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Histamine aggravated levothyroxine-induced cardiomyopathy in guinea pigs

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KEY WORDS levothyroxine; histamine; heart

AIM: To study effects of histamine on cardiomyopathy. **METHODS**: Cardiomyopathy model was developed in guinea pig by ip levothyroxine 0.5 $mg \cdot kg^{-1} \cdot d^{-1}$ for 10 d. Langendroff's hearts were perfused. ECG and contractile force were recorded. Histamine (5 μg) was given by intra-aortic injection. Histamine content of coronary venous effluent was determined fluorometrically. **RESULTS**: Attack of histamine on cardiomyopathy was severer than that in normal hearts. Tachycardia was more prominent; atrioventricular conduction block occurred earlier; decrease in coronary flow was more marked. Uptakes of histamine were 37 % in the model and 19 % in the normal hearts ($P < 0.01$). **CONCLUSION**: Histamine aggravated levothyroxine-cardiomyopathy.

Ventricular hypertrophy (VH) is easily developed by ip levothyroxine in guinea pigs as an experimental cardiomyopathy model[1-3]. Histamine induces inotropic and chronotropic effects on normal heart[4]. This paper is to study the effects of histamine on cardiomyopathy.

MATERIALS AND METHODS

Guinea pigs of either sex ($n = 6$, weighing $412 \pm s$ 35 g) were injected ip levothyroxine (Paper chromatographic pure, Shanghai Dongfeng Biochemical Techincal Co), mixed with 0.5 % CMC-Na before use) 0.5 $mg \cdot kg^{-1} \cdot d^{-1} \times 10$ d[1].

Guinea pigs were stunned. The heart was mounted via an aortic cannula in Langendorff's apparatus and perfused (80 cm of water) with oxygenated Ringer-Locke solution at 37.5 ℃[5]. After an equilibration period of 25 - 30 min, histamine (Purity, 98 %, 5 μg, Shanghai Dongfeng Biochemical Technical Co) was administrated by the intra-aortic injection. ECG and myocardial contractile force (MCF) were recorded, and coronary perfusate was collected at interval of 1 min.

Histamine content of coronary effluent was determined by a fluorometric method[6].

Statistical analysis was made using t test.

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RESULTS

Effect of histamine on MCF of isolated hearts MCF in normal and cardiomyopathic hearts were 0.76 ± 0.18 g and 1.01 ± 0.20 g ($P < 0.05$), respectively. After injection of histamine, change of MCF in normal and in model hearts were 252 ± 37 % and 173 ± 21 % ($P < 0.05$) at 30 s, respectively, a biphasic effect on MCF was weaker in cardiomyopathic hearts than in normal hearts (Tab 1).

Effect of histamine on heart rate and P-R interval At 0 time, an increase in heart rate was observed in cardiomyopathic hearts. Tachycardia induced by histamine was more prominent in the model than in normal hearts, atrioventricular conduction block caused by histamine occurred earlier and severer, and lasted longer in cardiomyopathic hearts than in normal hearts (Tab 1).

Effect of histamine on coronary flow and histamine content A fall in coronary flow induced by histamine was found, which was more marked in cardiomyopathic hearts than in normal hearts (Tab 1). Histamine contents in effluent samples were 4.05 ± 0.46 μg in normal, and 3.15 ± 0.76 μg ($P < 0.01$) in the model, indicating a more uptake of histamine by hypertrophic hearts.

Evaluation of cardiomyopathy model After experiment, heart atrium and ventricle were dried at 80 ℃ for 4 h and weighed. Heart index (heart weight/100 g body weight) and ventricle index (ventricle weight/100 g body weight) were calculated, heart index was 0.52 ± 0.03 % in normal, and 0.68 ± 0.04 % in model, ventricle index was 0.40 ± 0.03 % in normal, and 0.53 ± 0.04 % in model. Levothyroxine increased heart index and ventricle index.

DISCUSSION

Histamine induced biphasic effect on MCF, an

Tab 1. Effects of histamine on myocardial contractile force (MCF), heart rate (HR), PR interval (PR), coronary flow (CF), histamine content (HC). N: normal, M: model. $n = 6$, $\bar{x} \pm s$. $^{a}P>0.05$, $^{b}P<0.05$, $^{c}P<0.01$ *vs* 0 time; $^{d}P>0.05$, $^{e}P<0.05$, $^{f}P<0.01$ *vs* normal.

