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Management of metabolic syndrome in young population

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Abstract

Metabolic Syndrome is a complex disorder associated with several cardiovascular risk factors resulting in a 2.5-fold increase in cardiovascular mortality in adults. However, over the last 20 years, the same association has been demonstrated in the young population and it is also related to a parental history of the syndrome. However, the root of the problem could be a high risk factor profile for metabolic syndrome in children and adolescents as it has been demonstrated over the last 20 years. It has been shown that the association of obesity, alterations on glucose and lipids metabolism and high blood pressure are responsible for early atherosclerotic lesion at autopsy observed in young people. The prevalence of several risk factors for cardiovascular diseases has increased in the Brazilian population, as has that of obesity, a cause of great concern due to its importance as one of the metabolic syndrome components. The anthropometrics patterns of the Brazilian population have changed over the last 30 years from undernourishment to weight excess, regardless of age, sex and socioeconomic level. The identification of such individuals, followed by primary preventive measures, changes in lifestyle, and the pharmacological treatment should be implemented aiming at reducing the cardiovascular risk in countries undergoing an economic transition, such as Brazil. The measures recommended for that age group should be focused on changing the life style trough out adoption of healthy habits such as avoiding the excessive intake of calories, salt, saturated fat and cholesterol, engagement in regular physical activity without smoking.

Key Words: Metabolic syndrome in young people; Cardiovascular risk; Overweight; Prevention; Cardiovascular disease.

Cardiovascular diseases and metabolic syndrome in underdeveloped countries

Cardiovascular diseases represent the first cause of death in developed countries, but their importance in underdeveloped ones and in those with a transitional economy has increased[1] As responsible, a set of risk factors, identified as metabolic syndrome (MS), represented by arterial hypertension, overweight/obesity, elevated levels of triglycerides, reduced levels of HDL-cholesterol, and intolerance to glucose/type 2 diabetes are rapidly evolving[2,4]. The way such association leads to coronary arteriosclerosis, which accounts for the great majority of the deaths in affected individuals, has not yet been clearly understood. However, one of the important factors is the presence of insulin resistance/hiperinsulinemia, is frequently identified in a cluster in affected individuals. The latter seems to play an important role in the pathophysiology through the activation of the sympathetic nervous system and sodium retention, in addition to stimulation of cell growth. Obesity/hiperinsulinemia seem to be the driving forces related to multiple risk factors and the development of cardiovascular diseases[3,4].

The root of the problem is a high risk factor profile and metabolic syndrome in children and adolescents

The presence of cardiovascular risk factors in the adult population is a common fact in clinical practice. However, over the last 20 years, this same association has been demonstrated in the young population and is also related to a parental history of the syndrome[5,8]. In children and adolescents, the initial alterations in each of such factors may occur in varied associations, which, even being small, ultimately determine an unfavorable cardiovascular profile for those young individuals. Bogalusa carried out a study with 4,522 individuals, whose ages ranged from 5 to 38 years, selected between 1988 and 1996, to assess

the components of the metabolic syndrome (fat index; serum insulin, glucose, triglyceride and HDL-C levels; and BP). The author suggested two independent models to explain the cause of the syndrome. One of the models included fat index and insulin, lipid, and glucose levels, and the other included only insulin levels and blood pressure. The two models explained 54.6% of the total variance in the sample, suggesting a link between the metabolic alteration and the homodynamic factor, whose common substrate was hyperinsulinemia / insulin resistance[8]. Those same clinical alterations could cause the early atherosclerotic lesions at autopsy observed in those population[9-11] .

In Brazil, the Study of Rio de Janeiro, initiated in 1983, was designed to determine the blood pressure curve in 7,015 young individuals aged from 6 to 15 years, stratified by sex and socioeconomic level, and evolved to the search of the aggregation of other cardiovascular risk factors, not only in that population, but also in their relatives. The major results of that study showed a very direct relation between blood pressure and body weight[12], aggregation of blood pressure and body mass between the members of a same family[13], anthropometrics indices, blood pressure and left ventricular mass in adolescents[14], aggregation of blood pressure and metabolic risk factors in adolescents and their relatives[15] and hyperglycemia, hyperinsulinemia, overweight, and elevated blood pressure in young adults[16].

