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AGE-RELATED IMPAIRMENT OF RELAXATION TO ATP IN RABBIT AORTAS

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Abstract - Effect of aging on endothelium-dependent and independent relaxation was studied in rabbit aorta. Response to Ach was similar in young and adult animals. ATP and NaNO₂ showed both lower potency and efficacy in adult animals. Vascular smooth muscle might be of relevance in the age-related impaired relaxation to ATP.

Cardiovascular homeostasis depends on several factors that results liable to be altered in elderly subjects. The effect of aging on the cardiovascular system and on the related phenomena have been studied in several animal models. In aged rabbits it was observed an increase in blood pressure as well as in the vascular connetive component accompanied with tickening of the vessel wall (1). A great deal of information on the role of endothelium in maintaining vascular homeostasis has recently become available (2-4).

Two different subtypes of ATP receptors are present in vessels: P_{2y} on endothelial cells mediating vasodilatation and P_{2x}, on smooth muscle cells mediating contraction. P₁ receptors that are also present on smooth muscle, could be activated by adenosine produced by enzymatic ATP hydrolysis.

This study was performed to evaluate the effects of ageing on endothelium-dependent and independent relaxation of thoracic aorta from New Zealand rabbits 4-6 months old (young) and 7-12 months old (adult), by using vasodilator agents: adenosine triphosphate, acetylcholine and sodium nitrite.

Experiments were carried out on New Zealand male rabbits aged 4-6 months and 7-12 months. Thoracic aortas were cut into transverse rings approximately 3 mm long and suspended in a tissue bath containing a modified Krebs-bicarbonate solution gassed with 95%O₂-5%CO₂ pH 7.4 at 37°C. Isometric tension was recorded at a basal tension of 35 mN. In some rings the endothelium was gently removed rubbing the intimal surface of the vessel with a pipe cleaner.

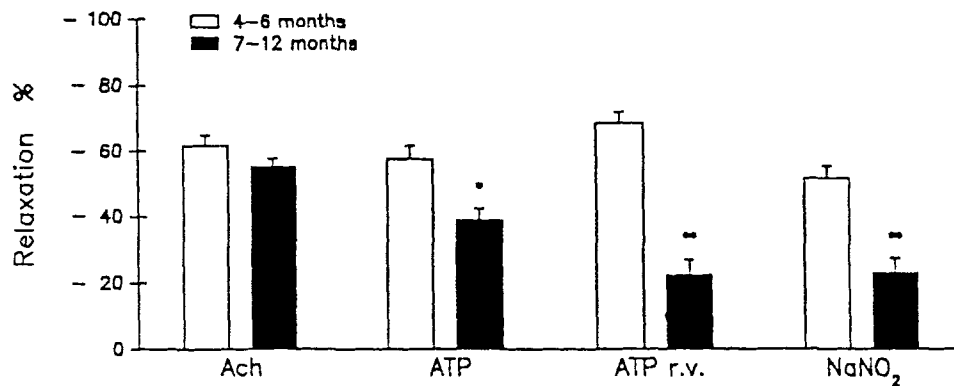


Fig.

Relaxation obtained with vasodilator agents in aortic rings from 23 rabbits of different age (12 young and 11 adult). Data are the mean \pm SEM.

* $p < 0.005$ ** $p < 0.001$; r.v. = rubbed vessels

Aortic chains were contracted by EC_{50} noradrenaline (NA) and separate cumulative concentration curves by adenosine triphosphate (ATP), acetylcholine (Ach) or sodium nitrite ($NaNO_2$) were obtained. Relaxation was expressed as percent of the contraction induced by EC_{50} NA. Results have been summarized in the figure.

The relaxation to Ach ($0.03\mu M$ to $3\mu M$) on EC_{50} noradrenaline-induced contraction was similar in aortas from young and adult rabbits. Relaxation to ATP ($30\mu M$ to $3mM$) was reduced in adult aortic rings showing both lower efficacy and potency. In rubbed adult aortic rings response to ATP increased, whereas in young rabbits the maximal relaxation was similar both in aortas with and without endothelium. Relaxation to $NaNO_2$ ($10\mu M$ to $1mM$) was reduced in aortas from adult rabbits.

These data suggest that with ageing ATP impaired relaxation is not dependent on endothelium mediated mechanisms, which appeared not to be altered. We hypothesize that functional and/or morphological variations mainly in smooth muscle might play a relevant role.

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