arab- Americans3	28.0%	43
China1	9.8 -17.8%	44
China2	10.2 -15.7%	17
Europe3	14.2 – 15.7%	45
Europe3	5.0 – 36.0%	46
Finland3	22.2 – 38.8%	47
France1	11-16%	48
Greece1	24.5%	49
India1	22.9 - 39.9%	50
Israel1	26%	51
Japan1	10.3 – 30.2%	52
Korea1	20.8 - 26.9%	53
Korea1	5.2 – 9.0%	54
Mexico3	13.6%	55
Mexico1	26.6%	55
Mexico1	39.9 - 59.9%	56
Sweden3	10 - 15%	57
Turkey1	23.7 – 39.1%	58
USA1	24.1 – 27.0%	40
USA1	26.3 - 29.3%	59
USA1	24.7 – 30.3%	60
USA1	28.1%	61
USA3	21.0%	61
Venezuela1	31.2%	62

Criteria used to define the metabolic syndrome:
1) NCEP/ATP III; 2) CDS; 3) WHO; 4) EGIR

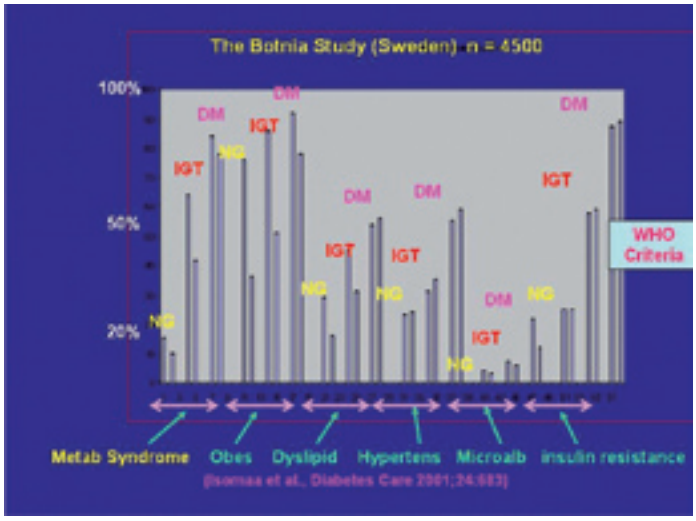

Figure 3. Prevalence of metabolic syndrome (according to the WHO criteria) and its various components in various groups (first bar for males and the second bar for females): normoglycemic individuals (NG); subjects with impaired glucose tolerance (IGT); subjects with type 2 diabetes mellitus (DM). (Adapted from Isomaa et al.[57])

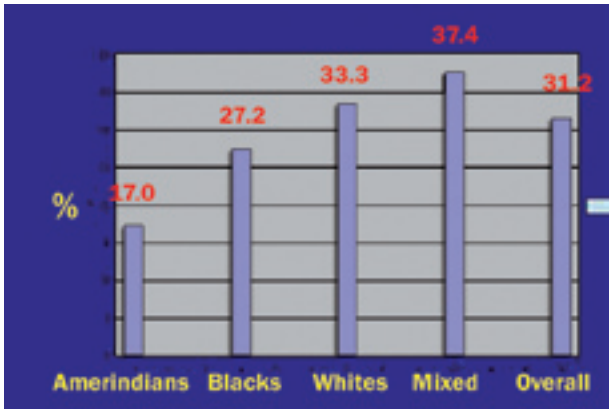

Figure 4. Prevalence of metabolic syndrome in various ethnic groups in Zulia State, Venezuela (1999-2001) (Adapted from Florez et al.62)

Underlying causes of the metabolic syndrome

The disorder of insulin resistance is the most accepted unifying hypothesis to describe the pathophysiology of the metabolic syndrome[22], although, this concept has been challenged[68], and not every individual with this syndrome has insulin resistance[69]. The biologic mechanisms at the molecular level between insulin resistance and metabolic risk factors aren't fully understood and appear to be complex[53,70,71]. A four-factor model (blood pressure, obesity, insulin resistance, and lipid profile) has been suggested, which relates all the components of the metabolic syndrome[72,73]. Although, abdominal obesity is considered as a central element of the metabolic syndrome, obesity as a single factor has recently been proposed to unify all the risk factors related to the metabolic syndrome[74]. Obesity is positively correlated with higher BP, fasting insulin, triglycerides, and negatively associated with HDL-cholesterol[75]. Since, obesity is also associated with a prothrombotic state[76], increased BMI is associated with higher risk of myocardial infarction and coronary heart disease[77]. Never-the-less, not all individuals who have the metabolic syndrome are obese, since non-obese people can have other components of the metabolic syndrome, such as high BP, low HDL-cholesterol, high triglycerides, insulin resistance, etc.

In general, the underlying causes of this syndrome are excess body weight (visceral/ central/ android obesity), physical inactivity/sedentary lifestyle, an atherogenic diet (high carbohydrates, low fiber, high saturated fat)[78], high alcohol intake[53], and smoking[71,79]. The development of metabolic syndrome has been found to be inversely related to dietary intake of magnesium[26,80]. Chronic work stress has also been reported to be associated with the development of metabolic syndrome, possibly due to the involvement of chronic stimulation of autonomic nervous system and neuroendocrine activity.[81] (81Chandola et al., 2006). Polycystic ovary syndrome has many features in common with the metabolic syndrome and the two syndromes may share common pathogenesis.[34] The use of certain drugs (high dose diuretics, βblockers, corticosteroids, oral contraceptives, antipsychotics, protease inhibitors and niacin), which promote weight gain and/or alteration of lipid or glucose metabolism, may also increase the risk of the development of the metabolic syndrome.[82] A genetic predisposition to development of metabolic syndrome is also possible as a result of K121Q polymorphism of the ENPP1/PC-1 gene, which regulates insulin response, and is linked to obesity and type 2 diabetes.[70] The K121Q polymorphism of the ENPP1/PC-1 gene is associated with insulin resistance/atherogenic phenotypes, including earlier onset of type 2 diabetes and myocardial infarction.[83] The ACE gene insertion/deletion polymorphism is significantly associated with the metabolic syndrome.[84] Other genetic bases of metabolic syndrome have also been suggested.[85-87]

Consequences of the metabolic syndrome

The metabolic syndrome is a risk factor for CV disease, stroke, chronic kidney disease, and type 2 diabetes. Individuals with the metabolic syndrome have significantly higher risk for heart disease (2 to 3-fold), stroke (2-fold), and diabetes (5-fold)[42,51,57,60,61,63,88-90].

The presence of metabolic abnormalities commonly result in endothelial dysfunction, which leads to atherosclerosis[91,92]. Although, each abnormality associated with the metabolic syndrome promotes atherosclerosis independently, but, when clustered together, the metabolic abnormalities, especially the combination of dyslipidemia and high BP, are highly atherogenic and enhance the risk of coronary heart disease and other diseases related to plaque buildup in artery walls (e.g., stroke and peripheral vascular disease), as well as all-cause mortality (Table 3)[6,59,61,88,93-98]. Several components of the metabolic syndrome, such as insulin resistance/hyperinsulinemia are associated with LV hypertrophy and diastolic dysfunction in non-diabetic hypertensive patients[99-101]. In addition, glucose intolerance and dyslipidemia (low HDL-cholesterol and high triglycerides) accelerate LV diastolic dysfunction even in treated hypertensive patients[102,103]. In the West of Scotland Prevention Study (WOSCOPS), individuals with the metabolic syndrome had 76% higher risk of coronary heart disease event and a 3.5-fold increase in the risk of new-onset diabetes over 5 years, compared to those without the syndrome[104]. Metabolic syndrome may also hasten the development of diabetes-related complica-

tions, such as nephropathy, retinopathy, and distal neuropathy[105]. Patients with the metabolic syndrome are also at high risk for the development of many hypertension-associated target organ damage both in diabetic[106] and non-diabetic patients[107,108]. Patients with the metabolic syndrome have significantly higher prevalence of microalbuminuria compared to those without it (12.3% versus 4.7%; p = 0.004)[109]; patients with microalbuminuria are at a higher risk of developing CV disease[110]. The metabolic syndrome is also an important risk factor for the development of chronic kidney disease in people without diabetes; this risk is significant even after adjustment for other factors, and increases along with the number of metabolic syndrome risk factors present. This suggests that the metabolic syndrome directly contributes to the development of chronic kidney disease[109,111]. There are suggestions that Insulin resistance syndrome may also be a risk factor for some cancers, such as breast and prostate cancer[112-114].

Table 3. Prediction of risks by NCEP/ATP III and WHO definitions of the metabolic syndrome*

Definition:	NCEP/ATP III	WHO	Population-attributable fraction
All cause mortality	1.27	1.37	~ 6-7%
Cardiovascular disease	1.65	1.93	12-17%
Diabetes	2.99	2.60	30-52%

* As reported by Schillaci et al.,154 and Ford et al.88

Clinical significance of the metabolic syndrome

There is a difference of opinion in terms of the significance and utility of the metabolic syndrome in clinical practice. Those who favor that metabolic syndrome should be a definite diagnosis requiring special clinical management put forward the argument that the presence of metabolic syndrome (impaired fasting glucose and impaired glucose tolerance) effectively predicts the development of type 2 diabetes and CV disease[22], and that insulin resistance syndrome (another name for the metabolic syndrome) should be categorized as a specific medical diagnosis. Thus, a version of the metabolic syndrome (dysmetabolic syndrome X) has its own ICD-code (ICD-9 Code 277.7) for the diagnosis and clinical management,41 and it is recommended that this syndrome should be treated to reduce the risk of CVD and diabetes[88,89,115,116]. There is even a journal named, "Metabolic Syndrome & Related Disorders," dedicated to this entity. The American Heart Association and National Heart, Lung, and Blood Institute (USA) recommend that the metabolic syndrome should be diagnosed and treated initially with diet and exercise[117], and an aggressive global approach to screening and to the management of the metabolic syndrome should be taken to slow the growth of the syndrome throughout the United States and other countries with high prevalence of the metabolic syndrome. It may be noted that the metabolic syndrome is an incomplete predictor of absolute risk. To predict absolute risk for individuals, sometimes called 'global risk,'it is necessary to include all of the risk factors related to the outcome. For CV disease, these include age, gender, total cholesterol, HDL-cholesterol, triglycerides, BP, body mass index, glucose status, tobacco usage, and family history, depending on the risk-assessment algorithm employed[118,119].

However, an opposite view is that the metabolic syndrome cannot be a definite diagnosis, because of certain concerns regarding the definition of the metabolic syndrome, in that a) the criteria are ambiguous, poorly defined or incomplete, and the list of risk factors comprising the cluster (metabolic syndrome) is not according to one well-defined, uniformly accepted criteria and the rationale for thresholds are ill defined; b) insulin resistance as the unifying etiology is uncertain, as there is no solid evidence that insulin resistance is the main cause of the syndrome; c) the value of including diabetes (such as the WHO criteria) in the definition is questionable, and there is no clear basis for including or excluding other CV risk factors; d) the underlying pathophysiology of the syndrome is unclear, although, several CV disease risk factors may occur together, the risks with the "syndrome" appear to be no greater than the sum of its parts; e) the CV risk value is variable and dependent on the specific risk factors present, and the notion that the metabolic syndrome is a useful marker of CV risk above and beyond the risk associated with its individual components is uncertain; f) the medical value of diagnosing the syndrome is unclear and the treatment of the syndrome is no different than the treatment for each of its components[68,120].

To counteract the criticism, at least partially, the International Diabetes Federation has proposed a unifying definition of the metabolic syndrome, which is somewhat an amalgam of the three major definitions (WHO, EGIR, NCEP/ATP III) (see earlier). It is expected that the new definition may be used worldwide and remove some of the confusion,[121] and facilitate early detection by routine screening, identifying those at high risk for developing CV disease and diabetes, and implementing more intensive management to reduce the long-term risk of CV disease and diabetes[121] (http://www.idf.org/webdata/docs/ accessed August 2005). Never-the-less, the use of any metabolic syndrome definition is driven by the objective, such as epidemiological studies, clinical trials, assessment of intervention programs, public health campaigns, or clinical management of at-risk individuals.