However, of all risk factors of the metabolic syndrome, the presence of overweight/obesity emerges as the most important, especially in the United States, where its prevalence increased 2 to 4 times, particularly among the African Americans and Latin Americans[17]. But this same phenomenon has also been observed in countries with a transitional economy, such as Brazil, as shown in the research carried out by the Brazilian Institute of Geography and Statistics [18], which has confirmed an effective evolution in the anthropometrics-nutritional profile of the entire Brazilian population, including children and adolescents, in the time period between 1974-1975 and 2002-2003 (Figures 1 and 2). In such period, a significant decrease was observed in the prevalence of under nutrition, more marked in the male sex, while a continuous and intense increase was observed in overweight and obesity in both sexes, although greater among women. The findings in children and adolescents should be emphasized: in the same regions and in the same period, the prevalence of undernourished children and adolescents decreased by approximately 50%, while that of overweight/obesity doubled[19,20].

The dietary pattern has also been assessed in that same study, showing that, regardless of their socioeconomic level, Brazilians have a wrong dietary pattern as follows: an excessive amount of sugar, an insufficient amount of fruits and vegetables, and an excessive amount of fat in general, and specially of saturated fat, particularly among the higher-income families living in the most developed regions of the country (South, Southeast, and West Central)[18].

In addition, there is a great tendency towards a sedentary lifestyle, observed in all studies assessing metabolic syndrome, which propitiates the appearance of alterations related to the glucose and lipid metabolism and an increase in blood pressure, which are well-known important risk factors for the development of cardiovascular diseases. Such findings point to a real probability of an increase in the future cardiovascular morbidity and mortality rates, which have a great socioeconomic impact not only for Brazil, but also for all countries with a transitional economy.

Table 1. Components of metabolic syndrome according to NCEP-ATP III

Components	Defining level
Abdominal obesity, given as waist circumference	
Men	>102cm
Women	>88cm
Triglycerides	≥150mg/dL
HDL Colesterol	
Men	<40mg/dL
Women	<50mg/dL
Blood pressure	≥130mmHg / ≥85mmHg
Fasting glucose	≥110mg/dL

Table 2. Goals for the treatment of metabolic syndrome in young people

Glucose (mg/dL)	
Fasting glucose	<100mg/dL
Impaired glucose tolerance (2h)	<140mg/dL
HgA1c (%) in diabetes	<7%
Cholesterol (mg/dL)	
Total	<170mg/dL
HDL-c	>40mg/dL
LDL-c	<110mg/dL
Triglycerídes (mg/dL)	<150mg/dL
Blood Pressure (mmHg)	
Systolic	<130mmHg
Diastolic	<80mmHg
Weight (kg)	Weight reduction 5-10%

Therapeutic approach

Although MS comprises variables that increase the risk for cardiovascular diseases, there is a lack of specific prospective studies about that syndrome that allow the elaboration of a table of risk similar to that of the Framingham study. However, because of its high unfavorable prognostic potential, MS should be

treated seriously, as earlier as possible, as should the other risk factors occasionally present, aiming at reducing the significant cardiovascular risk associated with that condition.

The goals for the treatment of MS are shown in table 2[21]. It is worth emphasizing that its success will depend on the patient's commitment, the persistence of the health professional, and the socioeconomic conditions of those involved. This objective requires non-pharmacological and pharmacological therapeutic measures.

Non-pharmacological treatment

Non-medicaments measures aiming at a change in lifestyle, focusing on regular physical activity and a balanced diet, are the first action to be taken[22].

Excessive weight, sedentary lifestyle, and an inappropriate diet are determinants of MS, the correction of such matters being an absolute priority[21].

A well-balanced diet is one of the major measures recommended for individuals with MS, and it should be individualized for the needs of each patient. The diet should be directed to weight loss and a reduction in visceral fat, aiming at normalizing blood pressure levels, correcting dyslipidemia and hyperglycemia, and, consequently, reducing the cardiovascular risk. Evidence favors fiber-rich diets with a low content of saturated fat and cholesterol, and a reduced amount of simple sugars[21,23]. The Mediterranean diet[24] proved to reduce cardiovascular events, and the DASH diet[25] proved to reduce blood pressure levels.

