Nebivolol and carvedilol induce NO-dependent coronary vasodilatation that is unlikely to be mediated by extracellular ATP in the isolated guinea pig heart

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Abstract:
In contrast to classical β-adrenoceptor antagonists, nebivolol and carvedilol possess endothelium-dependent vasorelaxant properties. It has been proposed that nebivolol and carvedilol activate microvascular endothelium into producing NO by the release of extracellular ATP and subsequent stimulation of endothelial P2 receptors. Here we tested this hypothesis in the coronary circulation of the isolated guinea pig heart. We analyzed the role of NO in the coronary vasodilatation induced by nebivolol and carvedilol as well as a possible involvement of extracellular ATP in these responses. Nebivolol and carvedilol (3–30 × 10⁻⁶ M) induced a concentration-dependent coronary vasodilatation that was inhibited by NO-synthase inhibitor, L-NAME (10⁻⁴ M). In contrast to nebivolol and carvedilol, neither atenolol nor labetalol acted as a coronary vasodilator. Vasodilatation induced by nebivolol and carvedilol was affected neither by the P₁ receptor antagonist, 8-sulfophenyl theophylline (8-SPT, 10⁻⁵ M), nor by the P₂ receptor antagonist, suramin (10⁻⁵ M).

On the other hand, ATP-induced coronary vasodilatation (0.3–10 × 10⁻⁶ M) was strongly inhibited by L-NAME (10⁻⁴ M), partially inhibited by 8-SPT (10⁻⁵ M), while suramin (10⁻⁵ M) had a minor effect.

In conclusion, in the isolated guinea pig heart nebivolol and carvedilol, but not their classical counterparts (atenolol, labetalol), act as NO-dependent coronary vasodilators. It seems unlikely that this response is mediated by the release of extracellular ATP.

Key words:
β-adrenoceptor antagonist, nebivolol, carvedilol, nitric oxide, ATP, coronary endothelium.