Clinical management of the metabolic syndrome

Because of the complex etiology of the metabolic syndrome, a multi-targeted, integrated therapeutic approach is required to simultaneously treat all the risk factors, at first by lifestyle (behavioral) modification (weight control, diet, exercise, smoking cessation), based on the observations that weight control enhances lowering of LDL-cholesterol and reduces many other risk factors associated with the metabolic syndrome, and exercise decreases VLDL-cholesterol and LDL-cholesterol, increases HDL-cholesterol, and decreases markers of inflammation[122]. If lifestyle modification is not sufficient to decrease the risk factors, then pharmacotherapy be added to treat simultaneously the conventional lipid (dyslipidemia) and non-lipid CV risk factors (high BP, glucose intolerance, prothrombotic state, etc.)[90,123].

Optimal management of hypertensive patients with the metabolic syndrome

Optimal management of hypertensive patients with the metabolic syndrome requires that such patients be managed differently than patients who do not have the disorder[124], in that a multi-targeted, integrated therapeutic approach is required to simultaneously treat hypertension, obesity, lipid disorders and diabetes (if present), to fully protect CV, cerebrovascular and renal systems[42,78,90,123,125] . Lifelong lifestyle modification (weight control, diet, exercise, smoking cessation) should be instituted to be followed by pharmacologic therapy in patients with the metabolic syndrome.

a) Treatment of obesity/weight reduction

Lifestyle intervention (exercise, prudent diet) and antiobesity drugs, such as Orlistat (selective lipase inhibitor)[126-128], sibutramine (serotonin antagonist)[129-132], and rimonabant (cannabinoid-1 receptor blocker)[133,134], are useful for weight reduction. The antiobesity drugs often improve lipid profile (reduction in LDL-cholesterol, VLDL-cholesterol and triglycerides, and increase in HDL-cholesterol) in patients with dyslipidemia 130, improve glycemic control in diabetic patients[127,129], and decrease risk for CV disease[133].

b) Treatment of dyslipidemia

Lifestyle modification, cholesterol-lowering drugs, such as statins, and triglyceride-reducing drugs such as fibrates and niacin, and fatty acids of omega-3 series correct dyslipidemia[135-137]. Antiobesity drugs are sometime used to treat severely obese patients. A statin should be used initially for hyperlipidemia unless contraindicated. Statins decrease total cholesterol, LDL-cholesterol, and triglycerides[138], improve endothelial function and fibrinolytic activity (by increasing fibrinogen activator and decreasing plasminogen activator inhibitor-1, and increasing thrombin activatable fibrinolysis inhibitor)[139]; they have no effect on glycemic control. As shown by large clinical trials, reduction in total cholesterol by statins results in a significant decrease in CV events and all-cause mortality[10]. Statins can cause muscle cramps, rhabdomyolysis, and have the potential to cause or worsen congestive heart failure or diastolic dysfunction[140,141], but these may be reversed by the administration of coenzyme Q10[140,141]. Fibrates [peroxisome proliferator-activated receptor (PPAR)-β agonists] reduce LDL-cholesterol, VLDL-cholesterol and triglycerides, and increase HDL-cholesterol; they improve insulin sensitivity.

Combined statin and fibrate therapy is effective in patients with complex lipid disorders[142]. Addition of ezetimibe, a cholesterol-absorption inhibitor, to fibrate therapy further reduced LDL-cholesterol by 23% compared to statin alone[143]. In this regards, several drug combinations are being developed to aggressively treat dyslipidemia, including niacin/lovastatin, ezetimibe/simvastatin, atorvastatin/CETP inhibitor, statin/PPAR agonist, and extended-release niacin/simvastatin and pravastatin/aspirin

c) Treatment of diabetes

First of all, multifactorial strategies should be adopted to prevent the development of diabetes in individuals with the metabolic syndrome. In randomized trials, lifestyle modification, antiobesity drugs, and drugs increasing insulin sensitivity (such as metformin) prevented the development of type 2 diabetes in subjects with impaired glucose tolerance[144]. However, if diabetes is already present then aggressive treatment to control blood sugar should be instituted.

Metformin should be considered as the first drug for glucose control in patient with type 2 diabetes[123]; sulfonylureas also improve glycemic control. Metformin and thiazolinediones (such as pioglitazone and rosiglitazone, which improve insulin resistance) appear promising in the treatment of diabetic patients. However, metformin can cause lactic acidosis. Among other anti-diabetic drugs, acarbose, which inhibits postprandial hyperglycemia, can be helpful in preventing postprandial hyperglycemia. The PPAR agonists may alter the process of atherosclerosis in patients with the metabolic syndrome and type 2

diabetes. These agents have a beneficial effect on the heart: the fibrates (PPAR-β agonists) and insulin-sensitizing thiazolidinediones (PPAR-β agonists) improve LV hypertrophy and diastolic function in normotensive diabetic patients[145,146]. Pioglitazone improves LV diastolic function without an effect on LV mass in hypertensive patients in proportion to amelioration of insulin resistance and increase in the levels of adiponectin and matrix metalloproteinase-2 (MMP-2)[147]. The thiazolidinediones also have a favorable effect on BP[148]. However, the use of thiazolidinediones may cause fluid retention, edema, and idiosyncratic hepatocellular injury[149].

d) Treatment of clotting disorders

Patients with the metabolic syndrome have several disorders of coagulation that makes it easier to form blood clots, which are often a precipitating factor in developing myocardial infarction. Such patients should generally be placed on daily low-dose aspirin therapy to help prevent such clotting events[150].

Hypertension is a key component of the metabolic syndrome. More than 50% of individuals with the metabolic syndrome have hypertension[46,48,151]; patients with insulin resistance have a higher prevalence of hypertension compared with subjects without insulin resistance[152]. (152Haffner, 1997). In turn, up to 50% of hypertensive patients may have insulin resistance and other components of the metabolic syndrome[106,108,153,154]. Elevated systolic and diastolic BP independently increases the risk of atherosclerosis and coronary heart disease[1]; high BP may also exacerbate other metabolic abnormalities. Dyslipidemia, a strong predictor of CV disease, may also lead to the subsequent development of hypertension[155]; control of BP often improves lipid profile[156,157].

The presence of the metabolic syndrome amplifies hypertension-related cardiac and renal target organ damage over and above the potential contribution of each single component of this syndrome. For example, hypertensive patients with the metabolic syndrome, as compared to those without it, have higher LV mass and greater prevalence of LV hypertrophy[99,106,108], a 2-fold higher CV event rate[154], increased risk of retinopathy and microalbuminuria[158]; the later being an independent risk factor for CV death[108,159]. Metabolic syndrome is also associated with large artery stiffness, a strong predictor of CV morbidity and mortality in hypertensive patients[154].

Treatment of hypertension

The recommended target BP level (JNC-7) in treated hypertensives with the metabolic syndrome is <140/<90 mm Hg.[1] However, a substantial proportion of patients with the metabolic syndrome have diabetes and/or chronic kidney disease, and, for such individuals, the JNC-7 and ADA recommend a goal of <130/<80 mm Hg[1,160].

The first step in lowering BP should be lifestyle intervention [sodium restriction, weight control, exercise, smoking cessation and moderation of alcohol consumption (for those who smoke and/or drink), and consumption of an overall healthy diet], since such intervention has been shown to lower BP[161-163]. Lifestyle modification can also prevent the development of new onset type 2 diabetes as shown by the Diabetes Prevention Program Research Group[144]. (144Knowler et al., 2002). However, for the overwhelming majority of patients with established hypertension, drug therapy is the mainstay of treatment and lifestyle modification is merely adjunctive.

Lifestyle changes (through dietary means such as weight loss and salt restriction) are also the best way to prevent or delay the onset of hypertension in prehypertensive individuals as was shown by the Trials Of Hypertension Prevention[164,165]. However, the transition from prehypertension to hypertension is inevitable, since people who are prehypertensive have a very high risk (90%) of eventually developing hypertension[1]. The selection of drugs should be tailored to the individual, taking into account the pathophysiological determinants of the metabolic syndrome present and the presence of comorbidity (Table 4)[1-150,166].

Table 4 Recommended Antihypertensive Agent

Compelling Indication	Diuretic	Beta-Blocker	ACE-inhibitor#	ARB#	CCB#	Aldosterone-antagonist
Heart failure	XX	XX	XX	XX		XX
Post-myocardial infarction		XX	XX			XX
High **coronary** disease risk	XX	XX	XX		XX	
Recurrent **Stroke** prevention	XX		XX			
Diabetes	XX*	XX	XX	XX	XX	
Microalbuminuria			XX	XX		
Chronic **kidney** disease			XX	XX		
Obesity	X		XX	XX	X	

* Low doses; #ACE = angiotensin converting enzyme; ARB = Angiotensin AT1- receptor blocker; CCB = Calcium channel blocker

It has been recommended that antihypertensive therapy in hypertensive patients with the metabolic syndrome should begin with an angiotensin-converting enzyme (ACE) inhibitor, unless there is a compelling indication for another class of drug[123]. A number of

clinical trials and meta-analyses show that ACE inhibitors and angiotensin receptor blockers (ARBs) reduce the odds of developing new onset type 2 diabetes and also decrease albuminuria[167,168]. However, ACE inhibitors or the ARBs do not reduce the odds of mortality, CV or cerebrovascular outcomes vs standard therapy[168]. ACE inhibitors also increase bradykinin levels, which results in the stimulation of the production of the vasodilator prostacyclin and nitric oxide, and the release of tissue plasminogen activator.

Several large clinical trials, including the Heart Outcomes Prevention Evaluation (HOPE) and MICRO-HOPE sub-study, have demonstrated that ACE inhibitors provide cardioprotective and renoprotective benefits beyond their effect on BP[1,160,169]. These drugs also improve insulin resistance by increasing insulin-mediated glucose uptake, and hence may be especially appropriate in treating hypertensive patients with the metabolic syndrome.1The other advantages of using the ACE inhibitors include absence of fatigue and many other adverse effects associated with-blockers and diuretics. However, ACE inhibitors cannot be given to pregnant women in the second and third trimester. Among the adverse effects associated with the use of ACE inhibitors include the induction of cough (more in women than in men), and on rare occasions, angioneurotic edema[170]. ACE inhibitors may also cause symptomatic hypotension in salt-and/or volume-depleted patients, and hyperkalemia in patients on potassium-sparing diuretics.

Several large clinical studies, such as the Valsartan Antihypertensive Long-term Use Evaluation (VALUE) trial[171], Irbesartan in Diabetic Nephropathy Trial (IDNT)[172,173], Reduction of Endpoints in Non-insulin-dependent Diabetes Mellitus with the All Antagonist Losartan (RENAAL)[173], Candesartan in Heart Failure Assessment of Reduction in Mortality and morbidity (CHARM)-Overall[174], and the Losartan Intervention For Endpoint reduction in hypertension study (LIFE)[173,175], indicate that the ARBs, in addition to their renoprotective effect and excellent safety profile, are cardioprotective. Some ARBs (such as irbesartan and telmisartan) have partial PPAR-β agonist activity[176,177], which makes them useful as antilipidemic, antiatherosclerotic and cardioprotective agents[178,179].

Traditionally, thiazide diuretics and -blockers have been avoided in patients with glucose intolerance abnormalities, however, the safety and efficacy of these drugs has been demonstrated in large clinical trials (for example, the ALLHAT[107,179] and UK Prospective Diabetes Study[180] trials). Based upon these studies thiazides (at low doses) and -blockers have been recommended in hypertensive patients with the metabolic syndrome. In the ALLHAT study (randomized, double-blind, active-controlled clinical trial of hypertensive patients aged > 55 years who had one other risk factor for coronary heart disease), in which patients were randomized to receive either chlorthalidone, amlodipine, or lisinopril, plus open-label step-up drugs (reserpine, atenolol, clonidine, hydralazine or others) to reach goal BP, there was no difference between the drugs in the primary outcome in patients followed for a mean of 4.9 years (Figure 5)[179]. Furthermore, the presence or absence of metabolic syndrome did not make any difference in the control of BP (Figure 5). In the secondary outcomes, the diuretic was superior to the calcium channel blocker and ACE inhibitor[179]. In a post hoc analysis, neither amlodipine nor lisinopril was superior to chlorthalidone in non-diabetic patients with or without the metabolic syndrome (Figure 6), although the diuretic was more likely to induce new-onset diabetes in both groups[107,181]. In the UKPDS, atenolol was as good as captopril in target organ protection (stroke, heart failure, MI, total mortality)[180].