At first, a diet abiding by all those recommendations is of difficult acceptance, leading to low patient's compliance. Therefore, the dietary guidance should, whenever possible, consider the socioeconomic and cultural habits of each individual. The help of a nutritionist may be useful to improve the dietary planning and to increase the patient's adherence to treatment. The total caloric value should be calculated so that the pre-established weight may be reached, considering that even a 5% to 10% reduction in weight is associated with an improvement in blood pressure levels, in metabolic control, and even in the diabetes-related mortality.

Physical activity should also be strongly stimulated, always considering each individual's age group and fitness[26]. The practice of moderate exercise for 30-40 minutes per day is undoubtedly associated with cardiovascular benefit. More intense physical activities are usually required to induce greater weight loss, and, in such cases, both for the type and intensity of the exercise, patients should be individually assessed and occasionally undergo cardiovascular evaluation.

Excessive ingestion of alcoholic beverages is related to an increase in blood pressure and triglyceride levels, and in the total caloric load[27]. A limit of alcohol ingestion of 30 mL/day is recommended for men and 15 mL/day for women.

Pharmacological treatment

The medicaments treatment may be necessary and, although it should not desirable, it has been increasingly used in young patients with elevated blood pressure, dyslipidemia, and diabetes[28]. The use of medication to treat obesity may also be considered, although the experience is still small and lacks a long-term assessment[28].

The pharmacological treatment is always indicated when no satisfactory therapeutic response is obtained with the non-pharmacological measures.

Hypertension

Decrease in blood pressure levels reduces the cardiovascular and renal morbidity and mortality. Therefore, any of the following 5 major classes of antihypertensive drugs should be used for the initial treatment of arterial hypertension: diuretics, beta-blockers, calcium antagonists, angiotensin-converting enzyme inhibitors, and angiotensin-receptor blockers[29]. Those drugs do not significantly differ regarding the cardiovascular benefits. Depending of the blood pressure level most studies assessing blood pressure control have reported that the majority of patients were on an association of anti-hypertensive drugs.

Blockade of the renin-angiotensin system has proved to be useful for the MS treatment when diabetes is present[30]. Some clinical studies on diabetic nephropathy with proteinuria have shown that renal protection is beneficial in type-1 (ACEI) and type-2 (angiotensin-receptor blocker) diabetic individuals[31].

In hypertensive individuals with BP ≥160/100mmHg, the combination of drugs should be considered since the beginning of the antihypertensive treatment. In approximately two thirds of the hypertensive patients, 2 or more drugs are required for blood pressure control, especially when the blood pressure levels are more elevated or when the goals to be achieved are strict. When drugs are combined, a diuretic should be used.

In patients with MS, a blood pressure reduction to levels lower than 130/85mmHg may be useful, considering the elevated cardiovascular risk associated with hypertension. In a type-2 diabetic patient, blood pressure should be reduced to a level below 130/80mmHg, regardless of the drug combination necessary for achieving that objective. The presence of nephropathy with important proteinuria is indicative for a reduction in blood pressure to values below 120/75mmHg[31].

Type 2 diabetes

Most patients with hyperglycemia do not properly respond to the non-pharmacological treatment. In

such cases, one or more hypoglycemic agents should be introduced to control glycemia and promote a decrease in the glycosylated hemoglobin A1c level[32] .

Diabetes is currently considered a cardiovascular disease. This change in paradigm implies a new direction in the treatment of the disease. In addition to the objective of normalizing glycemia, strategies should be directed to reducing the incidence of cardiovascular events. The adoption of stricter goals, not only in regard to glycemic levels, but also to the other associated risk factors, should be sought[33]. In regard to the oral hypoglycemic agents used in the treatment of type 2 diabetes, the ideal drug should have, in addition to the antihyperglycemic effect, an antiatherogenic action.

Type 2 diabetes results from the following 2 basic defects: insulin resistance and insulin deficiency. In the initial phases of the disease, the factor "insulin resistance" predominates, and the use of insulin-sensitizing drugs, such as metformin and glitazones, is indicated. Acarbose can also be used in that situation.

The natural history of type 2 diabetes shows that, as years go by, a progressive deterioration in glycemia occurs due to the installation of insulin deficiency. In this phase, sulfonylureas may be used in association with insulin sensitizes. Insulin deficiency may worsen, requiring the association of insulin with oral agents, and, finally, therapy with insulin alone.

Glinides and acarbose are auxiliary drugs indicated for the treatment of postprandial hyperglycemia.

