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Nebivolol for improving endothelial dysfunction in cardiac syndrome-x; Is it ready for clinical use?

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Letter to Editor

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Dear Editor

It is assumed that endothelial dysfunction (ED) of coronary arteries is one of the important underlying mechanisms for cardiac syndrome-X (CSX). ED reduces coronary vasodilatation capability, causes abnormal arterial contraction, and impairs endothelium dilatation. These events of ED along with reduced bioavailability of endogenous nitric oxide (NO) reduce blood flow in microvasculature of myocardium.[1] For this reason, this syndrome is also called microvascular angina. Accordingly, the principal component of treatment in patients with CSX is improving ED. However, the optimal treatment for this pathological mechanism has not yet been determined.[1]

In the not-too-distant past, the promising results of several individual studies showed that nebivolol has beneficial effects on improving endothelial function in patients with CSX, by increasing NO release in endothelial cells.[2] However, after that, the researchers did not show much interest in repeating that research. The reason for discontinuing research in this area is unclear; but the findings of pharmacological studies imply that nebivolol, as a highly potent selective β-adrenoceptor antagonist, can affect L-arginine/NO pathway, and therefore, can lead to endothelial vasodilatation.[2,3]

Regarding the effect of nebivolol on endothelial dysfunction in patients with CSX, clinical research began in 2009 and then disappeared in 2010. In 2009, nebivolol (5 mg daily) was compared with metoprolol (50 mg daily) in a randomized clinical trial with 34 patients with CSX.[4] Patients received these interventions for 12 weeks. Researchers found that nebivolol therapy could increase exercise duration, reduce exercise-induced myocardial ischemia, lower the number of angina attacks, and increase plasma L-arginine/NO levels. As a result, coronary microvascular function and exercise-induced myocardial ischemia were improved in patients with CSX.

In another study in 2010, Kayaalti et al. compared 5 mg nebivolol with control group (the authors did not specify what drug or placebo was prescribed for control group) to investigate the effect of nebivolol on endothelial function on 38 patients with CSX.[5] Patients received these interventions for 4 weeks. In this study, instead of a cardiac function, patients were evaluated for their brachial artery response (lumen diameter) as well as biochemical and inflammatory markers. They found that nebivolol therapy was associated with increased brachial artery lumen diameters and decreased inflammatory markers by improving endothelial function.[5]

The effect of nebivolol (5 mg/day) on oxidative stress also was compared with metoprolol (50 mg/day) in patients with CSX. They found that nebivolol could increase plasma level of NO, and therefore improve exercise stress test results.[6]

Based on the current evidence, it seems that nebivolol, as a highly selective beta-adrenergic blocker, can increase plasma levels of NO. This increase indirectly indicates the effects of this drug on improvement of endothelial cells function. Although pharmacological studies have confirmed these effects,[2,3] limited clinical studies have examined the efficacy of this drug in improving endothelial function of coronary arteries in patients with CSX. Only one study[4] directly evaluated the efficacy of nebivolol on endothelial function, and there is a need to further well-designed clinical trial studies to investigate whether nebivolol can improve endothelial function in patients with CSX.

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Conflict of Interests

Authors have no conflict of interests.

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