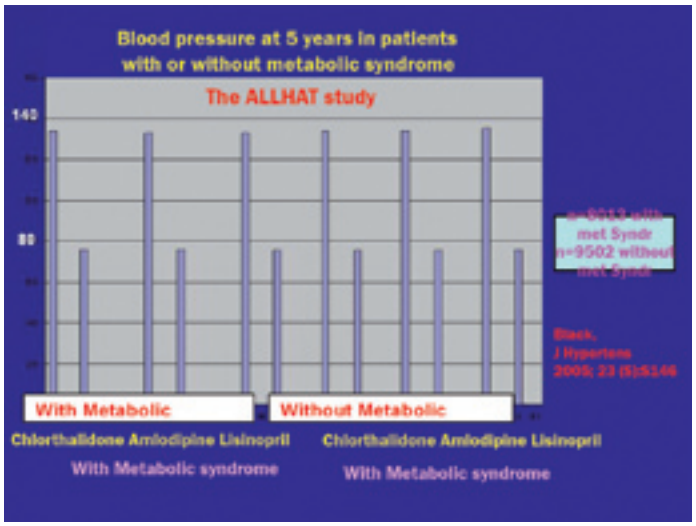

Figure 5: Control of blood pressure (systolic/diastolic) after 5 years of treatment with chlorthalidone, amlodipine or lisinopril in patients with and without metabolic syndrome (adapted from Black et al.[107])

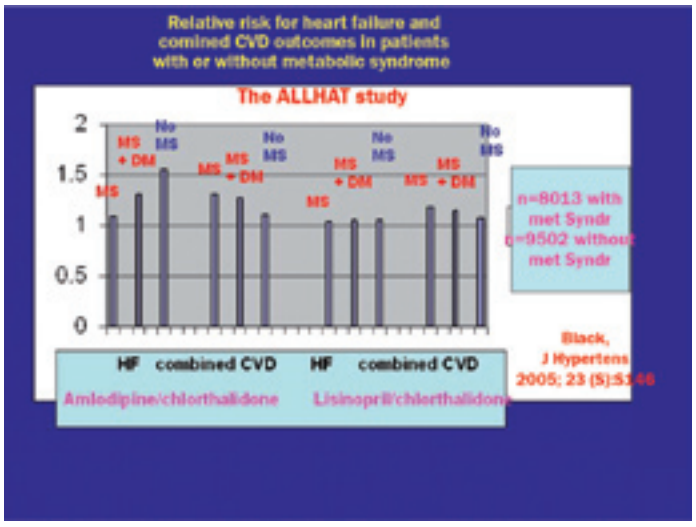

Figure 6: The relative risk for heart failure and combined cardiovascular outcomes in patients with or without metabolic syndrome (MS) and type 2 diabetes mellitus (DM) treated with combination of amlodipine/chlorthalidone or lisinopril/chlorthalidone in the AALHAT study. The ALLHAT trial (adapted from Black et al.107).

Like the ACE inhibitors, the long-acting calcium channel blockers improve insulin sensitivity[182]. The results from a large number of clinical trials show no difference in the primary endpoints between -blockers/diuretics, calcium channel blockers and ACE inhibitors[183]: [Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial [ALLHAT, n = 33,357)[179]; Controlled Onset Verapamil Investigation of Cardiovascular Endpoints (CONVINCE, n = 16,602)[184]; International Nifedipine Gastrointestinal Therapeutic System study—Intervention as a Goal in Hypertension Treatment (INSIGHT; n = 6,321)[185-187]; INVEST = International Verapamil Slow-Release/Trandolapril Study (INVEST, n = 22,576)[188]; NORDIL = Nordic Diltiazem (NORDIL, n = 10,881)[189]; Swedish Trial in Old Patients with Hypertension (STOP-Hypertension-2, n = 6614)[190,191]; United Kingdom Prospective Diabetes Study (UKPDS, n = 1414)[180]; VHAS = Verapamil in Hypertension and Atherosclerosis Study (VHAS)[192]].

Other drugs, such as celiprolol in combination with diuretics was found to have a favorable effect on glucose tolerance/insulin sensitivity in patients with essential hypertension and metabolic syndrome[193], and spironolactone added to ACE inhibitor or ARB therapy had an added reno- and CV protective benefits in patients with diabetic nephropathy[194]. Carvedilol, a β blocker with vasodilating properties, added to ACE inhibitor or ARB therapy, was more effective in preventing worsening of microalbuminuria than metoprolol in hypertensive patients with the metabolic syndrome[195]; carvedilol also improved insulin sensitivity and glycemic control[196]. Nebivolol, another βblocker with vasodilating properties, is also useful in the treatment of hypertensive patients with CV risk factors[197]; it has no effect on insulin sensitivity[198,199].

Among the newer drugs, moxonidine, a centrally active imidazoline-1 receptor agonist, effectively lowers BP and has a beneficial effect on lipid and carbohydrate metabolism[200]. Moxonidine, as an add-on drug, caused a significant reduction in BP in elderly hypertensives who were poorly controlled with two or more antihypertensive agents[201]. Moxonidine is also being used as an add-on drug to ramipril (MARRIAGE study) in hypertensive patients[202], and ramipril or eprosartan and hydrochlorothiazide in diabetic patients with severe hypertension[203]. Rilmenidine, a selective imidazoline I1 receptor agonist is an effective antihypertensive agent, which improves glucose utilization and reduces microalbuminuria[204.205].

Most patients eventually require two or more antihypertensive drugs to reach BP goal[1-160,206]. It is recommended that therapy in patients whose BP is more than 20/10 mm Hg above target at diagnosis be initiated with a combination of antihypertensive drugs[1,206]. The combinations may be given as individual prescriptions or as fixed-dose formulations[206]. Treatment with fixed-dose combinations, such as irbesartan + hydrochlorothiazide has provided with good BP control in more than two-thirds of hypertensive patients (of different ethnic groups) with the metabolic syndrome in the Irbesartan/HCTZ Blood Pressure Reductions in Diverse Patient Populations (INCLUSIVE)[207,208]. Lipid and BP targets were reached in a high % of hypertensive patients with coronary heart disease treated with a combination of amlodipine + atorvastatin[209-212].

In conclusion, the recommendations for treatment of hypertensive patients with the metabolic syndrome are that each metabolic abnormality should be treated along with hypertension to provide CV, cerebrovascular and renal protection. The ACE inhibitors or ARBs are the drugs of choice, unless contraindicated. Diuretics (at low dose), calcium channel blockers have been used effectively, and that βblockers can be used in certain cases. Fixed drug combination may also be quite useful.

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Impacto de la Unidad de Hipertensión Arterial en la Prevalencia de Presión Arterial Elevada en el área sur-oeste de Caracas años 2001-2005

*Esteban Enrique Hamilton Berti,ª * Miriam Pichardo,ª Janette Thomas,ª Salomón Benzaquen,ª Elías Chuki,* Francisco Fragachán.**
ªUnidad de Hipertensión Arterial Dr. Ángel Vicente Ochoa. Instituto Venezolano de los Seguros Sociales El Cementerio. Caracas.
**Unidad de Hipertensión Arterial del Hospital Universitario de Caracas. Universidad Central de Venezuela. Caracas. Venezuela.*
estebanhamilton@hotmail.com estebanhamilton@universia.edu.ve
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Resumen

La primera causa de consulta en los Ambulatorios del Instituto Venezolano de los Seguros Sociales a nivel nacional es la Presión Arterial Elevada, con una prevalencia de 30%. A partir del 1º Febrero del 2003 se crea la Unidad de Hipertensión Arterial del Ambulatorio del I.V.S.S. Ángel Vicente Ochoa de El Cementerio, Caracas. Realizamos un estudio retrospectivo de la consulta externa del Ambulatorio, desde Julio de 2001 hasta Diciembre de 2005. Estos son los resultados por años: Presión Arterial Elevada 2001 28%, Presión Arterial Elevada 2002 29%, Presión Arterial Elevada, 2003 18%, Presión Arterial Elevada 2004 16%, Presión Arterial Elevada 2005 16%. Total de pacientes atendidos en el Ambulatorio: año 2001 174.404, año 2002 137.328, año 2003 146.201, año 2004 219.078, año 2005 235.661. Podemos concluir que, el impacto de la Unidad de Hipertensión Arterial fue disminuir la prevalencia de Presión Arterial Elevada a 16%.

Palabras Claves: Prevalencia, Impacto, Unidad de Hipertensión Arterial.

Abstract

The first cause of consult in the Ambulatories of the Venezuelan Institute of Social Security at national level is High Blood Pressure, with a prevalence of 30%. Since February 2003 begin to work the Arterial Hypertension Unit in the Ambulatory of I.V.S.S. Angel Vicente Ochoa of El Cementerio. Caracas. We realized a retrospective study from the external consult of the Ambulatory since July 2001 to December 2005. These are the results: High Blood Pressure 2001 28%, High Blood Pressure 2002 29%, High Blood Pressure 2003 18%, High Blood Pressure 2004 16%, High Blood Pressure 2005 16%. Total attendants patients in the Ambulatory by years: 2001=174.404, 2002=137.328, 2003=146.201, 2004=219.078, 2005=234.661. We conclude that, the Impact of the Arterial Hypertension Unit was the diminution of the prevalence for High Blood Pressure to 16%.

Key Words: Prevalence, Impact, Arterial Hypertension Unit.

Introducción

Según los datos estadísticos presentados por la Dirección de Epidemiología del Instituto Venezolano de los Seguros Sociales del año 2004[1], dan como resultado que la 1ª causa de consulta en todos los Ambulatorios de esa Institución, a nivel nacional es la Presión Arterial Elevada, con una prevalencia de 30%. Debido a esta alta prevalencia de Presión Arterial Elevada se decide crear y poner en funcionamiento a partir del 1º de Febrero de 2003, la Unidad de Hipertensión Arterial del Ambulatorio Dr. Ángel Vicente Ochoa de El Cementerio, Caracas; como extensión de la Unidad de Hipertensión Arterial del Hospital Universitario de Caracas, de la Universidad Central de Venezuela. Todo esto, para mejorar las estadísticas y disminuir la prevalencia de Presión Arterial Elevada en el área de cobertura de dicho Ambulatorio, que comprende el Sur-Oeste de Caracas.

Así mismo, realizar el proyecto de crear una red de Unidades de Hipertensión Arterial en cada uno de los estados que comprenden el territorio venezolano; teniendo como misión disminuir la prevalencia de Presión Arterial Elevada a nivel nacional.

Materiales y Métodos

Se realizó un estudio retrospectivo, con las estadísticas provenientes de la consulta externa del Ambulatorio Dr. Angel Vicente Ochoa perteneciente al Instituto Venezolano de los Seguros Sociales, desde Julio de 2001 hasta Diciembre de 2005. Tomando en cuenta mensualmente las 10 primeras causas de consulta externa. Se promediaron los porcentajes de Presión Arterial Elevada por trimestres y por años. Se sumó el total de pacientes atendidos en el Ambulatorio para cada año. Todos los datos fueron aportados por el Departamento de Historias Médicas[2] de dicho centro. Se tomaron los datos estadísticos obtenidos de las investigaciones de la Unidad de Hipertensión Arterial de El Cementerio. Además, se utilizaron los datos del Departamento de Estadísticas[3] del Ambulatorio. Se tomaron en cuenta como parámetros de Presión Arterial el JNC VI[4], OMS año1.999[4], JNC VII[5] año 2003. El personal de la Unidad de Hipertensión Arterial fue homologado en la toma de Presión Arterial según las Normas de la Unidad de Hipertensión Arterial del Hospital Universitario de Caracas[6].

