

26 Medical Management of Metabolic Syndrome

Abstract: The metabolic syndrome, a combination of unhealthy body measurements and abnormal laboratory test results, may identify persons at high-risk for developing cardiovascular disease. Preventive measures should be adopted and curative measure should be strictly followed.

Management of metabolic risk factor include lifestyle modification, exercise, decrease atherogenic diet. Medical management include, treatment of the atherogenic dyslipidemia, decrease blood pressure, decrease blood sugar and improving the prothrombotic and proinflammatory status. Smoking cessation, lowering the levels of LDL-C, and blood pressure management are primary targets for risk reduction.

Lifestyle intervention is the initial therapy recommended for treatment of the metabolic syndrome. If lifestyle changes are not sufficient, then drug therapy for abnormalities in the individual with risk factors may be indicated.

Researches are still going on to find out the appropriate and cheaper management strategies for metabolic syndrome.

INTRODUCTION

Through his famous Banting Oration (1988) Prof. Gerald Reaven¹ introduced the concept of insulin resistance, this syndrome has been christened as syndrome X and, now termed "Metabolic syndrome".

The prevalence varies significantly country wise and also in relation to sex and age. The incidence observed to be varies from 8% (India) to 24% (US) and in male the difference was 7% (France) to 46% (India) whereas it was 20-25% in female subjects.²

Criteria for Diagnosing Metabolic Syndrome

Various criteria defining metabolic syndrome are listed in Table 1 out of all ATP III is most commonly used and IDF is most recently introduced by American International Diabetic Foundation (Table 1).

Various clinical diseases associated with metabolic syndrome are: Type 2 diabetes, cardiovascular, essential hypertension, polycystic ovarian syndrome, non-alcoholic fatty liver disease, certain forms of cancer and sleep apnea disorder.

MANAGEMENT

"Prevention is better than cure", therefore following preventive measures are recommended:

1. Exercise regularly throughout to lead active life.
2. Encourage children to have daily physical activity at home and at school, and should be encouraged to develop taste for healthy foods.

3. Eat a healthy, balanced diet, low in saturated fat and large portion of that should include nutrient rich fruits and vegetables rich in nutrients.
4. Do not smoke or reduce it to a minimum 2-5 cigarettes per day. Similarly, alcohol intake should not be more than 50-100 ml per day (5 days/week).
5. Recognition of the fact that a genetic (inherited) predisposition could be responsible for diabetes, heart disease, and the metabolic syndrome.
6. Have regular medical check ups and initiate early treatment for high blood pressure and management of other risk factors.

Goals of Management

The primary goal of management of metabolic syndrome is to reduce risk for clinical atherosclerotic disease.⁵ Therefore first-line therapy is directed toward the major risk factors: LDL-C reduction, control of hyper-tension, and diabetes. Preventing of Type 2 diabetes mellitus is another important goal when it is not present in a person with the metabolic syndrome.

Table 2 summarizes the current goals and recommendations for management of each of the risk factors of the metabolic syndrome. These recommendations are derived in large part from existing NHLBI, AHA, and ADA guidelines for management of specific risk factors.

Abdominal Obesity

Weight reduction deserves first priority in individuals with abdominal obesity and the metabolic syndrome.³ Both weight reduction and maintenance of optimal bodymass index (BMI), best achieved by a combination of reduced calorie intake and increased physical activity and the use of principles of behavioral therapy. The aim of weight reduction is to achieve a decline of about 7 to 10% from baseline body weight during a period of 6 to 12 months. This can be achieved by decreasing the calorie intake by 500 to 750 calories per day and regular exercise. Achieving the recommended amount of weight loss will reduce the severity of most of the metabolic risk factors. The role of reduction in tea consumption have been investigated at the obesity clinic and found to be highly effective in reducing central obesity.

Currently available weight-reduction drugs, sibutramin, orlistat rimonabant has been observed to be effective in the management of obesity along with diet and exercise. In some patients with BMI above 40, bariatric surgery is often helpful.

Physical Inactivity

Increasing the physical activity assists in weight reduction and is observed to have a beneficial effect on the metabolic risk factors. Importantly, it reduces overall CVD risk.⁴ Current recommendations for the public call for sixty minutes or more of continuous or intermittent aerobic activity, preferably done every day, will promote weight reduction and maintenance of desired body weight. Preference is given to 60 minutes of moderate-intensity brisk walking or equivalent physical activity which includes using simple exercise equipment (e.g. treadmills), jogging, swimming, golfing, team sports, and engaging in resistance training. Avoidance of common sedentary activities (television watching and computer games) are highly recommended.^{5,6}

For high-risk patients (e.g. those with recent acute coronary syndromes or recent revascularization), physical activity should be carried out under medical supervision.

Dietary Measures

Besides weight control, reduction of total calories, and the intake of low glycemic index foods the diet should also be low in saturated fats, *trans* fats, cholesterol, sodium, and simple sugars.^{7,8} In addition, there should be ample intake of fruits, vegetables, and whole grains; fish (contain omega-3 fatty acids) intake should be encouraged with recognition of concerns about the mercury content of some fish. Various combinations of commercial diet having lipid, carbohydrate, protein in various proportions have been tried but none of these combinations showed satisfactory results in obtaining the goals of correcting metabolic risk factors.

Dyslipidemia

This condition consists of abnormally high levels of LDL-C, triglycerides and apoB and VLDL particles, and low HDL-C. According to ATP III,⁷ dyslipidemia can become a target for lipid-lowering therapy after the goal for LDL-C has been attained. Other lipid risk factors are secondary (Table 3).

After achieving the primary goal of LDL-C secondary goal to decrease TG and increase HDL-C should be tried (Table 4).

