EVALUATION OF VASCULAR FUNCTIONS IN BALLOOON-INJURED RAT CAROTID ARTERY

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The endothelial dysfunction and arterial remodelling are observed in various pathologies including restenosis after angioplasty (PTCA). Endothelial injury induced by different stimulus (mechanical damage, ox LDL, free radicals, bacterial products, growth factors etc.) lead to proliferation of intimal vascular smooth muscle cells (VSMC) with formation of neointima (1). The reactivity of damaged and remodelled vessel is altered and characterised by an anomalous responses to contracting and vasorelaxing agents depending on type of event that produce endothelial damage (2, 3). In this study we evaluated the alterations in vascular reactivity of rat carotid artery after mechanical damage and endothelial denudation with angioplastic balloon technique. Endothelial denudation of commune right carotid was performed in male Wistar rats (350-400 g) anaesthetised with ketamine (100 mg/Kg, i.p.) and xilazine (5mg/Kg i.p.) (4). Animals were sacrificed at different days (0, 1, 7, 14, 21, 28) after endothelial damage for vascular function evaluation. Arterial rings collected from injured and uninjured carotid were mounted in isolated organ bath for isometric force displacement by Power Lab Sistem.
At 0 day, injured vessels stimulated with phenilephrine (PE 0,3 µM) were enable to produce any contraction. Injured carotids collected at 1, 7, 14, 21 or 28 days showed reduction of phenilephrine-induced (PE 0,3 µM) contraction with a trend to disappear completely to the subsequent 3-4 stimulations. This effect was more evident at days 1, 7, 14 and 21. An imp rovement of PE induced contraction was observed at time 28.
Rings obtained from injured carotid artery showed a significant reduction of KCl (60 mM) induced contraction at any experimental time ($P<0.001$) compared to rings obtained from uninjured carotids. After 28 days injured vessels showed an improvement ($P<0.01$) of KCl induced contraction compared to 0, 1, 7 and 14 days.
At the same experimental time we evaluated the activity of *endhotelial-derived relaxing and hyperpolarizing factor* (EDRF and EDHF) induced by acetylcholine (ACh 0.001-1 µM) in presence of indomethacin (10 µM) and indomethacin+ L-NAME (10 µM+100 µM) respectively. At days 1, 7 injured carotid did not show any ACh-induced relaxation. At day 14 injured carotid exhibited a significant reduction ($P<0.01$) of EDRF induced relaxation, which improved at day 21 and 28. In contrast EDHF-induced relaxation, elicited by ACh, remained significantly reduced at all time points ($p<0.05$).
We also evaluated the relaxant properties of VSMC and of ATP-dependent potassium channels (KATP). A significant reduction of sodium nitropusside (SNP; 0.001-10 µM)-induced relaxation was observed at time 1, 7, 14 and 21 ($p<0.001$). An improvement of SNP induced relaxation was observed at 28 days. In contrast, at days 14, 21, 28, injured carotid showed a non significant reduction of relaxation induced by diazoxide (DZX 3-300 µM), an opener of KATP channels.
These results suggest that, either mechanical damage or inflammatory process (1 and 7, 14, 21 days) may be involved in the hyporeactivity of PE, KCl and vasorelaxing agents. Furthermore the improvement to PE and KCl induced contraction and SNP induced relaxation observed at 28 days could indicate a recovery of functionality of the VSMC. The reduction of EDRF, EDHF induced relaxation may be related to a alteration of production/release of these factors, but we can not exclude the possibility of an impairment of guanilate cyclase/cGMP pathway.

References

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