Resultados

Estos son los resultados recopilados en promedios: Presión Arterial Elevada año 2001 28%, Presión Arterial Elevada año 2002 29%, Presión Arterial Elevada año 2003 18%, Presión Arterial Elevada año 2004 16%, Presión Arterial Elevada año 2005 16%(Figura 1). Total de pacientes atendidos en el Ambulatorio por años: año 2001 174.404, año 2002 137.328, año 2003 146.201, año 2004 219.078, año 2005 235.661(Figura 2). Total de pacientes con Presión Arterial Elevada: año 2001 1.397, año 2002 3.392, año 2003 7.595, año 2004 7.787, año 2005 3.954 (Figura 3).

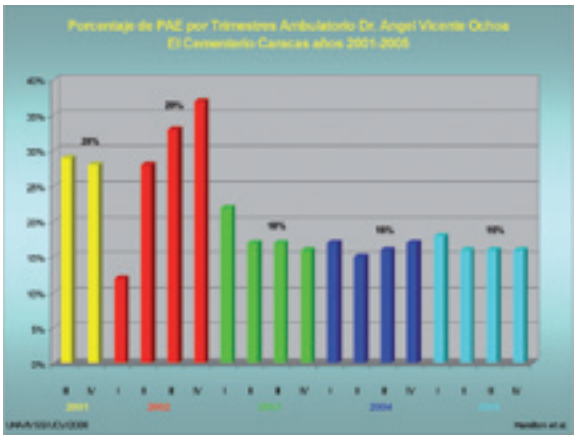
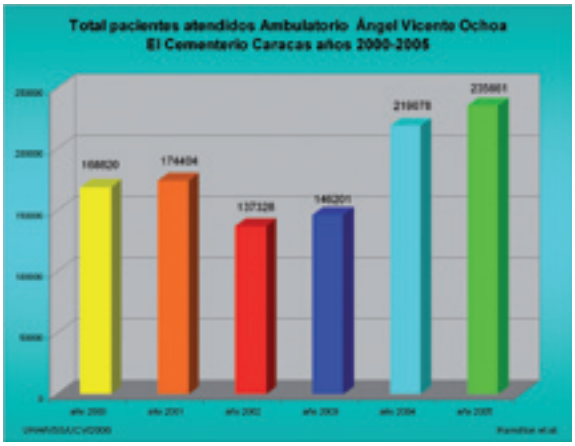


Figura 1



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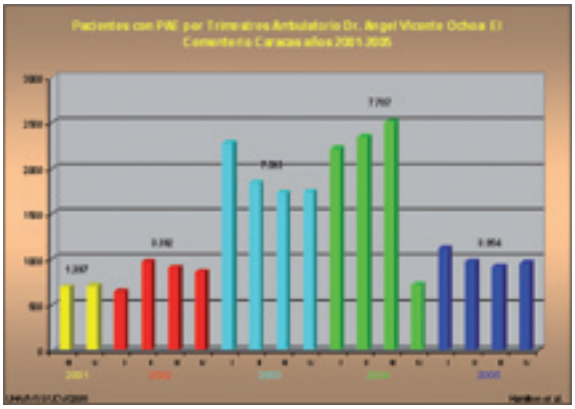

Figura 3

Primera causa de consulta Enero 2003 Presión Arterial Elevada 21%, segunda causa de consulta Virosis 17% (Figura 4). Primera causa de consulta Diciembre 2005 Virosis 18%, segunda causa de consulta Presión Arterial Elevada 16%(Figura 5). Además, de los datos obtenidos en la investigación realizada de Presiones Arteriales en zonas Altas y Llanas en los años 2003-20047, el 0,5% de pacientes menores de 19 años presentaron Presión Arterial Elevada. Así mismo se observó 7,5% de Presión Arterial Elevada Grado I y Normal Alta en niños de 2 a 6 años8 de edad durante los primeros 6 meses de 2005.

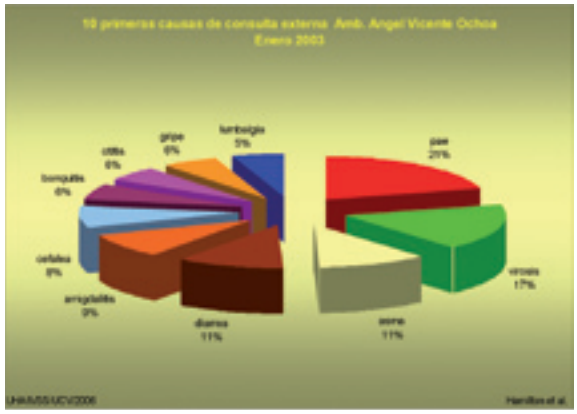

Figura 4

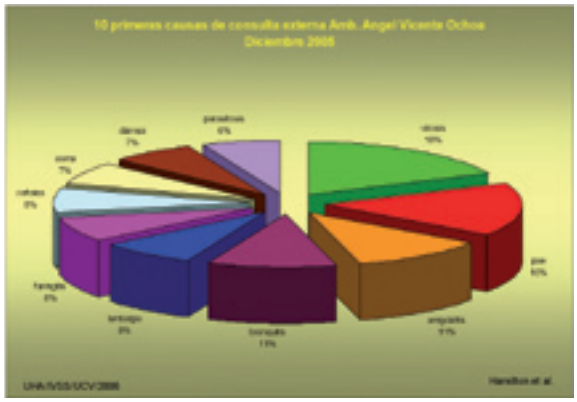

Figura 5

Discusión

Se puede concluir que, el impacto del funcionamiento de la Unidad de Hipertensión Arterial en el Ambulatorio Dr. Ángel Vicente Ochoa fue, disminuir la prevalencia de Presión Arterial Elevada de 29% en el año 2002 a 16% en el año 2005. A partir del año 2003, la Presión Arterial Elevada pasó de la 1ª causa a la 2ª causa de consulta externa, habiendo aumentado el número de pacientes atendidos en la consulta externa por año en dicho Ambulatorio. Se observó un aumento en el número de pacientes con diagnóstico de Presión Arterial Elevada en los años 2003 y 2004; por la novedad de la Unidad de Hipertensión Arterial, pero sin embargo disminuyó la prevalencia a 18% y 16% respectivamente. Se obtuvieron varios datos epidemiológicos en los años 2003-2004-2005 los cuales fueron: Presión Arterial Elevada 0,5% en menores de 19 años, Presión Arterial Elevada Normal Alta y Grado I 7,5% en niños de 2 a 6 años. Todo esto debido a que, la Unidad de Hipertensión Arterial implementó programas para la educación del paciente, investigación clínica, homologación de criterios diagnósticos y optimización de los tratamientos antihipertensivos en adultos y niños.

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Oat derived - glucan significantly improves HDLc and diminishes LDLc and Non-HDL cholesterol in overweigh individuals with mild hypercholesterolemia

Reyna-Villasmil Nadia[¥]; Bermúdez-Pirela Valmore[¥]; Mengual-Moreno Edgardo[¥]; Arias Nelly[¥]; Cano-Ponce Clímaco[¥]; Leal-Gonzalez Elliuz[¥]; Souki Aida[¥]; Inglett George E[£].

[¥]Center for Metabolic and Endocrine Research. The University of Zulia. Maracaibo-Venezuela
[£]USDA-ARS, National Center for Agricultural Utilization Research, Cereal Products and Food Science Research Unit, Peoria, USA.

Nadia Reyna- Villasmil
Address: Facultad de Medicina. Cátedra de Bioquímica. Universidad del Zulia. Maracaibo- Venezuela
Telephone number and fax: (58) 0261-7597279.
e-mail: nadiareyna@hotmail.com, nadiareyna@yahoo.com.

Abstract

Objective: To investigate the effect of bread formulated with 6 g.β- glucan in normotensive subjects with overweight and mild-to moderate hypercholesterolemia.

Design: The 38 eligible patients ate an isocaloric diet for 1-week period; they were divided in two groups. Group A was treated with step II American Heart Association (AHA) diet and Group B, treated with AHA step II diet plus bread containing β-glucan for 8 weeks. Plasma lipids were measured during baseline and after weeks 8 in all patients.

Results: There was a significant increase in plasma HDLc in the oat βglucan group from 38,9±1,9 to 48,8±2,1mg/dl;p<0,001, while B group remained without change. Oat βglucan consumption significantly reduced plasma total cholesterol and LDLc from 231,5±4,0 to 195,2±4,1md/dl and 167,6±4,0 to 122,2±3,5md/dl (p<0.001) respectively. Both diet's showed a significantly drop in total cholesterol and LDL-c total cholesterol and LDLc with no significant differences between treatments. In the ß-glucan diet, TC-LDL/HDLc ratios showed significant decreases when compared with the AHA diet. Oat β-glucan consumption diminished significantly non-HDL cholesterol compared with the AHA diet p<0.04.

Conclusions: Six gramsβglucan (Nutrim-OB) from oat administered in bread added to AHA diet and exercise can reduce lipidic risk factors associated with CVD in overweigh and mild hypercholesterolemic male subjects.

Key Words: β -glucan, oat soluble fiber, HDL cholesterol, LDL cholesterol, Non-HDL cholesterol.

Introduction

In, 1963, De Groot et al[1] were the first report that the addition of an oat product to the diet of human lowered blood cholesterol concentrations. Since the report, many animal and human studies have investigated the beneficial effects attributed to the ingestion of oat products, including improvements in gastrointestinal function, modulation of glucose metabolism, and decreased blood cholesterol concentration[2, 3].

Oats, an important source of water-soluble fiber, have long been reorganized as a potential cholesterol- lowering dietary component. In January 1997, the US Food and Drug Administration passed a unique ruling that allowed oat brand to be registered as the first cholesterol-reducing food, with a recommended dosage of 3 g β β glucans incorporated into a palatable cereal product[4].

A diet high in fiber has been linked to a decreased risk of mortality from cardiovascular disease (CVD), independent of energy intake, dietary fat intake, and other dietary factors[5]. Meta- analyses have shown that the consumption of soluble fiber, such as β -glucans in oat products, reduces blood total-cholesterol and LDL-cholesterol concentrations[6,7]. Thus, the ability of soluble fiber to reduce CVD risk is in part related to its ability to favorably modify blood lipids and lipoproteins.

The importance of decreasing low-density lipoprotein cholesterol (LDLc) levels for CVD prevention has been well recognized in clinical trials[8,9]. The risk of nonfatal myocardial infarction (MI) and coronary death was reduced by 20%-40% following treatment with LDLc-lowering drugs[10,12].

The importance of low HDLc levels (40 mg/dl) as a risk factor for the development of CVD is recognised by current British, European and US guidelines[13], although a target for raising HDLc is not specified. The National Cholesterol Expert Panel guidelines[14] (NCEP ATP III) has placed a greater emphasis on low HDLc levels and has revised the level below which HDLc is considered to be a CVD risk factor from 35 mg/dl to 40 mg/dl. Furthermore, the guidelines recommend the use of drugs for raising HDLc in individuals with isolated low HDLc levels and CVD or CVD risk equivalents[14].

No specific treatment goals are defined for HDL cholesterol and triglycerides, but the lipidic fractions are use as markers of increased risk and should also be used to guide the choice of drug therapy[13]. Current lipid-modifying therapies that raise HDLc concentration include bile acid binding resins, fibrates, nicotinic acid and statins[14,20]. Niacin[21,25] raises HDLc levels by up to 30%, and increases of 10%-15% have been reported with fibrates[22,25]. Statins and well tolerated, effective LDLc-lowering drugs with beneficial effects upon HDLc[23,28]. However, long term effects of chronic use of these drugs in dyslipidaemic patients should be considered, especially taking into account post-marketing toxicity reports about some statins and combined therapy with fibrates.

The aim of the study was to investigate the effect of bread formulated with 6 g. β - glucan in normotensive subjects with overweight and mild-to moderate hypercholesterolemia.