Blood Pressure Control

Hypertension is present without diabetes or chronic kidney disease, the goal for antihypertensive therapy is a blood pressure of <140/90 mm Hg. In the presence of diabetes or chronic kidney disease, the blood pressure goal is <130/80 mm Hg.⁹ Mild elevation of blood pressure often can be effectively controlled with lifestyle therapies: weight control, increased physical activity, alcohol moderation, sodium reduction, and increased consumption of fresh fruits and vegetables and low-fat dairy products, as per dietary approaches to stop hypertension (DASH) diet.⁸ If hypertension cannot be adequately controlled by lifestyle therapies, antihypertensive drugs are added to the regime. The benefits of therapy extended to patients with type 2 diabetes mellitus whose blood pressure is above goal level, and presumably to hypertensive patients with the metabolic syndrome. Nowadays many investigators support angiotensin-converting enzyme (ACE) inhibitors as first-line therapy for hypertension in the metabolic syndrome, especially when either type 2 diabetes mellitus or chronic renal disease is present.⁹

ARBs may be used in those who cannot tolerate ACE inhibitors or as an alternative to ACE inhibitors in people who have left ventricular dysfunction.¹⁰ The role of diuretic in treating metabolic syndrome patients is still debatable because some authors argue that they may convert Impaired Fasting Glucose (IFG) and Impaired Glucose Tolerance (IGT) to frank diabetes mellitus while according to others their benefit outweighs harms.

Elevated Fasting Glucose

In the metabolic syndrome diagnosis, elevated fasting glucose (≥ 100 mg/dL) includes both IFG and Type 2 diabetes mellitus. In metabolic syndrome patients with IFG (or IGT if assessed), weight reduction, increased physical activity, or both will delay (or prevent) the onset of Type 2 diabetes mellitus. In addition, thiazolidinediones,^{11,12} metformin,¹³ and acarbose¹⁴ will lower the risk for Type 2 diabetes mellitus in people with IFG or IGT. Except for a preliminary trial with acarbose,¹⁵ no clinical trial evidence is yet available to document that oral hypoglycemic agents will lessen the risk for cardiovascular events. Moreover, neither metformin nor thiazolidinediones are recommended in this statement solely for the purpose of preventing diabetes because their cost-effectiveness and long-term safety have not been documented. Priority should be given first to treat dyslipidemia¹⁶ and hypertension and maintain HbA1C <7%.

Prothrombotic State

In metabolic syndrome there are elevations of fibrinogen, plasminogen activator inhibitor-1, and other coagulation factors. For primary prevention, the only available long-term approach to counter their contribution to arterial thrombosis is low-dose aspirin or other antiplatelet agents. In metabolic syndrome patients who are at moderately high risk for CVD events, aspirin prophylaxis is an effective therapeutic option to lower vascular events.¹⁷

Proinflammatory State

In metabolic syndrome there is elevated cytokines (e.g. tumor necrosis factor- α and interleukin-6) and acute-phase reactants (e.g. CRP, fibrinogen). Measurement of CRP is the simplest way to identify a proinflammatory state in clinical practice. CRP levels >3 mg/L can be taken to define such a state in a person without other detectable causes. Weight reduction, will reduce CRP levels and presumably will mitigate the underlying inflammatory stimulus. No drugs that can act exclusively through this mechanism are available for reducing the cardiovascular risk. However, several drugs used to treat other metabolic risks are reported to reduce CRP levels (e.g. statins, nicotinic acid, fibrates, ACE inhibitors, thiazolidinediones).¹⁸

CONCLUSION

Statins and other LDL-lowering drugs effectively reduce the risk for CVD; adequate therapies for dyslipidemia either are not available or have not yet been proved to reduce the risk in combination with LDL lowering drugs. Insulin resistance is an attractive target. New investigational pharmacological agents like glucagons like peptide (GLP-1), dipeptidyl peptidase (DPD)-IV inhibitors and the endocannabinoid receptor blocked rim-onabant have also demonstrated promising results.

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Multiple Choice Questions

1. **Who was the first person to describe the term metabolic syndrome:**
 - A. Dr Rudolf Virchove
 - B. Dr Gerald Raevan
 - C. Dr JD Brunzell
 - D. Dr J Gustat
 2. **Which one is the latest criteria for metabolic syndrome:**
 - A. WHO
 - B. ADA
 - C. ATP III
 - D. IDF
 3. **Which is false regarding in ATP III criterias:**
 - A. Fasting blood sugar more than 100 mg/dl
 - B. Blood pressure above 130/85 mm Hg
 - C. Triglyceride above 150 mg/dl
 - D. HDL-C < 40 mg/dl in men
 4. **What is the drug of choice in treating hypertension in metabolic syndrome:**
 - A. Diuretics
 - B. Beta-blocker
 - C. ACE inhibitors
 - D. Calcium channel blockers
 5. **Which dyslipidemia in metabolic syndrome should be corrected first:**
 - A. HDL -C
 - B. LDL-C
 - C. VCDL-C
 - D. Triglyceride
 6. **In very high-risk patients for CVD what should be the optimal goal for LDL-C:**
 - A. < 150 mg/dl
 - B. < 130 mg/dl
 - C. < 100 mg/dl
 - D. < 70 mg/dl
 7. **All drugs reduces the CRP level *except*:**
 - A. Statins
 - B. Nicotinic acid
 - C. Calcium channel blocks
 - D. ACE inhibitors
 8. **All are include in metabolic syndrome *except*:**
 - A. ISH (Isolated systolic hypertension)
 - B. Obesity
 - C. Hyperinsulinism
 - D. Dyslipidemia
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1. B 2. D 3. A 4. C 5. B 6. D 7. C 8. A