Metabolic syndrome, with the main clinical manifestations of obesity, dyslipidemia, elevated blood pressure, and elevated blood glucose levels, has become an increasingly prevalent global public health concern.

Metabolic syndrome is a convergence of multiple risk factors related to cardiovascular disease. When the concept of metabolic syndrome was initially proposed, some researchers thought the concept was unnecessary, since there were already measures in place to describe the separate cardiovascular risk factors such as dyslipidemia, hypertension and diabetes. However, a large number of epidemiological investigations confirmed that even if blood glucose or blood pressure did not reach the cutoff point of the diseases, the superposition of multiple risk factors serves to amplify the damage of a single factor to the cardiovascular system. A meta-analysis of 87 clinical studies including 951,083 cases showed that the relative risk (RR) of metabolic syndrome for cardiovascular disease is 2.35, RR of death from cardiovascular disease is 2.40, and RR of stroke is 2.27. The study showed that even the non-diabetic individuals who suffered from metabolic syndrome may still have an increased risk of cardiovascular diseases[1]. Therefore, having a clear definition for the diagnosis of metabolic syndrome provides guidelines for clinicians and patients to recognize the early warning signs for a high-risk population.

This can properly inform early interventions to prevent and control cardiovascular risk factors derived from obesity and abnormal distribution of fat, as well as appropriate management of actual cardiovascular disease[2].

The report of the National Heart, Lung, and Blood Institute/American Heart Association Conference on scientific issues related to the definition of metabolic syndrome issued a comprehensive explanation on the existing and emerging trends of the therapeutic development for metabolic syndrome[3]. According to the report, the first target of intervention for metabolic syndrome was obesity, but weight-loss drugs such as sibutramine and orlistat were not suitable due to their potentially serious side effects. Hence, weight loss relies mainly on controlling diet and increasing exercise, but patient have poor compliance in these areas.

Insulin-sensitizing medications play an important role in the treatment of metabolic syndrome. The United Kingdom Prospective Diabetes Study showed that metformin could significantly reduce the incidence of cardiovascular diseases in obese diabetic patients and prevent or delay impaired glucose tolerance from deteriorating into type 2 diabetes. However, there is no official consensus on the relationship between the application of metformin to metabolic syndrome patients and the incidence of cardiovascular disease. Therefore, the application of metformin is not currently recommended for metabolic syndrome patients to reduce the risk of cardiovascular diseases. The use of rosiglitazone, an insulin sensitizer, is severely restricted because it may increase the risk of cardiovascular diseases including myocardial infarction, stroke, heart failure, and death. It is only used for patients with type 2 diabetes who cannot control the disease with anti-hyperglycemic agents; it is not recommended as a prophylaxis for patients with metabolic syndrome or diabetes[4].

Statins can reduce the risk of cardiovascular events in metabolic syndrome patients. Fibrates may decrease lipid abnormality that then results in atherosclerosis, or even directly reduce atherosclerosis. Recently, several clinical trials on fibrates have shown that they can decrease death...
rate of cardiovascular disease of patients with metabolic syndrome or with lipid abnormality-resulted atherosclerosis. In addition, clinical studies have also demonstrated that combination therapy of statins-fibrates provides enhanced therapeutic effects, but close attention must be paid in order to avoid strong side effects.\[5\]

Metabolic syndrome patients with high blood pressure should change their lifestyles, and at the same time, their hypertension should be treated according to the recommendations of the hypertension treatment guidelines. Currently, it is difficult to distinguish which kinds of antihypertensive drugs are best for metabolic syndrome patients. Angiotensin-converting-enzyme inhibitor (ACEI) or angiotensin II receptor blocker (ARB) may be better choices, considering that metabolic syndrome patients tend to develop microalbuminuria.

There is still no specific chemical medicine targeting plasminogen activator inhibitor 1 and fibrinogen. Small doses of aspirin can reduce cardiovascular events in both primary and secondary prevention, thus aspirin can be used as part of the primary prevention treatment for metabolic syndrome. However, it does not exert therapeutic effects via modulating fibrinolytic activity.

Attention to anti-inflammatory drugs is growing. It is known that several lipid-lowering drugs are effective in reducing the level of C-reactive protein, which implies anti-inflammatory effects by these medications.

Metabolic syndrome patients with type 2 diabetes are a high-risk group among cardiovascular disease patients. Reducing cardiovascular risk factors should be a major goal. Lifestyle changes and using anti-hyperglycemic agents are necessary to reduce the hemoglobin A1c (HbA1c) levels below the target level according to the guideline. Although pharmaceutical treatment on metabolic syndrome has advantages in tackling hyperglycemia, hypertension or dyslipidemia, it remains restricted within the framework of each disease component. There is no one drug, or class of drugs, that can comprehensively intervene in multiple cardiovascular risk factors. The establishment of the concept of metabolic syndrome has not brought about the breakthrough in pharmaceutical treatment, which has several obvious reasons. First of all, there is a shortage of drugs that effectively address obesity, especially central obesity. Second, there are no ideal insulin-sensitizing agents. Third, there is a lack of drugs that have effective fibrinolytic properties. And last, there is insufficient indication for the usage of drugs in patients whose disease measurements fall below the cutoff point of their diagnosis parameters, i.e., having elevated blood pressure and blood glucose, but not reaching the diagnosis of hypertension or hyperglycemia. In contrast, traditional Chinese medicine (TCM) is able to compensate for these insufficiencies to some extent. Therefore it is reasonable to use a combination of traditional Chinese and Western medicine strategies to better cope with the challenges of treating metabolic syndrome.

