EDİTÖRYEL YORUM
EDITORIAL COMMENT

Comparing Two Different Therapies

İki Farklı Tedavi Yaklaşımı Karşılaştırılırken

Endothelial cells, which are strategically located between circulating blood – blood cells and vascular smooth muscle, release humoral factors that control relaxation and contraction, thrombogenesis and fibrinolysis, and platelet activation and inhibition. Therefore the functional integrity of endothelium is of paramount importance for the maintenance of blood flow and antithrombotic capacity (1). Endothelial dysfunction plays a key role in various disease processes including atherosclerosis (2), hypercholesterolemia (3), essential hypertension (4), menopause (5), diabetes mellitus (6) and congestive heart failure (7,8). Angiotensin converting enzyme inhibitors including lisinopril have been reported to favorably effect endothelial functions in patients with hypertension, and simvastatin was demonstrated to improve the endothelial functions of spontaneously hypertensive rats (9-12).

In the prospectively-designed study (13) published in the current issue of The Anatolian Journal of Cardiology, patients with essential hypertension were randomized to two types of drug therapy in order to investigate whether some additional improvement in blood pressure control and endothelial functions could be demonstrated through adding simvastatin to lisinopril despite the absence of hyperlipidemia. Besides performing an arterial blood pressure follow-up, high resolution ultrasonography that is increasingly used as a noninvasive tool was employed to determine changes in endothelial function. This noninvasive method when applied on the brachial artery permits in vivo assessment of how the artery responds to endothelium dependent and independent stimuli induced by a rapidly increased blood flow and sublingual nitroglycerin, respectively (14).

Blood pressure follow-up revealed that both groups treated with lisinopril alone and lisinopril plus simvastatin showed comparable reductions of 20-23% in systolic and diastolic blood pressure levels that were both similar between them before starting drugs. Although a more prominent reduction of pulse pressure was observed in the combined therapy group, higher initial mean pulse pressure level in this group (61±11 vs. 54±14), decrease of pulse pressure levels in both groups to a mean of 46 in identical manner, and the absence of systolic-diastolic blood pressure ranges in the manuscript should be noted before interpreting that finding.

The initial levels of brachial artery ultrasonography parameters and their changes after the therapies demonstrate another example of a troublesome patient selection bias as the authors shortly stated in the discussion. At the beginning, flow mediated vasodilatation ratios were 16±7% and 13±8% in combined and monotherapy groups, respectively. Lisinopril alone increased the latter to 18.7%, while it's combination with simvastatin has provided a blunted response of the former in the level 16.7%. In this situation, simvastatin seems to have inhibited the favorable effect of lisinopril on the endothelial functions, which is certainly very difficult to explain under the light of our current knowledge. It is clear that this finding could not be interpreted as "the absence of a statistically significant additional effect" of a drug to another, but should be established as a finding suggesting that simvastatin inhibits the 38% improvement provided by lisinopril when two drugs are combined.

Nonparametrical statistical computations utilized in small sample sizes are particularly prone to result in such statistical anomalies, and a p value of >0.05 in such a comparison should not be automatically translated to "similar initial levels", as it was very demonstrative in the above-mentioned parameters assessed in this study, which evaluated a very meaningful hypothesis developed under currently focused subjects utilizing a modern methodology. The work could be appreciated as a stimulus to further research including larger sample sizes and longer follow-up, and the results on the drug effect should be considered as some preliminary observations influenced by the selection bias.

Osman Akdemir, MD,
Trakya University, School of Medicine,
Cardiology Department, Edirne, Turkey

Address for correspondence: Osman Akdemir, MD - Trakya University, School of Medicine, Cardiology Department, Edirne, Türkiye

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