

基础研究

磷酸二酯酶抑制剂对C型钠尿肽作用下家兔心房机械活动的影响

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摘要:

目的: 观察磷酸二酯酶抑制剂(PDEI)对C型钠尿肽(CNP)作用下家兔心房机械活动及心房肌细胞内环核苷酸(cAMP,cGMP)浓度的影响。方法: 采用大耳白兔麻醉后立即开胸取出心脏置于氧饱和的36.5℃生理盐水中, 剥离左心房后立即固定在心房灌流装置上, 用CNP及不同浓度PDEI检测心房搏出量和心房搏动压, 采用放射免疫法测定cAMP和cGMP浓度。结果: ①与对照循环组比较, CNP(30.0 nmol/L)组心房搏出量和心房搏动压明显降低(P<0.01), cGMP的含量显著增加(P<0.001), cAMP含量则无显著性变化(P>0.05)。②与对照循环组比较, 磷酸二酯酶(PDE)非选择性抑制剂IBMX组(1 000.0 nmol/L)心房搏出量和心房搏动压显著增加(P<0.001), cAMP及cGMP的含量显著增加(P<0.001); 与IBMX组比较, IBMX(1 000.0 nmol/L)加CNP(30.0 nmol/L)组心房搏出量、心房搏动压、cAMP含量、cGMP含量则无显著性变化(P>0.05)。③与对照循环组比较, PDE₂抑制剂EHNA(30.0 nmol/L)组心房搏出量和心房搏动压明显降低(P<0.05), cAMP含量无显著性变化(P>0.05); EHNA(30.0 nmol/L)加CNP(30.0 nmol/L)组心房搏出量和心房搏动压显著降低(P<0.01), cAMP含量无显著性变化(P>0.05); 与EHNA组比较, EHNA加CNP组心房搏出量和心房搏动压明显降低(P<0.05), cAMP含量无明显变化(P>0.05)。④与对照循环组比较, PDE₃抑制剂milrinone(1.0 nmol/L)组心房搏出量和心房搏动压增加, 但差异无显著性(P>0.05); cAMP含量则明显增高(P<0.05); milrinone(1.0 nmol/L)加CNP(30.0 nmol/L)组心房搏出量和心房搏动压显著降低(P<0.001), cAMP含量明显增高(P<0.05)。与milrinone组比较, milrinone加CNP组心房搏出量、心房搏动压显著降低(P<0.001), cAMP含量则无明显变化(P>0.05)。结论: CNP抑制家兔心房机械活动, 其机制与增加细胞内cGMP含量有关; 不同PDEI对CNP抑制心房机械活动产生不同的影响。

关键词: 心钠素; 磷酸二酯酶; 心房; 环核苷酸

Effects of phosphodiesterase inhibitors on atrial dynamics induced by C-type natriuretic peptide in isolated beating rabbit atria

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Abstract:

Abstract: Objective To investigate the effects of phosphodiesterase inhibitors (PDEI) on atrial dynamics induced by C-type natriuretic peptide (CNP) and the contents of cyclic nucleotide (cAMP,cGMP) in isolated beating rabbit atria. Methods After the rabbits had been anesthetized, the hearts were removed rapidly. The left auricles were isolated and fixed on the atrial perfusion system. The atrial stroke volume and the pulse pressure were observed by CNP with or without PDEIs pretreatment. The contents of cAMP and cGMP were measured by radioimmunoassay. Results ① Compared with control cycle group, CNP (30.0 nmol/L) obviously decreased the atrial stroke volume and pulse pressure (P<0.01) and increased the cGMP content (P<0.001), while the content of cAMP had no change (P>0.05). ② Compared with control cycle group, IBMX (1000.0 nmol/L), a non-selective inhibitor of PDE, significantly increased the atrial stroke volume, pulse pressure, cAMP and cGMP contents (P<0.001), but there were no differences of the indexes mentioned above between IBMX (1 000.0 nmol/L) plus CNP (30.0 nmol/L) group and IBMX group (P>0.05). ③ Compared with control cycle group, EHNA (30.0 nmol/L), an inhibitor of PDE₂, obviously decreased the atrial stroke volume and pulse pressure (P<0.05) and cAMP content had no change (P>0.05). EHNA (30.0 nmol/L) plus CNP (30.0 nmol/L) showed similar roles with EHNA only. ④ Compared with control cycle group, milrinone (1.0 nmol/L), an inhibitor of PDE₃, significantly increased the content of cAMP (P<0.05) and slightly increased the atrial stroke volume and pulse pressure, but had no significant differences (P>0.05). CNP (30.0 nmol/L) obviously decreased the atrial stroke volume and pulse pressure (P<0.001), and increased the cAMP content (P<0.05) by pretreatment of milrinone. Compared with milrinone

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group,milrinone plus CNP decreased the atrial stroke volume and pulse pressure ($P<0.001$),and the cAMP content had no change($P>0.05$). Conclusion CNP can inhibit atrial dynamics by increasing the content of cGMP,the different inhibitors of PDEs play different roles in the CNP-induced inhibition of atrial dynamics in isolated beating rabbit atria.

Keywords: atrial natriuretic; phosphodiesterase; heart atria; cyclic nucleotide

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