

# Introduction of Taiwan Hypertension Guideline

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Hypertension is one of the most important risk factors for atherosclerosis-related mortality and morbidity. According to the Prospective Studies Collaboration, hypertension produced the greatest mortality burden in year 2001, accounting for more than 9 million deaths worldwide, more than any other known risk factors. About 54% of stroke and 47% of ischemic heart disease worldwide were attributable to high blood pressure. Overall, about 80% of the attributable burden occurred in low-income and middle-income economies.

The definition of HT was still based on office BP. The BP targets differ according to various pre-existing diseases. For high risk patients, such as patients with diabetes, and established coronary heart disease (CHD), a BP target of 130/80mmHg is reasonable. For patients with chronic kidney disease and ischemic stroke, and for patients without any co-morbidity (primary prevention), a BP target of 140/90 mmHg is generally accepted.

Home BP monitoring has better correlations with target organ damage and future CV events. It can also improve patient's adherence to treatment regimens. This guideline highly recommends home BP monitoring before and during treatment. White-coat HT and masked HT can be detected without difficulty by the use of home BP monitoring.

Life style modification should be undertaken in all patients with high normal blood pressure, prehypertension, patients with definite hypertension, and those required drug treatments. The purpose is to lower blood pressure, to control other risk factors, and to reduce numbers or doses of anti-hypertensive drugs. The lifestyle measures that are widely recommended to lower blood pressure and cardiovascular risks are smoking cessation, weight reduction in the overweight, moderation of alcohol consumption, physical activity, adoption of diet, and reduction of salt consumption.

When a patient needs drug treatment, physicians should "PROCEED" to decide the optimal agent for the patient: First, Previous unfavorable experience of the individual patient to a given class of antihypertensive drug should be carefully sought out because adverse events are the most important cause of non-adherence. Second, Risk factors for an individual patient should be considered. Third, Organ damage, even sub-clinical, or previous associated cardiovascular conditions may favor certain classes of drugs or certain combinations. Fourth, Contraindications or unfavorable conditions should be examined. Fifth, Expense or cost may be taken in account. Sixth, Expert's or doctor's judgment is of paramount importance in managing patients. Any guideline can only served as reference in treating individual patient. Finally, Delivery and compliance issue is the key to successful treatment of HT. Physicians should motivate patients and have good communication with individual patient. Simplified treatment with long-acting drugs or by using single-pill combination formula may be required to obtain higher adherence rate.

The main benefits of antihypertensive agents are derived from lowering of blood pressure per se, and are generally independent of the drugs used. Although there are some clinical trials supporting the superiority of one drug or combination over another or other combinations in reducing stroke, end-stage renal disease, or cardiovascular events, controlling blood pressure to goal is more important than choosing drug class. There are some conditions for which preferred drugs might be considered. Nevertheless, in more than 75% of patients single agent would not be enough, so it seems futile to emphasize the identification of the first preferred drug.

To estimate the extent of blood pressure reduction or to predict how many drugs are needed to achieve blood pressure goal, “Rule of 10” and “Rule of 5” can be used to predict the reduction in systolic blood pressure and diastolic blood pressure, respectively. In a meta-analysis of 354 randomized, double-blind, placebo-control trials comprising 40,000 drug-treated patients and 16,000 placebo-treated patients, a standard dose of either one of the 5 major classes of anti-hypertensive agents could produce approximately a 10-mmHg decrease in systolic blood pressure (Rule of 10) and a 5-mmHg decrease in diastolic blood pressure (Rule of 5) (all after placebo-subtraction) when the baseline pre-treatment systolic blood pressure was 154/97 mmHg. For a 10 mmHg higher in baseline systolic blood pressure or diastolic blood pressure, further decrease of 1.0 mmHg in systolic blood pressure and 1.1 mmHg in diastolic blood pressure were observed. When the doses were doubled, there were only 2 mmHg incremental decrease in systolic blood pressure and 1 mmHg incremental decrease in diastolic blood pressure. Alternatively, when 2 drugs in standard doses but with different mechanisms were taken together (except the combination of ACEI and ARB), the decrease in blood pressure is the sum of the decrease of the individual agents (approximately 20 mmHg in systolic blood pressure and 10 mmHg in diastolic blood pressure).

Combination of different drugs is frequently needed in patients with stage 2 HT or in high risk patients when lower targets are pursued. The 2 or 3 different drugs with independent mechanisms could be used in low or standard doses to achieve more BP lowering than up-titration of the monotherapy alone, obviating the frustration of searching for effective monotherapy. A decrease of 20/10 mmHg in SBP/DBP could be expected with a 2-drug combination. The combination of different drugs in low or standard doses is more likely to be free of side effects compared to higher doses of monotherapy. Furthermore, it may have a favorable tolerance profile since the complementary mechanisms of action of the components minimizing their individual side effects.

For pathophysiological consideration, the A (ACEI or ARB) + C (CCB) or D (thiazide diuretic) formula will be a reasonable first-step combination. The frequently used 2-drug combinations include the following:

ACEI + CCB

ARB + CCB

ACEI + thiazide diuretic

ARB + thiazide diuretic

CCB + beta-blocker

The recommended 3-drug combination is A+C+D, except in patients with heart failure or CHD in that beta-blockers are indicated. Combination of a beta-blocker and a thiazide diuretic should be used with great caution because of higher diabetogenic potential. Combination of ACEI and ARB is also undesirable. In the ONTARGET study, the combination of ACEI with ARB not only has no additional benefits comparing to each individual component but also increases the incidence of renal impairment and other side effects.

In the recently published ACCOMPLISH study, 2 single-pill combinations (SPC) were compared. Unexpectedly, the ACEI and CCB combination group has better cardiovascular and renal outcomes than the ACEI

and diuretic combination group. The safety profile is similar, suggesting A+C combination might be better than A+D combination.