Subjects

A total of 38 mildly hypercholestolemic male subjects [total cholesterol: 200-240 mg/dl (5,18 - 6,2 mmol/L)] patients with body mass index (in Kg/m^2) between 25-30 were recruited from an overweigh population consulting at the Center for Endocrine and Metabolic Research (CIEM), The University of Zulia, Maracaibo-Venezuela. At entry, subjects ranked between 55 and 72 years (Mean 59,84 ± 0,61 years), with a mean BMI of 28,30 ± 0,56 Kg/m^2, mean plasma total cholesterol of 232,3 ± 2,4 mg/dL and HDLc of 40,73 ± 1,62 mg/dl. Individuals were excluded if they reported or were observed to have CVD, to have self-reported diabetes or a fasting blood glucose concentration >7,0 mmol/L, to be a systolic blood pressure >140 mm Hg or a diastolic blood pressure >90 mm Hg, to have tobacco use, to have a history of eating disorders or of thyroid gland disorders, or renal disease or to use any medications known to affect any of the dependent variables in the study. The research protocol was approved by the bioethics committee of CIEM. All subjects provided written, informed consent before participation.

Study design and measurements

The subjects were selected and well motivated. All eligible participants were committed to take an isocaloric diet for one week (wash out period). After 12-hours, fasting venous blood sample was drawn in order to measure total Cholesterol, triglycerides and HDLc by an enzymatic method (Human GmbH, Germany). LDL cholesterol (mg/dL) and VLDLc were calculated by Friedewald´s formula[33] and Non-HDLc was calculated by addition of LDLc and VLDLc[34]. After adaptation during this period, subjects were randomly assigned to one of two interventional groups: **A** control group (n=19): American Heart Association (AHA) Step II diet[31], plus whole wheat bread as main fiber 6 g/day and walking 60 minutes/day or **B** experimental group (n=19): AHA Step II diet, walking 60 minutes/day plus bread containing soluble fiber 6 g/day (Nutrim-OB, provided by USDA-ARS Cereal Products and Food Science Research Unit, Peoria, USA). β-glucan and whole-wheat bread Composition was not significantly different (Table 1). Subjects returned weekly for 8 weeks to be weighed and to obtain more bread. A combination of change in body weigh and reported physical activity were under supervision at the Nutrition Unit. Finally, at week 8, 12-h fasting concentrations of all parameters described above were assessed again.

The American Heart Association dietary guidelines for healthy American Adults recommend a diet that provides <10% of calories from SFA, up to 10% from PUFA, and as much as 15% from MUFA. The recommendation to limit total dietary fat to 30% of calories is intended to facilitate the reduction of SFA and to help control calories to manage weight in the group B, the MUFA were provided in 20%.

To evaluate the organoleptic properties of both breads, was used a test of qualification[29], which each subject completed questionnaires designed to rank acceptability, evaluating appearance, colour, aroma, texture and flavour that were rated on a scale of 0 to 9, with 0 being the worst attribute and 9 the best one[30].

Table1. β-glucan and whole-wheat bread Composition		
	Whole-wheat bread per each 100 gr.	β-glucan bread per each 100 gr.
Energy (Kcal)	306,5	244,6
Protein (gr)	9,35	9,64
Fat (gr)		
Total	5,98	1,47
SFAs		
MUFAs		
PUFAs		
Carbohydrates (gr)	52,9	48,2
Dietary fiber (gr)		
Total	2,1	8,68
Soluble (β-glucan)	0,37	6,14
Insoluble	1,73	2,54
SFA, saturated fatty acid; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid		

Statistical analyses

Data are presented as means ± EE, except for satiety, tolerance, and acceptability, which are presented as medians. Treatment effectiveness is also presented as increment or diminution percentages. Paired student t test was used to compare means before and after treatment in each group. One tailed t test was used to compare percentage increments or decreases after treatment between both interventional groups. Mann and Whitney U was used to assess differences between whole wheat bread and βglucan bread on acceptability variables. All statistical procedures were performed with SPSS version 11.01 and differences with a value of p<0,05 were considered significant.

Results

Body weigh and BMI behaviour

As noted above, a total of 38 subjects completed the study. Subjects were middle to old-aged (59,84 ± 0,61 years) and overweigh according to body mass index (in kg/m^2; 28,30 ± 0,56). Baseline energy intake (isocaloric diet) was 2582 ± 250 Kcal/day and energy intake during β-glucan diet or AHA Step II diet was 2254 ± 220 Kcal/day and 2265 ± 250 Kcal/day respectively with no significantly differences found between them.

All patients experienced a significant weight loss. However, group B had a better response from 76,8±2,6 at baseline to 71,0±2,4 Kg post-treatment (IMC: 28,4±0,8 to 26,2±0,8 Kg/m2) Vs. only 76,0±2,2 to 72,2±2,3 Kg (IMC: 28,2±0,8 to 26,8±0,8 Kg/m^2) in group A, p<0,002. Table 2.

Table 2. Body weight, fasting plasma glucose and lipid profile in group A (AHA diet alone) and group B (AHA diet plus β -Glucan supplementation)

	Group A (n=19)			Group B (n=19)			Mean treatment difference (%)[€]		
	Baseline	After treatment	p	Baseline	After treatment	p	Group A	Group B	p
Body weight (Kgs.)	76,0 ± 2,2	72,2 ± 2,3	<0,001	76,8 ± 2,6	71,0 ± 2,4	<0,001	↓4,9	↓7,5	<0,002
Body Mass Index (Kg/mts2)	28,2 ± 0,8	26,8 ± 0,8	<0,001	28,4 ± 0,8	26,2 ± 0,8	<0,001	↓4,9	↓7,5	<0,002
Fasting Plasma Glucose (mg/dl)	83,8 ± 2,6	85,6 ± 1,8	NS	88,3 ± 2,0	82,3 ± 1,9	<0,04	↑4,0	↓5,9	NS
Triacylglycerol (mg/dl)	127,7 ± 9,6	119,8 ± 7,0	NS	112,8 ± 4,3	109,9 ± 7,0	NS	↓1,8	↓4,2	NS
Total cholesterol (mg/dl)	232,8 ± 2,7	202,7 ± 6,7	<0,001	231,8 ± 4,3	194,2 ± 4,3	<0,001	↓12,7	↓15,9	NS
HDL-cholesterol (mg/dl)	42,1 ± 2,6	41,7 ± 2,4	NS	39,4 ± 2,0	49,5 ± 2,1	<0,001	↓2,2	↑27,8	<0,001
LDL-cholesterol (mg/dl)	160,3 ± 2,8	133,2 ± 5,4	<0,001	167,9 ± 4,3	120,9 ± 4,3	<0,001	↓16,8	↓27,3	<0,04
VLDL-cholesterol (mg/dl)	32,4 ± 4,2	27,1 ± 2,1	NS	23,5 ± 1,7	22,8 ± 1,5	NS	↓6,6	↓4,9	NS
Non HDL-c (mg/dl)	192,7 ± 5,7	160,3 ± 6,4	<0,001	191,5 ± 4,0	143,7 ± 3,7	<0,001	↓16,1	↓24,5	<0,04
TC/HDL-c	6,0 ± 0,4	5,2 ± 0,4	NS	6,1 ± 0,3	4,0 ± 0,2	<0,001	↓8,4	↓33,3	<0,003
LDL/HDL-c	4,1 ± 0,3	3,4 ± 0,3	<0,03	4,5 ± 0,3	2,5 ± 0,1	<0,001	↓13,3	↓42,1	<0,001

The date are mean ±EE; n=38.

[€]Treatment difference (%) = [(after treatment x 100) / baseline] – 100, where baseline and after treatment represent the mean of the absolute values from weeks 1 and 8.

NS: no significant differences

Total Cholesterol (TC), LDLc, Non-HDLc and TC-LDLc to HDLc ratios

Significant changes were found in TC (p< 0,001), LDLc (p< 0.001), and Non-HDLc (p<0,001) for both, the β glucan and wheat whole group and AHA diet (Table 2). However, ß-glucan supplementation achieved a stronger LDLc reduction from 167,9 ± 4,3 to 120,9 ± 4,3 mg/dl Vs. only 160,3 ± 2,8 to 133,2 ± 5,4 mg/dl obtained in group A. This represents a highly significantly 27,3 % fall in LDLc concentration when comparing with a smaller 16,8 % reduction in group A.

Non-HDLc exhibited a significantly drop in βglucan group from 191,5 ± 4,0 to 143,7 ± 3,7 mg/dl (-24,5%) compared with 192,7 ± 5,7 to 160,3 ± 6,4 mg/dl (-16,1%) reduction in group A, p<0.04.

The mean LDLc to HDLc ratio declined during wheat fiber from 4,1±0,3 to 3,4±0,3, p<0,03) and βglucan supplementation from 4,5±0,3 to 2,5±0,1, p<0,001). Comparing both schemes, this study showed a greater reduction in βglucan group (-42,1% vs.-13,3%, p<0,001) as well as TC to LDLc ratio (-33,3% Vs -8,4 %; p<0,003).

No significant differences were observed for VLDLc and triglycerides within and between groups, when comparing baselines at week 8.

HDLc behaviour

During the study period, HDLc concentrations increased significantly only in βglucan intervention group from 39,4 ± 2,0 to 49,5 ± 2,1 mg/dl, p<0,00. Considering percentages, we found a strong 27,8% increase in HDLc concentration compared to a 2,2 % decrease in whole wheat diet, p<0,001.

Acceptability

Data were made available for all participants explaining potential adverse effects of fiber (such as diarrhea, nausea, abdominal discomfort, abdominal distension, and flatulence). These factors were minimal for both diets, indicating slight awareness of symptoms that were easily tolerated.

All nutritional interventions were well accepted (Table 3). Each of the five attributes rated (appearance, color, aroma, flavour, and texture) had a median of 4 to 6 points in whole wheat bread and a median of 6 to 8 points in oat-derived βglucan, on a scale of 0 to 9 (Table 2). When comparing both breads, significant scores differences were found favoring to β-glucan bread in terms of appearance (p<0,001), flavor (p<0,003), and texture (p<0,001). No differences were found in aroma and color (Table 3).

Table 3. β-glucan and whole-wheat bread sensorial evaluation[€]

	β-glucan bread	Whole-wheat bread	p
Appearance	8	5	<0,001
Color	6	6	NS
odor	8	6	NS
flavor	8	4	<0,003
Texture	8	5	<0,001
Total	38	26	--

[€]Median score

High plasma levels of low-density lipoprotein cholesterol, triglycerides and reduced levels of high-density lipoprotein cholesterol, is significantly associated with an increased incidence of CVD and the improvement of this states leads to a significant reduction of cardiovascular mortality[12,14]. Thus, the combination of two lipidic risk factor calculated as index like LDL/HDL and TC/HDL ratios has also been used to estimate cardiovascular risk because improve sensitivity and specificity (6-8,20). Increasing evidence suggests that besides pharmacological treatment also lifestyle changes reduce the CVD risk[18,21]. In this context, lifestyle factor such as physical activity and dietary behavior, particularly in subjects with an increased CVD risk, are in the center of interest[16], whereas the positive physiological properties and metabolic benefits of complex carbohydrates such as fiber are still underestimated in prevention of atherosclerosis[5,8].

Presently, the National Cholesterol Education Program/ American Heart Association (NCEP/AHA) Step I and Step II diets are recommended when attempting to lower cholesterol levels. These diets are low in saturated fat as well as total fat and are considered a high-carbohydrate diet. They have been shown to lower total and LDL cholesterol by 5-14%. However, an unfortunate side effect of a high carbohydrate diet is an increase in plasma triglycerides as well as a decrease in the beneficial HDL cholesterol, two factors that increase the risk of cardiovascular disease. An alternative diet in the treatment of hypercholesterolemia is one high in monounsaturated fatty acids (MUFAs). These diets replace the saturated fat typically consumed with foods high in MUFAs, resulting in a total fat consumption greater than that of the Step I and II diets. In contrast to the NCEP/AHA diets, diets high in MUFAs do not raise triglycerides or lower HDLs and may even promote a rise in HDL

cholesterol. The majority of research performed on MUFAs has utilized olive or canola oil, both excellent sources of MUFAs, as primary food sources. By investigating other sources of MUFAs, researchers may potentially discover additional foods that will have the same beneficial effect as olive and canola oils. An increase in food sources of MUFAs known to combat high cholesterol may promote increased adherence to a high-MUFA diet.

