

# Diabetes May Influence Blood Pressure on Antihypertensive Drug

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## Commentary

As to metabolic syndrome (Met-S), the frequency of hypertension and diabetes increases with the progress of arteriosclerosis. Its pathophysiological mechanism also involves the control of the nervous system. In other words, regarding the adjustment of blood pressure in humans, the blood pressure will fluctuate by adjusting mechanism of the nervous system, corresponding to the body position, movement, exercise and psycho-psychiatric changes in various situations. There is no problem in normal persons concerning these regulatory mechanisms. However, in the patients associated with hypertension or previous stroke, the mechanism for instantaneously regulating blood pressure has been impaired. Therefore, blood pressure may rise or fall suddenly in such patients.

In this article, I would like to describe recent various findings related to Met-S, hypertension and diabetes and introduce our study results concerning discontinuation of antihypertensive drug. Met-S was originated and studied from syndrome X in 1980s [1,2]. Since then several kinds of diagnostic criteria have been found in each association and country [3]. In recent years, prevalence of Met-S has been gradually elevated for decades, including medical, social and economic problems [4-6]. This tendency has been spread in every country [7].

Met-S has been also defined as a cluster of interconnected metabolic abnormalities accompanied by glucose metabolism. They also include dyslipidemia, elevated blood pressure and central obesity [8].

According to lots of reports so far, Met-S increases the risk of death from all causes including type 2 diabetes and cardiovascular disease [9]. Furthermore, Met-S is also associated with other co-morbidities including thrombosis and pro-inflammatory conditions, non-alcoholic steatohepatitis and reproductive disorders and certain types of cancer [10].

Hypertension included in Met-S has been called 'silent killer'. Without any symptoms, it always exacerbates arteriosclerosis for years. The frequency is high in each country worldwide and its treatment, care and prevention for hypertension would be important from adulthood to middle-aged and elderly. Therefore, in recent years, various guidelines have been presented in each country.

There have been several guidelines for hypertension and heart disease, in Japan [11], in North American region [12,13] and in European countries [14,15]. In addition, some related guidelines for patients with lipid and obesity are found [16,17] and guidelines for young generation and the elderly have been also presented in recent years [18,19]. In the future, treatment and management for hypertension would be continued for comprehensively utilizing these guidelines for patients with metabolic syndrome suffering from some diseases.

To investigate the treatment of many patients, two dimensional viewpoints of warp and weft are important, which is longitudinal thread and transverse thread, respectively. The former is medical treatments on hypertension for several decades. On contrast, the latter is to examine and evaluate various data in epidemiological way.

There are some examples as follows: how many people are already treating with hypertension, how many people have hypertension tendency in preclinical stage, how much extent does certain antihypertensive drug lower the blood pressure in the relevant population, what kind of treatment or care should be done for hypertension in a certain country, what kind of beneficial outcome will be expected by this policy and so on [20]. Among them, in addition to drug administration, it will be necessary to investigate and examine the contents and effects of "non-drug therapy" for hypertension [21].

Non-medicinal therapy usually means our lifestyle, including meal, exercise, rest, alcohol and smoking. There has been 2017 High Blood Pressure Clinical Practice Guideline, which is a Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines [13]. It showed six aspects for recommendations for non-pharmacological interventions at the level of 1-A.

These are summarized to weight loss [22], a heart-healthy diet such as the DASH (Dietary Approaches to Stop Hypertension) diet [21], sodium reduction [23], potassium supplementation [24], increased physical activity [25] and reduction in alcohol consumption [26].

The author and colleagues investigated lot of hypertensive cases who could discontinue the administration of anti-hypertensive drugs [27]. We have thousands of cases of hypertension in a year, in which 4.6%-6.1% cases could stop antihypertensive drugs in a few years. For example, 50 cases with each 25 in male and female were studied in detail. There were family histories of hypertension 33 cases (66%) in women, smoking 76% in men, alcohol consumption 60% in men, 42% for dyslipidemia 42% and type 2 diabetes mellitus (T2DM) 12%. The frequency of 12% may be lower than expected, in comparison with others.

For these results, some possible reasons were speculated. Diabetic status can cause microangiopathy and macroangiopathy associated with neuropathy including peripheral and autonomic regulation. Then, hypertensive patients with diabetes may be rather difficult to discontinue antihypertensive drugs because of impaired mechanism of neural and vascular regulation of blood vessels. Probably, the cases with successful discontinuation of drug may have several necessary factors with light hypertension, regular life, limited status of obesity, diabetes and other influential impairments.

Moreover, discontinuation of antihypertensive treatment is affected by a large number of factors in a real life setting [28]. They include type of antihypertensive treatment, co-treatments, clinical conditions, social and environmental factors where the patient lives.

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As for the diabetes guidelines, changes have been observed recently. American Diabetes Association (ADA) followed the joint algorithm of European Diabetes Society (EASD) 2012 [29] until 2017 [30]. For example, metformin is used as an initiator, and various drugs are listed as horizontal lines.

On contrast, recommendations were changed in the 2018 edition [31]. Metformin is used as a single agent. When HbA1c is 9% or more, 2 agents with metformin+other drug are used. When HbA1c is 10% or more, 3 agents with metformin+other drugs or insulin therapy would be considered.

Furthermore, American College of Physicians (ACP) showed official comments concerning diabetes in 2017 [32]. It has surprising recommendations with a paradigm change. There was Statement 2, in which clinicians should set the management goal for HbA1c in most T2DM patients to be 7% or more and less than 8%.

Consequently, we can find large paradigm changes in also diabetes field. We would continue medical practice with attention to the management of hypertension and diabetes using adequate and satisfactory guideline as well as respecting QOL/ADL and psychological desire of the patients from now.

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