Parameter	Group	0	1	2	3	4	5 min
MCF/%	N	100	142 ± 29^{b}	92 ± 8^{b}	75 ± 7^{c}	78 ± 15^{b}	88 ± 19^{a}
	M	100	101 ± 19^{ae}	88 ± 21^{ad}	82 ± 19^{bd}	84 ± 16^{bd}	82 ± 11^{bc}
HR/bpm	N	224 ± 34	264 ± 15^{b}	260 ± 29^{b}	235 ± 27^{a}	259 ± 23^{a}	249 ± 21^{a}
	M	273 ± 34^{e}	322 ± 45^{bf}	300 ± 39^{ae}	283 ± 48^{ae}	273 ± 48^{ad}	262 ± 41^{ad}
PR/ms	N	4.4 ± 0.1	4.4 ± 0.2^{a}	4.4 ± 0.2^{a}	4.5 ± 0.3^{a}	4.6 ± 0.5^{a}	4.8 ± 0.6^{a}
	M	4.2 ± 0.4^{d}	4.2 ± 0.4^{ad}	4.8 ± 0.2^{be}	5.0 ± 0.3^{be}	5.4 ± 0.6^{be}	5.5 ± 0.7^{be}
CF/mL·min^{-1}	N	7.4 ± 0.4	7.2 ± 0.7^{a}	7.7 ± 0.7^{a}	7.2 ± 0.5^{a}	7.1 ± 0.6^{a}	6.7 ± 0.3^{b}
	M	7.4 ± 0.4^{d}	6.4 ± 0.7^{bd}	6.3 ± 0.6^{be}	6.4 ± 0.6^{be}	6.7 ± 0.7^{ad}	6.7 ± 0.7^{ad}
HC/μg·min^{-1}	N	0.39 ± 0.08	4.01 ± 0.46^{c}	0.81 ± 0.15^{b}	0.39 ± 0.05^{a}	0.39 ± 0.04^{a}	0.39 ± 0.03^{a}
	M	0.36 ± 0.05^{d}	2.88 ± 0.85^{ce}	0.99 ± 0.24^{bd}	0.38 ± 0.05^{ad}	0.37 ± 0.04^{ad}	0.36 ± 0.03^{ad}

increase in heart rate, atriventricular conduction block, and decrease in coronary flow were observed as [6]. Levothyroxine-cardiomyopathy in guinea pigs accompanied by an increase in heart rate, myocardial contractile force and ventricular index. These results were in agreement with previous investigation[7]. After injection of histamine, tachycardia was more prominent; atrioventricular conduction block occurred earlier and severer, decrease in coronary flow was more marked; but biphasic effect on MCF was weaker in cardiomyopathy than in normal, which could be related with a decrease of histamine content of every minute.

Histamine exerts its cardiovascular actions by stimulating H_1 and H_2 receptor; and levothyroxine produced cardiovascular manifestation by direct effects on the heart[8]. Both histamine and levothyroxine joined together and affected heart by different mechanisms. Thus, histamine aggrevated levothyroxine-cardiomyopathy.

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组胺对豚鼠左甲状腺素诱导的心肌病的影响

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关键词 左甲状腺素; 组胺; 心脏

目的: 研究组胺对心肌病的影响. **方法**: 豚鼠 ip 左甲状腺素 0.5 mg·kg^{-1}·d^{-1} × 10 d, 造成心肌病模型. 心脏置于 Langendorff's 装置中, 以任-乐氏液灌流. 记录心电图、心肌收缩力, 收集每分钟冠流量. 经主动脉上方注入 5 μg 组胺, 立即连续记录上述指标 10 min. 冠流液中组胺含量用荧光法测定. **结果**: 组胺对心肌病模型心脏打击更严重, 心率加快更显著, 房室传导阻滞出现更早, 冠流量下降更突出, 组胺摄取增加. **结论**: 组胺加重左甲状腺素诱发的心肌病.