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Passive smoking induced hypertrophy of the left ventricle: effect of captopril

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Both active and passive long term cigarette smoking affects negatively the cardiovascular system causing atherosclerosis of the coronary arteries, focal myocardial lesions and arrhythmias [1]. Acute cigarette smoking increases heart rate, arterial blood pressure [2], cardiac output, contractility [3], and reduces peripheral artery compliance [4]. Changes are primarily mediated by activation of the sympathetic nervous system [5]. Since several studies have indicated that haemodynamic and vessel reactivity alterations may be provoked by smoking, it is reasonable to suppose that smoking might stimulate adaptive growth of the left ventricle (LV). The aim of the study was to show whether prolonged passive smoking can induce growth and alter hydroxyproline concentration of the LV and whether these potential changes may be influenced by the ACE inhibitor captopril.

Four groups of rabbits were investigated in a three-week experiment: control (c), control + Captopril (c + C) (7.5 mg twice daily intramuscularly), passive smoking (S) (3 cigarettes twice daily), and passive smoking + captopril (S + C) (as above). The left and right ventricle of the heart were detached and weighed separately. The ratios of the weight of the individual parts of the heart to the body weight were calculated in each animal. Hydroxyproline, as an indicator of collagen concentration, was measured in the left ventricle according to Kesava et al. [6]. Student's t-test was used for statistical analysis.

In the S group the weight and relative weight of the LV was increased (by 16%, $p < 0.02$) and (by 23%, $p < 0.01$) respectively. Simultaneous treatment with captopril (S + C) had not significant effect on the hypertrophic growth of the LV. Neither passive smoking nor captopril did provoke significant changes in the weight of the RV. The hydroxyproline concentration in the LV was slightly increased in the S group (by 24%, $p < 0.06$), and significantly increased in the S + C group (by 18%, $p < 0.05$).

To our best knowledge, it is for the first time that hypertrophy of the left ventricle is described after prolonged period of passive smoking. However, in the same model of passive smoking in rabbits hypertrophy of the whole heart was described [7], and hypertrophy of the left ventricle was observed in heavy smokers [8]. As we did not perform haemodynamic measurements in our model, we can only speculate on the mechanisms involved in the hypertrophic growth observed. As captopril did not prevent either hypertrophy or fibrosis of the LV in this experiment and since in this model of passive smoking renin levels were not found to be increased [9], the renin-angiotensin system does not seem to play a substantial role in the growth of the LV in this particular model. Alterations of other humoral systems participating in the hypertrophy of the LV, like nitric oxide [10] and the sympathetic system [3], should be considered. As we found an increased norepinephrine level in our previous study with this model [9], activation of the sympathetic system, probably with blood pressure elevation [2], might be decisive. We conclude that the RAS was not involved in the hypertrophy and fibrosis of the left ventricle induced by three week passive smoking in rabbits.

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References

1 Leone, A.: Int. J. Cardiol. **38**, 113 (1993)
2 Trap-Jensen, J.: Am. Heart J. 115 (1Pt2), 263 (1988)
3 Winniford, M. D.: J. Hypertens. Suppl. **8**, S17 (1990)
4 Giannattasio, C.; Mangoni, A. A.; Stella, M. L.; Carugo, S.; Grassi, G.
5 Mancia, G.: J. Hypertens. **12**, 691 (1994)
6 Kesava Reddy, G.; Enwemeka, Ch. S.: Clin. Biochem. **29**, 225 (1996)
7 Gvozdjáková, A.; Kucharská, J.; Bada, V.; Gvozdják, J.: Čs. fysiol. **37**, 90 (1988)
8 Shasha, S. M.; Kamal, H.; Kristal, B.; Galetzky, G.; Roguin, N.; Shkolnik, T.: Atherosclerosis **98**, 91 (1933)
9 Török, J.; Gvozdjáková, A.; Kucharská, J.; Balažoviech, I.; Gvozdják, J.; Kyselá, S.; Simko, F.: J. Mol. Cell. Cardiol. **30**, A194 (1998)
10 Babál, P.; Pecháňová, O.; Bernátová, I.; Švrtina, S.: Histol. Histopathol. **12**, 681 (1997)

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Table: Changes in the weight and relative weight of the left and right ventricle and left ventricular hydroxyproline concentration

	Control	Control + captopril	Smoke	Smoke + captopril
Body weight (b.w.) (kg)	3.256 ± 0.064	3.146 ± 0.074	3.107 ± 0.083	3.075 ± 0.176
Heart weight (g)	6.171 ± 0.251	6.729 ± 0.316	6.578 ± 0.263	6.422 ± 0.353
Heart weight/b.w. (g/kg)	1.896 ± 0.067	2.143 ± 0.102	2.121 ± 0.086	2.111 ± 0.112
RV weight (g)	1.191 ± 0.061	1.388 ± 0.079	1.202 ± 0.075	1.289 ± 0.077
RV weight/b.w. (g/kg)	0.366 ± 0.018	$0.441 \pm 0.023^*$	0.386 ± 0.021	0.424 ± 0.026
LV weight (g)	2.522 ± 0.071	2.726 ± 0.149	$2.913 \pm 0.126^*$	2.813 ± 0.166
LV weight/b.w. (g/kg)	0.775 ± 0.018	0.869 ± 0.050	$0.951 \pm 0.042^*$	$0.923 \pm 0.047^*$
Hydroxyproline in LV (mg/g w.w.)	0.343 ± 0.016	0.386 ± 0.015	0.424 ± 0.034	$0.405 \pm 0.011^*$

* $P < 0.05$, LV: left ventricle