

Introduction: nebivolol is primarily a β_1 selective adrenergic receptor blocker and used in the treatment of hypertension and heart rate. Nebivolol also elicits an endothelium dependent nitrogen monoxide (NO) mediated dilation in peripheral vessels (Ignarro et al.). However, the cerebrovascular effects of nebivolol are unknown. We hypothesized that nebivolol increases the diameter of the isolated arteries from the rat brain.

Methods: Basilar arteries (BA) were isolated from male Wistar rats. The arteries were cannulated and placed in a pressure-flow myograph chamber containing Ca^{2+} -KREBS solution. Experiments were conducted with zero flow and 80 mmHg intraluminal pressure. The vasomotor functions of the arteries were measured with sodium nitroprusside (SNP), Nifedipin (NIF) and nebivolol (NEB). N ω -nitro-L-arginine methyl ester (L-NAME) was used for the blockade of nitric oxide synthase. 1H-[1, 2, 4]oxadiazolo[4, 3-a]quinoxalin-1-one (ODQ) was used for the blockade of soluble guanylate cyclase.

Results: the active diameter was (AD) $222 \pm 14 \mu\text{m}$ and the passive diameter of the BA was measured $400 \pm 7 \mu\text{m}$ (n=9). Nebivolol induced significant vasodilation (10-5M: $289 \pm 15 \mu\text{m}$, 30 ± 7 AD% p<0.05). In response to L-NAME the active diameter remained decreased significantly until the end of the experiment (from $187 \pm 7 \mu\text{m}$ to $162 \pm 11 \mu\text{m}$; -11 ± 2 AD%). In case of incubation with L-NAME there was no significant difference compared to the control response in vasodilation to nebivolol. (10-5M $211 \pm 12 \mu\text{m}$, 25 ± 5 AD%). In case of incubation with ODQ there was no significant differences in vasodilation to nebivolol compared to the control response (10-5M: $311 \pm 20 \mu\text{m}$; 31 ± 5 AD%), in contrast the vasodilation to SNP significantly decreased. (10-4M from $347 \pm 10 \mu\text{m}$ to $229 \pm 17 \mu\text{m}$; from 60 ± 7 AD% to $0,6 \pm 0,3$ AD%).

Conclusion: these data suggest that nebivolol is a potent vasodilator in cerebral arteries and that the NO-cGMP pathway does not play role in the underlying mechanisms. Nevertheless, nebivolol by increasing cerebral blood flow may have therapeutic significance.

Grant support: TÁMOP 4.2.4.A/2-11-1-2012-0001; TÁMOP-4.2.2.A-11/1/KONV-2012-0024; TÁMOP-4.2.2.A-11/1/KONV-2012-0017; OTKA: K-71591