EDITORIAL

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Oxidative stress, point-of-care test, and metabolic syndrome

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Recently, there has been a tremendous interest in the role of reactive oxygen species (ROS) and reactive nitrogen species and their imbalance in the pathogenesis of various human diseases [1]. The overproduction of ROS poses a damage to cell structures, including membranes, proteins, and DNA, which seem to be linked to diverse disease states, such as diabetes, atherosclerosis, hypertension, cardiovascular diseases, cancer, and neurodegenerative diseases [1,2]. Moreover, there are mounting evidence to support that oxidative stress is closely related to metabolic syndrome, which is a cluster of cardiovascular risk factors composed of hyperglycemia, hypertension, dyslipidemia, and abdominal obesity [3].

Although the earliest reference to metabolic syndrome goes far back to the mid 1960's by Camus, and it has gained even greater interests since 1989 when Reaven termed it syndrome X, there is no clear understating as to how each components of metabolic syndrome are linked to one another, and how they cause cardiovascular diseases [3]. Meanwhile, oxidative stress has been shown to be related to each components of metabolic syndrome. For example, abdominal obesity, or more precisely, visceral fat accumulation induces increase in systemic lipid peroxidation and damage through excess free fatty acids and cytokines like tumor necrosis factor-α, which then trigger systemic oxidative alterations [4]. Secondly, patients with metabolic syndrome displayed significantly lower superoxide dismutase (SOD) and glutathione peroxidase activities, and type 2 diabetes patients showed positive associations with systemic oxidative stress, measured by increased concentrations of urinary 8-epi-prostaglandin F2a and 11-dehydro-thromboxane B2 [5]. Oxidative stress may contribute to the development of type 2 diabetes by activating stress-signaling pathways such as nuclear factor-κB pathway as well [5]. As for hypertension, antioxidant and oxidant imbalance is a well known physiological regulator of arterial pressure, and recent studies s showed that oxidative stress causes endothelial dysfunction, leading to increased blood pressure and coronary artery disease [6]. Hypertensive subjects show elevated oxidative stress and compromised antioxidant capacities [6]. In terms of dyslipidemia, many animal and human studies show increased ROS production, nicotinamide adenine dinucleotide phosphate oxidase activity, and many oxidative stress markers and lowered SOD and endothelial nitric oxide synthase in

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dyslipidemia [3].

Based on abundant data on correlations between oxidative stress and components of metabolic syndrome, namely atherosclerosis, hypertension, type 2 diabetes, adiposity, and insulin resistance, some researchers suggest oxidative stress as an early event in the pathology of metabolic syndrome or a candidate for a central pathogenic role [3,4]. Strong associations have been found between oxidative stress and metabolic syndrome itself. Increase in advanced oxidized plasma protein, which are indicators of nitrosative stress, have been found in metabolic syndrome [7], and a significant decrease in total antioxidant status and vitamins C and E were observed in metabolic syndrome [8]. Various markers related to oxidative stress and antioxidant status have been studied so far, and many were shown to be in close relations to the presence of metabolic syndrome, each components of metabolic syndrome as well as proportional to the number of factors of metabolic syndrome.

The authors in this issue measured the antioxidant capacity using Biological Antioxidant Power (BAP) test and assessed relationships with the present of metabolic syndrome and related factors [9]. BAP test is based on the capacity of a colored solution containing a source of ferric ions bound to a special chromogenic substrate to discolor when ferric ($Fe3^{+}$) ions are reduced to ferrous ($Fe2^{+}$) ions. The intensity of chromatic change is proportional to the capacity of plasma to reduce ferric ions to ferrous ions, or the antioxidant capacity [9]. BAP test is a relatively simple point-of-care test (POCT) to measure antioxidant capacity that requires only a single drop of capillary blood and a short incubation period of 5 minutes. There are several other POCTs to measure oxidative stress, including free oxygen radicals testing test, free oxygen radicals defence test, and ferric-reducing ability assay, and each method is sensitive to different antioxidants in a different manner and the interaction between antioxidant components may affect the results. There is no single assay that is more representative of the antioxidant capacity or oxidative stress [9,10].

While many studies have shown a close relationship between metabolic syndrome and various conventional markers of oxidative stress, not much has been studied with antioxidant capacity measured by POCT, which can be readily done anywhere. Kim et al. [9] have demonstrated a close correlation between total antioxidant capacity from BAP test and the presence of metabolic syndrome as well as related factors, including homeostasis model assessment-estimated insulin resistance, high sensitivity C-reactive protein, and serum adiponectin level. However, there are several points to be considered. First, not all antioxidant reduce ferric ions to ferrous ions, which means that some antioxidants will be not determined by BAP assay, and some nonantioxidant reducers reduce ferric to ferrous ions exist that would cause falsely high result. Also, confounding factors such as uric acid and ascorbic acid which are major antioxidants contributors of the assay must be taken into account.

Oxidative stress, indeed, seems to play a major role in metabolic syndrome, and a simple, cheap way of measurement may be beneficial in screening patients with metabolic syndrome. However, more extensive well-controlled studies are required in different and larger groups of patients to test reliability and reproducibility to test these POC testing methods, and since each assay is based on different redox system with various limitations, more than one method may not be adequate to evaluate the total antioxidant capacity.

Conflict of interest

No potential conflict of interest relevant to this article is reported.

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