Integration of complex carbohydrates into the everyday food patterns by unprocessed food components such as oat products seems to be well feasible and has been shown to be a safe approach for cholesterol reduction without unpleasant side effects[32,35,37].

The beneficial effect of oat products on the lipoprotein profile are ascribe to their soluble fiber compound, β -glucan[34,36]. β-glucan from oats is nonstarch polysaccharide that is composed of β-(1→4)-linked glucose units, which are separated every 2-3 units by a single B-(1→3)-linked glucose unit[37,40].

Most research studies using food as the soluble fiber source have fed oats or oat products. Brown et al[44] performed a meta-analysis of 67 controlled dietary studies and calculated that, for each gram of soluble fiber from oats, psyllium, or pectina, total cholesterol and LDL concentration decreased by ≈1.55 mg/dl (0.04 mmol/L). The meta- analysis showed no significant change in triacilglycerols and HDL. The observed changes appeared to be independent of study design treatment length, and dietary fat content. Others studies showed significantly lower total cholesterol and LDL concentrations were reported after the consumption of oat bran. Generally, no significant change was reported in triaglycerol or HDL concentration when oatmeal or oat bran was included in the diet[34,37].

The present studies showed that a mean daily 8-wk intake of 6 g β-glucan from oat bran administered in bread, had favorable effects on the serum lipoprotein profile. The oat-derived ß-glucan use in this investigation (Nutrim-OB)[37,39] lowered total cholesterol and raised HDLc concentrations significantly, since, group B elicited a significant increase (27,8%; p<0,001) on HDLc, when compared with AHA diet. This HDLc increase represents a break-down in therapeutic approach of this common dyslipidaemia because previous research with statins, fibrates or nicotinic acid has not evidenced higher elevations than oat ß-glucan therapy. Although significant reductions in LDL concentrations were found in the present study (27,3% p<0,04).

A combination of factors and mechanisms appears to contribute to the reduction in lipids observed after the consumption of soluble fiber[41,43]. Mechanisms suggested for the reduction in cholesterol after increased consumption of soluble fiber include increased excretion of bile acids or neutral sterols, increased catabolism of LDL cholesterol, and reduced absorption of fat 1-3. Increased viscosity of the gastric and intestinal contests can delay gastric emptying, decrease nutrient absorption, and interfere in micelle formation. Soluble fibers were shown to be fermented in the colon[46,48] and thus to give rise to short-chain fatty acids that can be absorbed and may inhibit hepatic cholesterol synthesis. The viscosity in the intestine may depend, among other thing, on the solubility and molecular weight of β-glucan in their oat products, in turn, may lead to a low viscosity in the intestine[41,44,48].

The mechanism for the increase in HDLc concentrations by oat -glucan is unknown but some studies suggest that amount of ß-glucan is the key determinant of HDLc concentration increases. Six grams of oat ß-glucan were administered in this study that represents a higher amount than most of the studies in which oats were evaluated previously[1,3,44,47]. Behall et al[35], however, argued that the solubility and viscosity of the ß-glucan are more important than the amount consumed for the effect on serum lipids. An increase in HDLc levels was observed when oat gum was used (in contrast with oat bran) and the authors attributed this to the low solubility and the moderate molecular weight of the oat gum, which resulted in low viscosity in the gut[41,48]. The oat ß-glucan used in this study (Nutrim-OB)[40] also had a low solubility and a low viscosity, and taking this data together we suggest that our finding may be due to a combination of higher β-glucan concentration plus the particular chemo-physical properties mentioned above.

The types of oats products used in different studies varied considerably. The β-glucan content of a good-quality commercial oat bran varies between 6% to 10%; wide ranges in concentration are found as result of different processing methods of the oat bran. The linear structure of β-glucan is very susceptible to depolymerization during processing of the oats. This lead to reduced viscosity and physiologic activity.

Non-HDLc is an important predictor of cardiovascular disease and represents cholesterol carried by all potentially pro-atherogenic apo B-containing particles, primarily VLDL, IDL, LDL lipoprotein (a) and chylomicron remnant. The Strong Heart Study, a population-based study of CHD, suggests that Non-HDL cholesterol index may be particularly useful in predicting CVD risk in patients with diabetes[28]. According to our data -glucan elicited a significant decrease on Non-HDLc (24.5%) when compared with AHA diet alone (16.5%), p<0,04. These facts support oat-derived β glucan interaction with both, lipidic pro-atherogenic mechanism and the primary anti-atherogenic mechanism: the reverse cholesterol transport.

Oat β-glucan enriched-diet elicited a significantly reduction in body weight and body-mass-index when com-

pared with AHA step II diet. Weight loss enhances insulin sensitivity and thereby glucose and lipoproteins profiles, of substantial improvemed as observed in TC-LDLc to HDLc ratios, and reflected in CHD risk reduction.

We also did not observed any significant effect of the background bread formulated with the addition of β-glucan consumption on gastrointestinal symptoms. Thus, when comparing both breads, significant scores differences were found favoring to -glucan bread (experimental group) in terms of appearance ($p<0,001$), flavor ($p<0,003$), and texture ($p<0,001$). The dose of 6g β-glucan was practical, as reflected in the volunteers´ high compliance.

In conclusion, the result of the present study suggest that 6 g β-glucan from oat administered in bread and a high MUFAs diet, in addition AHA diet and exercise can reduce risk factors associated with CVD in overweigh and mild hypercholesterolemic male subjects. These results changes in food ant nutrient intake without changing energy intake without changing energy intake.

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Obesidad en pacientes adultos en el municipio Sucre del estado Miranda

Roberto Núñez, Alejandra Peña*, Betsy Pacheco**, Maribel Sánchez**, María Rivera****
**Médicos Internos Alcaldía del Municipio Sucre del Estado Miranda.*
*** Médico Interno Hospital "Victorino Santaella Ruiz" Estado Miranda.*
****Médico Internista, Profesor Asistente, Facultad de Medicina UCV. Caracas. Venezuela.*

Resumen

Se evaluó el estado nutricional de 360 adultos que consultaron los ambulatorios "Don Pedro del Corral", "Araguaney" y las Clínicas Móviles, entre abril y junio de 2005, para el diagnóstico de obesidad, la cual se determinó según el índice de masa corporal sugerido por la Organización Mundial de la Salud (OMS) y se clasificó la obesidad en tipo I, tipo II y tipo III según la OMS. RESULTADOS: 28,88% de los pacientes femeninos que consultaron presentaron obesidad y 23,33% de los pacientes masculinos fueron obesos. Hubo obesidad de tipo I en un 65,79%, de tipo II en un 23,68% y de tipo III en un 10,52%. Los datos obtenidos fueron significativamente superiores a los datos publicados internacionalmente en Europa, Estados Unidos y el resto de Latinoamérica.

Palabras clave: obesidad, índice de masa corporal, adultos.

Abstract

It was evaluated the nutritional state of 360 adults which were attended in the health centers "Don Pedro del Corral", "Araguaney" and the mobile clinics, between April and June of 2005, in order to determinate obesity, which was determinated by Body Mass Index suggested by the World Health Organization (WHO), and it was clasificated in Type I, Type II and Type III. RESULTS: 28,8 % of female patients who consulted presented obesity and 23,3 % of male patients were obeses. There was type I obesity in 65,79 % of cases, 23,68% were type II and 10,52 % presented type III obesity. The data obtained was significatively higher to international data publicated in Europe, United States of America and Latinmerica.

Keywords: Obesity, Corporal Mass Indice, Adults.

La obesidad es una enfermedad crónica cuya prevalencia va en aumento y que plantea un serio riesgo para el desarrollo de comorbilidad como diabetes mellitus, hipertensión arterial, cardiopatías, enfermedades de la vesícula biliar, ciertas formas de cáncer y enfermedades psicosociales. Esto tiene una gran importancia pues en las últimas décadas, Latinoamérica ha sufrido una "transición nutricional", que ha implicado agregar a las distintas expresiones de la dieta latinoamericana características de la dieta estadounidense (alta en grasas saturadas y carbohidratos) con un incremento de sobrepeso y obesidad[1]. Adicionalmente, el sedentarismo, el aumento del consumo de alcohol y cigarrillo y el estrés, presente en ciudades de rápido crecimiento en países en vías de desarrollo (como en Venezuela), resultan determinantes de la obesidad y otras enfermedades crónicas y degenerativas[1]. Esta investigación se realizó con la finalidad de responder a un problema sanitario del Municipio Sucre del Estado Miranda: el subregistro de las alteraciones nutricionales de su población además de demostrar el alto índice de obesidad de los pacientes que consultan a dichos centros. Debido a que no se brinda suficiente importancia a la obesidad en Venezuela, no se toman las medidas adecuadas de educación, prevención, diagnóstico, tratamiento, seguimiento y control de esta entidad mórbida y la comorbilidad asociada, lo cual representa un problema que afecta en gran manera, tanto la calidad de vida de los que la padecen como al gasto regional y nacional en problemas de salud pública. En los datos epidemiológicos de la OMS para el año 2000, se reportaron 200 millones de obesos en el mundo, un 30% más que los datos de 1995. Para el año 2005, se ha proyectado que está cifra se encuentre alrededor de los 300 millones[2]. Si a ello se suma la población con sobrepeso, no es necesario esperar al 2025 para tener una epidemia de sobrepeso y obesidad, tal y como se proyecta con la diabetes. Hoy la población está muriendo debido al síndrome metabólico y otros factores de riesgo cardiovasculares[3]. Los aportes que trae consigo esta investigación son la obtención de datos veraces, confiables y significativos de los ambulatorios del Municipio Sucre que se tomaron como objeto de estudio y que se podrían proyectar a la situación de todo el Municipio. Se incluyeron en el estudio ambos sexos y personas mayores de 20 años, lo cual pudiera proporcionar una visión a gran escala del estado real de la prevalencia de la obesidad de adultos en el Municipio Sucre.

Materiales y métodos

La población estuvo constituida por adultos de sexo masculino y sexo femenino mayores de 20 años, pacientes de los ambulatorios "Don Pedro de Corral", "Araguaney" y en Clínicas Móviles que residieran en el Municipio Sucre del Estado Miranda. Para la obtención de una muestra representativa se tomó el promedio de pacientes adultos mayores de 20 años de los meses febrero y marzo de 2005 que acudieron a los ambulatorios "Don Pedro del Corral", "Araguaney" y los evaluados en las Clínicas Móviles como el total de individuos y en base a esto se calculó el 30% de la muestra, lo cual constituye un nivel elevado de representatividad[4]. Se seleccionó una muestra representativa mediante un muestreo opinático conformada por 360 adultos, distribuidos de la siguiente manera: 270 de sexo femenino y 90 de sexo masculino, clasificados en 12 grupos de edades: 20 a 25, 26 a 30, 31 a 35, 36 a 40, 41 a 45, 46 a 50, 51 a 55, 56 a 60, 61 a 65, 66 a 70, 71 a 75 y 76 a 80.

Como criterio de inclusión se tomaron individuos mayores de 20 años que consultaran a uno de los siguientes centros de salud del Municipio Sucre: ambulatorio "Don Pedro del Corral", ambulatorio "Araguaney" y Clínicas Móviles. Los individuos debieron consultar en el tiempo estipulado para la recolección de los datos (abril a junio de 2005). Además, el individuo debía habitar en el Municipio Sucre. Se excluyó a los individuos menores de 20 años, a las mujeres embarazadas y a aquellos pacientes cuya enfermedad afectara de manera aguda al peso del individuo, entre las cuales figuran la deshidratación, neoplasias, edema en todos sus grados, disfunciòn tiroidea, síndromes diarreicos y síndromes eméticos.

Evaluación nutricional antropométrica:

Previo al estudio, los pacientes fueron informados acerca de los objetivos, procedimientos y beneficios de la evaluación, y manifestaron su decisión de participar en el estudio.