There are several reports on using TCM in the prevention and treatment of metabolic syndrome, covering TCM etiology, pathogenesis, classification and prescription. But consensus on its core pathogenesis and pattern differentiation is still lacking. The research community also lacks a solid scientific position on how best to exert the advantages of TCM in addressing metabolic syndrome.

The scientific research teams of Huashan Hospital of Fudan University and Yueyang Hospital of Integrated Traditional Chinese and Western Medicine of Shanghai University of TCM have established the therapeutic principle, treatment type, prescriptions and selected drugs for metabolic syndrome on the basis of analyzing the etiology and the core pathogenesis according to TCM theory through literature study and the summary of clinical experience. They have carried out the study of integrative medicine for the multiple components of metabolic syndrome. According to them, the main feature of metabolic syndrome is that the nutrients absorbed cannot be normally transformed into energy due to insulin resistance, which is considered “spleen-deficiency with failure in transportation” in TCM theory. Accumulated sugar and fats in the blood may lead to diabetes and hyperlipidemia, and those accumulating in the body may result in central obesity and fatty liver. These in turn are converted into pathogenic heat, phlegm turbidity and static blood over the time, eventually causing damage to the regulatory function of blood vessels, which may lead to the development of hypertension. Microalbuminuria can arise if pathogenic heat causes injuries to the kidneys, or blood stasis blocks collaterals and damages kidney function. According to the TCM theory, the research team has created a formula called “Yiqi Huaju Formula”, based on the purging-tonifying principle, to treat metabolic syndrome. “Yiqi” is to promote the spleen function of transformation and the absorption of nutrients to convert them into energy, which is the TCM view on improving insulin sensitivity; “Huaju” is to eliminate and dissipate the pathological products produced by metabolic disorder, which is the TCM view on decreasing the inflammatory response and promoting fibrinolytic activity.

In the treatment of a group of patients with central obesity, it was shown that Yiqi Huaju Formula exerted several important effects, including increasing insulin sensitivity and regulating adipocytokines; increasing adiponectin levels as well as lowering leptin levels, body mass index and waist circumference; changing the abnormal fat distribution; regulating lipid metabolism; as well as reducing postprandial triglyceride levels and inhibiting inflammatory cytokines, and in particular, promoting fibrinolysis, which is an area of weaknesses in the chemical drugs indicated
for anticoagulation\[7\]. These studies also showed that Yiqi Huaju Formula not only improves insulin resistance, but also has preventive and therapeutic effects on the six risk factors which play important parts in the development of cardiovascular disease and are the major areas of concern indicated by the report of the National Heart, Lung, and Blood Institute/American Heart Association, namely body weight, blood pressure, blood lipids, blood glucose, inflammation and coagulation status. The formula conforms to the basic requirements for the treatment of metabolic syndrome, and shows a good application prospect to meet the challenges of managing metabolic syndrome with integrative medicine.

Nonalcoholic fatty liver disease is one of the important diseases related to metabolic syndrome. Simple lipid-lowering therapy based on patient dietary and lifestyle education has some positive effects; with the addition of Yiqi Huaju Formula, treatment efficacy improves significantly, manifesting as enhanced insulin sensitivity, reduced waist circumference, improved serum lipid profile, and aspartate aminotransferase and alanine aminotransferase decreased almost to normal levels. Inflammatory cytokine levels are reduced and CT examinations show that more than 90% of patients with liver fatty infiltration are corrected\[8\].

As an important component of metabolic syndrome, microalbuminuria is one of the major clinical manifestations of early diabetic nephropathy and also an independent risk factor for coronary heart disease. Some patients still cannot control the progress of kidney disease after treatment with ACEI or ARB and anti-hyperglycemic medications. A clinical study showed that with the help of Yiqi Huaju Formula, patients had reductions in their homeostasis model assessment index, waist circumference, fasting and postprandial 2-hour blood glucose, HbA1c, the ratio of urinary microalbumin/creatinine and 24-hour urinary protein levels. The improvements in the experimental group was superior to the control group which only used chemical drug treatments, and achieve more comprehensive intervention on multiple cardiovascular risk factors. Integrative medicine combining TCM and chemical drugs can provide more optimal therapeutic effects on metabolic syndrome. It should be the one of the reasonable strategies to consider in the management of metabolic syndrome.

REFERENCES

English.
