Editorial

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Efonidipine, Another Beauty Relieving the Pressure

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In a variety of observational studies from the population level to various clinical situations, it is well known that, a lower heart rate is considered to be better.[1] However, in Anglo-Scandinavian Cardiac Outcomes Trial study, a vice versa was demonstrated showing an inferior protection for stroke by atenolol and bendroflumethiazide to amlodipine and perindopril.[2] Despite of several explanations on those contradictory findings, findings such as the pharmacodynamics actions, an explanation solely provided by the slow heart rate seems to be, at least from a statistical viewpoint, the most powerful.[3]

In the study by Komukai et al.[4] efonidifine, a dihydropiridine calcium antagonist on the actions of L-type as well as T-type calcium channels, showed a significant reduction in the heart rate as well as in the blood pressure. It is characterized by rapid onset and durable action which is independent of the administration time. In the previous study by Oh et al.[5] efonidipine also showed similar efficacy, in regards to, slowing down the heart rate by approximately 11% in the mild to moderate hypertension patients. Komukai et al.[4] postulated that heart rate reduction could be partially explained by slowly fading antihypertensive action, which was demonstrated by a non-linear fitting model, based periodic function.

In essential hypertension, slowing down the heart rate by atenolol is rather closely related to the worsening of central hemodynamics. Moreover, there is no evidence supporting the hypothesis that the slower heart rate is better, in any direct comparison study. Recently, a 12 month follow up study for the patient with diabetic nephropathy done by Sasake et al.[6] showed that efonidipine was better in reducing arterial stiffness than amlodipine, through the actions on aldosterone, renal function, and oxidative stress. Unfortunately, the blood pressure and the heart rate data were not demonstrated well enough to detect the difference between the groups.

Putting those altogether, there seems to be a possibility that intrinsic pharmakodynamic properties of efonidipine could compensate or overcome the potential or relative disadvantage caused by a deceased heart rate on the arterial stiffness.

Due to ethical issues, a study replacing heart rate slowing drugs for beta-blocker in the coronary artery disease is currently not allowed. Therefore, the beta-blocker therapy for coronary artery disease is not to be replaced by other rate slowing drugs, according to the current evidences. Even with a significant reduction in the secondary composite end points in the MorBidity-mortality EvAlUaTion of the I_f inhibitor ivabradine in patients with coronary artery disease and left ventricULar dysfunction (BEAUTIFUL) study subgroup of heart rate of 70 beat per minute or greater, it is needless to say that the efficacy of ivabradine is not to be extrapolated to the essential hypertension patients.[7] But at the same time, at least, ivabradine data did suggest that the harmful effects, demonstrated by atenolol, might not be universal to all the beta-blockers.[7]

Mechanism of action of efonidipine on the sinus node is quite similar to that of ivabradine.[8] Considering potential efficacy on the arterial stiffness, the "BEAUTIFUL-like action" in addition to modest antihypertensive efficacy, provided by efonidipine, is something "throbbing". Especially studies for central hemodynamics and a direct comparison study would be very interesting.

Another interesting hypothesis, regarding efonidipine, is that the dissociation of the durability on blood pressure and the heart rate could be an alternative to the trade-off between potent blood pressure lowering and the reflex tachycardia common in other dihydrophyridine calcium antagonists. Since the 24 hours blood pressure reduction is partly contributed by nocturnal blood pressure reduc-

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tion, modest efonidipine efficacy on nocturnal blood pressure needs to be considered for individualized patient care.

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