Para el diagnóstico nutricional se evaluaron las variables edad, sexo, peso y talla y se construyó el indicador índice de masa corporal (IMC) (peso/talla^2). Para el cálculo de la edad se consideró la fecha de nacimiento a la fecha de la evaluación antropométrica. Para la determinación del peso y la talla se utilizaron tres balanzas calibradas marca Health-o-Meter. Todos los participantes fueron pesados con ropa ligera y sin zapatos y la talla se determinó con un tallímetro usando como punto de referencia el oc-

cipucio. El personal que realizó las mediciones estaba previamente entrenado y estandarizado.

La evaluación antropométrica del grupo de estudio se realizó en un lapso de tres meses (abril-junio, 2005) y para la recolección de los datos se elaboró un formato ***ad hoc.***

El indicador índice de masa corporal (IMC) se determinó para todo el grupo.

De acuerdo al IMC se consideraron las siguientes categorías según la OMS[2]: obesidad como un IMC mayor o igual a 30 kilogramos entre metros cuadrados (kg/m^2), sobrepeso un IMC entre 25 a 29,9 kg/m^2, normal un IMC entre 18,5 y 24,9 kg/m^2 y malnutrición por déficit proteico calórico un IMC menor a 18,5 kg/m^2. A su vez, la obesidad se clasificó en: clase I (IMC entre 30 a 34,9 kg/m^2), clase II (IMC entre 35 a 39,9 kg/m^2) y clase III (IMC igual o mayor a 40 kg/m^2) según la OMS[5]. Posteriormente los datos fueron exportados al paquete estadístico SPSS 11.05 para el análisis de los mismos.

La distribución según el sexo fue de 75% para el sexo femenino y 25% para el sexo masculino. El 55% pertenecía al ambulatorio Don Pedro del Corral, 29,16% al ambulatorio Araguaney y 15,83% a las Clínicas Móviles.

En la distribución por sexo se observó en la población femenina un 28,88% de obesidad, un 31,11% de sobrepeso y 32,22% de peso normal. En la población masculina un 23,33% de obesidad, un 30% de sobrepeso y 40% de peso normal.

El Gráfico 1 presenta la distribución de la muestra según IMC. Hubo un 28,89% de obesidad, 31,11% de sobrepeso, 32,22% de peso normal y 7,78% de malnutrición por déficit proteico-calórico.

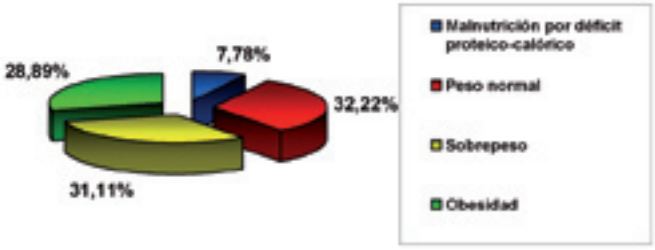

Gráfico 1. Clasificación según índice de masa corporal en adultos de los ambulatorios "Don Pedro de Corral", "Araguaney" y Clínicas Móviles (En ambos sexos).

El Gráfico 2 presenta la distribución de la muestra con obesidad según grupo etario. Se observa que de los pacientes adultos estudiados la obesidad se ve mayoritariamente reflejada en mujeres. En los siguientes grupos de edades se observó únicamente obesidad en el sexo femenino, de 41 a 45 años (12,12% prevalencia), 51 a 55 años (12,12%), 56 a 60 años (3,03%), 61-65 años (9,09%) y 66 a 70 años (3,03%). Los siguientes grupos etarios presentaron obesidad tanto en mujeres como en hombres: 20 a 25 años (9,09% de prevalencia en mujeres y 3,03% de prevalencia en hombres), 26 a 30 años (3,03% de prevalencia en mujeres y 6,06% de prevalencia en hombres), 31 a 35 años (6,06% prevalencia en ambos sexos), 36 a 40 años (6,06% de prevalencia en mujeres y 3,03% de prevalencia en hombres) y 46 a 50 años (prevalencia de 15,15% en mujeres y 3,03% en hombres).

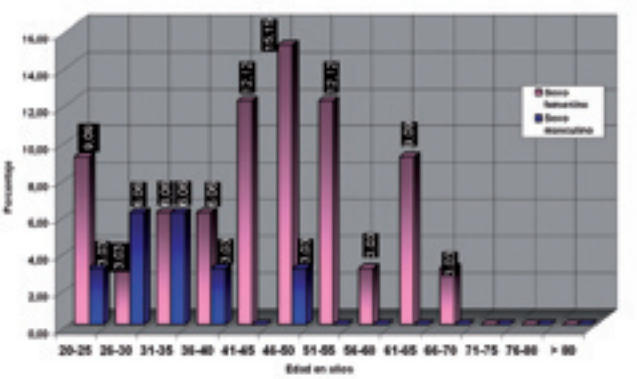

Gráfico 2. Obesidad en adultos de los ambulatorios "Don Pedro de Corral", "Araguaney" y en Clínicas Móviles (Por edad y sexo).

El Gráfico 3 presenta la obesidad clasificada en tipo I, tipo II y tipo III según grupo etáreo. Se observa que en adultos (ambos sexos) predominó la obesidad tipo I". Hubo obesidad tipo I en las edades de 20 a 25 años (10,53% de prevalencia), 26 a 30 años (2,63%), 31 a 35 años (5,26%), 36 a 40 años (2,63%), 41 a 45 años (10,53%), 46 a 50 años (10,53%), 51 a 55 años (10,53%), 61 a 65 años (7,89%) y 66 a 70 años (2,63%). Hubo obesidad tipo II en las edades de 26 a 30 años (2,63% de prevalencia), 31 a 35 años (2,63%), 36 a 40 años (5,26%), 46 a 50 años (2,63%) y 51 a 55 años (10,53%). Hubo obesidad tipo III en las edades de 26 a 30 años (2,63% de prevalencia), 31 a 35 años (2,63%), 46 a 50 años (2,63%) y 55 a 60 años (2,63%).

El Gráfico 4 presenta la distribución de la obesidad según el sexo. El 61,64% de los obesos fueron de sexo femenino y el 38,36% fueron de sexo masculino.

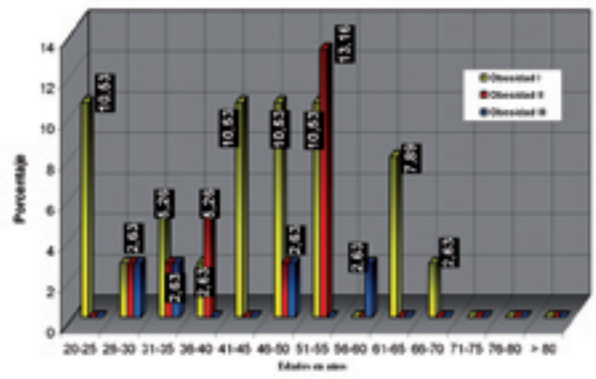

Gráfico 3. Tipo de obesidad en adultos en los ambulatorios "Don Pedro de Corral", "Araguaney" y en Clínicas Móviles (Por grupos etarios).

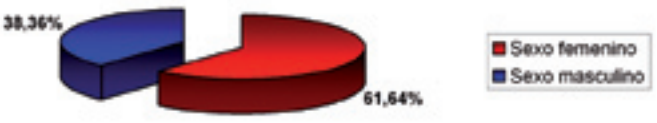

Gráfico 4. Obesidad en adultos en los ambulatorios "Don Pedro de Corral", "Araguaney" y en Clínicas Móviles (Por sexo).

peso pero en la población pediátrica, la cual muestra resultados similares a los publicados internacionalmente. Puede observarse en los resultados de este estudio que la obesidad en mujeres es mayor a la obesidad en hombres, lo cual también concuerda con los resultados internacionales donde la mujer siempre presenta una prevalencia mayor.

No se encontró estudios que cuantificaran la obesidad según la clasificación de la OMS, solo se menciona que la obesidad de tipo I es mayor que la de tipo II y ésta es más frecuente que la de tipo III[2]. En este estudio se encontró que los datos concuerdan con lo mencionado por la OMS, pues la obesidad de tipo I se presentó en el 65,79%, la de tipo II en un 23,68% y la de tipo III en un 10,52%.

En el estudio también se observó una mayor prevalencia de obesidad entre los 20 y 40 años en el caso de los hombres, y en el caso de las mujeres la obesidad tuvo mayor prevalencia entre los 31 y 55 años.

Discusión

Los resultados en este estudio revelan una prevalencia de obesidad superior a la obtenida a nivel internacional. Hubo una prevalencia de obesidad de 28,88% en el sexo femenino y 23,33% en la población masculina. Debe considerarse que los datos fueron obtenidos en las consultas de dos ambulatorios y en las Clínicas Móviles del Municipio Sucre del Estado Miranda, que llegan a ser muy representativos de la población en general. El estudio MONICA[6] de Europa publicado en 1999 reveló 15% de obesidad en hombres y 22% en mujeres en la población en general, menor a la prevalencia obtenida en el presente estudio. La Sociedad Española para el Estudio de la Obesidad (SEEDO) para el año 2000 publicó un estudio (SEEDO 2000)[7, 8] donde se determinó una prevalencia de obesidad de 15,57% en mujeres y 13,39% en hombres en la población española, menor a la prevalencia obtenida en este estudio. El National Health and Nutrition Exam Survey III (NHANES III)[9] entre 1988 y 1994 reportó una prevalencia de obesidad de 19,9% en hombres y 25,1% en mujeres, los cuales son datos más cercanos a los obtenidos en el presente estudio. En Brasil para 1989 hubo una obesidad de 6% en hombres y 13% en mujeres[10]. En Argentina, Colombia, México, Paraguay y Uruguay según datos de la OMS publicados en el 2003 se ha encontrado más de 15% de obesidad en la población[10]. Lamentablemente el Ministerio de Salud y Desarrollo Social no posee cifras de morbilidad de obesidad en Venezuela. Existen algunos estudios acerca de obesidad y sobre-

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Síndrome metabólico a propósito de un caso Hospital "Jesús María Casal Ramos" Araure- estado Portuguesa

Autoras: Dra. Jenny Paola, De Jesús Vielma; Dra. Iraima Yelitza, Rivero Meza
Araure, Estado Portuguesa. Venezuela.

Resumen

En la actualidad se considera a la Obesidad y a la Diabetes Mellitas como 2 nuevas epidemias, ya que su incidencia esta aumentando tanto en los países occidentales como en el mundo en desarrollo.

El síndrome metabólico es un conjunto de alteraciones clínicas, antropométricas y metabólicas en cuyo trasfondo existe algún grado de resistencia a la disposición de glucosa mediada por insulina; este síndrome es un complejo que predice el riesgo de diabetes Mellitas y su incidencia va en aumento.

El tercer panel para el tratamiento de adultos (ATP III) establece que dicho síndrome es una condición de riesgo cardiovascular y para determinar la existencia del mismo establecieron los siguientes parámetros: glicemia en ayunas 110 mg/dl, obesidad abdominal, hipertrigliceridemia, baja concentración de colesterol HDL e Hipertensión arterial. Según la Organización Mundial de la Salud (OMS) el diagnostico requería de una alteración visible en el metabolismo de la glucosa que este en valores 110 mg/dl.

Fisiopatologicamente el tejido adiposo excesivo presente en la obesidad juega un papel preponderante ya que este tejido libera sustancias como: ácidos grasos, factor de necrosis tumoral (FNT), leptina, resistina, factor inhibidor del plasminogeno (PAI), e interleucina 6 (IL6) entre otros, los cuales favorecen la aparición de un estado proinflamatorio de resistencia a la insulina y/o de daño endotelial.

Se calcula que para el año 2010 habrán en el mundo mas de 200 millones de personas con Diabetes Mellitas de allí la importancia de detectar y tratar oportunamente estos casos con un manejo eficaz, multifactorial e individualizado de los distintos factores de riesgo que lo definen.

Palabras claves: Síndrome Metabólico, Diabetes Mellitas, Obesidad, Insulino- resistencia.

Abstract

At the present time is considering the Obesity and Diabetes Mellitus as two news epidemics, because the incidence is increasing in the country's occidentals as soon as in the developed world.

The Syndrome Metabolic is a united of clinical, anthropometrics and metabolic alterations, in the depth exists any grade of Insulin resistance, this Syndrome is Diabetes Mellitus and the incidence is increasing.