Therapeutic combinations of metformin and glitazones, metformin and sulfonylureas, and glitazones and sulfonylureas have been widely used.

Dyslipidemias

The alterations in the lipid metabolism frequently bear a relation to atherogenesis, and, consequently, to atherosclerosis, and to high cardiovascular morbidity and mortality rates[27,34].

The goals of the treatment of a patient with MS regarding lipid levels are shown in table 2. It is worth emphasizing that although LDL-cholesterol levels are not one of the diagnosing criteria of MS, controlled clinical trials have reported the need for reducing LDL-cholesterol as a primary goal to be achieved with treatment, simultaneously with the correction of the HDL-cholesterol and triglyceride levels[28].

Statins are the drugs of choice to reduce LDL-cholesterol. Studies on primary and secondary prevention in adults have shown that statins reduce coronary events, the incidence of stroke, the need for myocardial revascularization, and total cardiovascular mortality[28]. Fibrates have proved to be beneficial in reducing cardiovascular events in individuals with HDL-cholesterol below 40 mg/dL, a frequent component of MS. Fibrates have also been indicated for the treatment of hypertriglyceridemia when diet and physical activity were not sufficient to correct it. Ezetimibe in association with statins causes a marked reduction in LDL-cholesterol and may be used to achieve the recommended lipid goals. The combined therapy of statins and fibrates or nicotinic acid may be an attractive option for individuals with MS who have elevated LDL-cholesterol and triglyceride levels and reduced HDL-cholesterol levels. Care should be taken regard the continuous use of statins and fibrates and Creatinophosfokinase levels should be measured 1, 3, and 6 months. If patients are stable, measurements can be repeated every 6 months. In the presence of myalgia this combination should be discontinued.

Obesity

If the non-pharmacologic measures recommended do not reduce weight by at least 1% of its initial value per month, after 1 to 3 months, the introduction of adjuvant drugs should be considered for individuals with a BMI ≥30kg/m^2, or for those with a BMI between 25kg/m^2 and 30kg/m^2 in the presence of co morbidities. Sibutramine and orlistat are the most frequently indicated drugs. Some studies have reported their favorable effects on weight loss and improvement in metabolic parameters with good tolerance and safety[35]. Drugs of the noradrenergic class, the selective serotonin reuptake inhibitors used as antidepressants are effective for weight loss but studies testing them are old and relating to the short time.

The importance of primary prevention in children and adolescents

The adoption of primary preventive measures in young individuals has been recognized as of great importance in approaching cardiovascular diseases. The demonstration of the presence of arteriosclerosis in children, adolescents, and young adults, in addition to a greater knowledge about the risk factors in those age groups, points to proposals of rational and effective programs aiming at interfering with those factors as early as possible[35,37].

The measures recommended for that age group focus on the adoption of healthy habits, such as avoiding the excessive ingestion of calories, salt, saturated fat, and cholesterol, and engaging in regular physical activity without smoking and control on alcohol intake. Health education focusing on improving nutrition, physical activity and healthy lifestyles for school children and their parents should become a leading role for physicians[38,39].

The specific prevention of obesity through diet and physical activity should be the number one priority, because its success will have a positive direct repercussion on dyslipidemia, arterial hypertension, and the alterations in the metabolism of carbohydrates[22,38,39].

The benefits associated with physical activity in young individuals include weight loss, improvement in met-

abolic parameters, a reduction in blood pressure and insulin resistance, psychic wellbeing, predisposition to maintain physical activity in adulthood, and, consequently, a decrease in the risk of cardiovascular disease and an increase in life expectancy[22,39].

In general, youngest people have been exercising less. Television, videogames, and computers tend to keep them indoors. The lack of safety in big cities inhibits walking and bike riding. At school, the new curricular requirements have reduced the time spent for physical activity. And, finally, the families have become increasingly sedentary. These observations point towards the need for actions directed to changes in the family as a whole.

Governmental programs providing specific areas for practicing physical exercise, a greater supply of physical education teachers, and improved public safety are absolutely necessary. It is also a consensus that such measures will only succeed within a context encompassing joint family, school, community, and government efforts.

Only interference at young age will be able to effectively guarantee a healthy adult lifestyle, as far as the cardiovascular system is concerned, thereby favorably influencing the elevated cardiovascular morbidity and mortality rates.

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