The Third Adults Treatments panel (ATP III) established the parameter following: glicemia fast 110mg/dl, abdominal Obesity, Hipertligliceridemia, low Cholesterol HDL, and Hypertension arterial.

According to the Organization mundial de la Salud (OMS), the diagnostic requires of the presence the observable alteration of glicemia fast whit levels 110mg/dl.

Fisiopathologically the excessive adipose tissue present in the Obesity plays a preponderant roll because this tissue continually to secrete substances as: fat acid, Factor of Necrosis Tumoral (FNT), leptina, resistina, factor inhibitor of Plasminogeno (PAI), and Interleucina 6 between others which favoring the apparition of pro- inflammatory condition of resistance insulina and damage of endothelium.

Probably for the year 2010 will have in the world more than 200 millions of people with Diabetes Mellitus, wherefore the importance of to find and to treat is cases with efficacious, multiple and individually handling preventing the distincts risk factors what compound it.

Keys word: Syndrome metabolic, Diabetes Mellitus, Obesity, resistance insulina.

Introducción

El síndrome metabólico (SM) –conocido también como síndrome plurimetabólico, síndrome de resistencia a la insulina o síndrome X- es una entidad clínica controvertida que aparece, con amplias variaciones fenotípicas, en personas con una predisposición endógena, determinada genéticamente y condicionada por factores ambientales.

Según la asociación americana de endocrinólogos clínicos (AAEC) se caracteriza por resistencia a la insulina medida por hiperinsulinemia y según la Guía Europea para la Prevención de la Enfermedad Cardiovascular en la Práctica Clínica (criterios NCEP ATP-III año 2002) se caracteriza por glicemia en ayunas mayor o igual a 110mg/dl asociada a 2 o más de los siguientes criterios:
1.- Obesidad abdominal: mas de 30 Kg /mts2 de índice de masa corporal (IMC) o cuando el perímetro abdominal supera los 102cm. en hombres y 88cm en mujeres o un índice cintura cadera (ICC) mayor de 0,9 en hombres y 0.85 en mujeres.

2.- Dislipemia: colesterol HDL < 45 mg/dl en mujeres y < 35 mg/dl en hombres o TG mayores de 150 mg/dl.

3.- Presión arterial ≥ 130-85 mmHg.

Asociada o no a criterios menores como:

Hipercoagulabilidad, síndrome del ovario poliquístico, disfunción endotelial, microalbuminuria o enfermedad cardiaca coronaria.

Caso clinico

El presente caso se trata de un paciente masculino de 49 años de edad con antecedente de hipertensión arterial de larga data quien refiere inicio de enfermedad actual el 03/01/06 en horas de la noche cuando comienza a presentar disnea paroxística nocturna de moderada intensidad que limito el sueño en vista de lo cual acude a Cardiólogo quien detecta cifras tensiónales elevadas que no responden al tratamiento por lo que decide referir a este centro medico donde ingresa el 04/01/06.

Antecedentes personales patológicos: HTA desde hace 20 años sin tratamiento.

Antecedentes familiares: Padre muerto por Infarto al miocardio e Hipertenso.

Madre hipertensa, abuela y 2 tías maternas hipertensas.

Hábitos psicobiologicos: Tabaquitos: 2 cigarrillos/día. Alcohólicos moderados (fines de semana). Cafeinicos. 3 tazas/día.

Examen funcional: refiere aumento de peso de 1 Kg. al mes y aumento del apetito, refiere amigdalitis a repetición durante el ultimo año, disneas paroxísticas nocturnas ocasionales durante 1 año sin estudio ni tratamiento, hábitos evacuatorios diarios sin alteración del aspecto de las heces, micciones presentes 4 veces/ día con orinas claras abundantes y nicturia.

Examen físico de ingreso: TA: 200/100, FR: 22, FC: 65, Peso: 122 Kg.

Paciente en Regulares condiciones generales, afebril, hidratado, eupneico, conciente y orientado, con evidente exceso de peso. Ojos: pupilas isocoricas normoreactivas; Boca: edéntula parcial con caries dental, Piel: sin lesiones; Tórax: cilíndrico, simétrico, sin signos de disnea, ápex no visible ni palpable, Cardiopulmonar: Ruidos cardiacos rítmicos normofoneticos con soplo grado I/IV; pulsos simétricos palpables; murmullo vesicular presente en ambos campos pulmonares con escasos crepitantes finos bibasales. Abdomen: globoso a expensas de panículo adiposo, blando, depresible, sin megalias, ruidos hidroaereos presentes. Miembros inferiores: con edema blando, fovea positivo, no doloroso, grado I/ IV, Neurológico: conciente y orientados en los 3 planos, reflejos osteotendinosos presentes, sensibilidad conservada, sin focalización neurológica, Glasgow 15/ 15 puntos.

Paraclinicos: HB: 12,6; HTO: 38%; GB: 9700; segmentados: 62%; linfocitos: 37%; eosinofilos: 1%; glicemia: 94; creatinina: 0,6; BUN: 12,7; colesterol total: 220; triglicéridos: 258; creatinina: 0.84; glicemia en ayunas: 119.

Electrocardiograma: TS/ 88/ 0.16/ 0.10/ 0.40/ trazo: Hipertrofia ventricular izquierda, SSVI, CAI.

Rx de tórax: marcada cardiomegalia con signos de estasis vascular.

Interconsulta con nutrición: peso actual: 120,7 kg. IMC: 42,76 Kg/cm2, con un diagnostico nutricional de obesidad e hiperlipidemia indicándosele tratamiento nutricional con 1900 Kcal/día con dieta hipocalórica, hipolipidica e hipoglucidica

(28 Kg/ Kg Pi) con proteínas 1,01gr/ Kg/p, grasas: 0,76 gr/kg/p, carbohidratos 4,13 gr/Kg/p.

Tratamiento recibido al ingreso (04/01/06): furosemida: 20 mg c/8h; simvastatina: 40mg OD; captopril:25mg c/8h; ranitidina: 50 mg c/8h; Clexane: 80mg SC OD; Asa: 100mg OD; posteriormente se aumenta dosis de Captopril a 50 mg c/8 h, se disminuye dosis de furosemida a C/12h y dosis de Clexane a 40 mg SC OD, el día 09 se observa que no se ha logrado mantener al paciente normotenso por lo que modifica el esquema antihipertensivo se omite furosemida, se mantiene captopril y se asocia Carvedilol. 25 mg c/12 h, Amlodipina 10 mg c/12h, di- eudrin 12,5 mg VO c/12 h.

Evolución clínica: paciente permanece durante su hospitalización asintomático desde el punto de vista cardiovascular pero mantiene cifras tensiónales elevadas evidenciándose en los controles:

04/01/06: 200/100mmHg; 05/01/06: 210/130mmHg; 06/01/06: 170/110mmHg; 07/01/06: 160/100mmHg, 08/01/06: 150/100mmHg, el día 09/01/06 se consigue con el tratamiento antihipertensivo indicado el control de la tensión arterial por lo que se decide su egreso con seguimiento ambulatorio del caso por endocrinología, nutrición y medicina interna.

Comentarios

De acuerdo al Centro Nacional de Información de la Salud de la Mujer (NWHIC siglas en inglés), el síndrome metabólico está conectado con la resistencia a la insulina. Y debe tener por lo menos tres de los siguientes factores de riesgo:

- Obesidad abdominal: indice cintura- cadera mayor de 102 en el hombre y 90 en la mujer.
- Alta presión arterial: 130/85 o más alta.
- Intolerancia glucosa: glucosa de 110 o más alta.
- Triglicéridos altos: 150 o más alta.
- HDL bajo: este es el tan conocido colesterol "bueno."

Sindrome metabolico según aaec. (Año 2002)

Criterios mayores

- Resistencia a la Insulina (medida por hiperinsulinemia dependiente de los niveles de glucosa.
- Acantosis nigricans.
- Obesidad abdominal (circunferencia abdominal >102 cm en hombres y > de 88 cm en mujeres).
- Dislipemia (colesterol HDL < 45 mg/dl en mujeres y < 35 mg/dl en hombres o TG › 150 mg/dl).
- Hipertensión arterial.
- Intolerancia a la glucosa o diabetes mellitus tipo II.
- Hiperuricemia

Criterios menores

- Hipercoagulabilidad.
- Síndrome del ovario poliquístico.
- Disfunción endotelial.
- Microalbuminuria.
- Enfermedad cardiaca coronaria.

Diagnosticos del sindrome metabolico: según la oms (1998):

- Alteración de la regulación de la glucosa (glicemia en ayunas ≥ a 110mg/dl y/o 2 horas poscarga ≥ a 140 mg/dl).
- Resistencia a la Insulina (captación de glucosa por debajo del P25 en clamp.)

  Presión arterial ≥ a 140-90 mmHg.
- Dislipemia (TG> a 150 mg/dl y/o colesterol HDL <35 -39 mg/dl en hombres y mujeres.
- Obesidad (índice cintura/cadera >0.9-0.85 en hombres y mujeres respectivamente y/o índice de masa corporal > 30 kg/m2).

- Microalbuminuria (excreción urinaria de albúmina ≥ 20 mg/min).

La OMS señala que es indispensable para el diagnostico de Síndrome Metabólico (SM) la presencia de resistencia a la insulina y/o alteración en la tolerancia a la glucosa.

Síndrome metabólico según Nacional colesterol educación programo NCEP (ATP III.)Año 2001

- Obesidad abdominal (circunferencia abdominal > 102 cm en hombres y >88 cm en mujeres.
- TG ≥150 mg/dl.
- HDL colesterol < 40 mg/dl en hombres y < 50 mg/dl en mujeres.
- Presión arterial ≥ 130-85 mmHg.
- Glicemia basal en ayunas ≥ 110 mg/dl.

Fisiopatologia del sindrome metabolico:

La patogénesis del síndrome metabólico es compleja, intervienen tanto factores genéticos como ambientales, que van a influir sobre el tejido adiposo y sobre la inmunidad innata.

La obesidad juega un rol preponderante ya que el tejido adiposo, es muy activo en la liberación de distintas sustancias: ácidos grasos, factor de necrosis tumoral β(FNT), leptina, Resistina, factor inhibidor de la activación de plasminógeno (PAI1), IL6, etc. Estos factores pudieran favorecer la aparición de un estado proinflamatorio, de resistencia a la insulina (RI) y/o de daño endotelial.

Por otro lado, la obesidad tiene una estrecha relación con la RI. Generalmente, la RI aumenta con el incremento del contenido de grasa corporal. Los ácidos grasos libres no eterificados (AG) que se generan aumentan en plasma y se encuentran con un hígado y un músculo resistentes a la insulina. Esta mayor oferta de AG en hígado conduce a:

Aumento de gluconeogénesis, incremento en la producción de triglicéridos: aumento de VLDL, LDL, con efecto aterogénico, disminución de HDL, mayor producción de sustancias con actividad protrombótica como: Fibrinógeno, PAI1, esteatosis hepática no alcohólica por deposito de triglicéridos.

Conclusiones

En vista del auge de esta patología metabólica en nuestra población general se hace necesario conocer los criterios para el diagnostico de esta enfermedad para así poder detectar y tratar oportunamente estos casos. La prevención primaria del SM es la del manejo eficaz, multifactorial e individualizado de los distintos factores de riesgo que lo definen, para reducir el riesgo de enfermedad cardiovascular. No basta con tratar por separado cada componente del síndrome, es preciso intentar detener su origen: la resistencia a la insulina. Según las circunstancias del paciente, puede ser más conveniente alcanzar pequeñas mejoras sobre varios FRCV que intervenir enérgicamente sobre un solo factor, sin actuar en los restantes.

Es útil la detección oportunista de factores de riesgo mediante programas preventivos específicos como la dislipemia, hipertensión arterial, obesidad o tabaquismo. El inicio del tratamiento en prevención primaria vendrá determinado por el riesgo cardiovascular global del paciente. La prevención secundaria del SM se centrará en efectuar su diagnóstico y tratamiento precoz, interviniendo sobre los factores de riesgo asociados.

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