

## Protective effects of histamine H<sub>1</sub> and H<sub>2</sub> antagonists, adenosine and hydrocortisone on cardiac anaphylaxis<sup>1</sup>

QIU Rong, GUO Zhao-Gui<sup>2</sup>

(Research Section of Pharmacology, Hunan Medical University, Changsha 410078)

**ABSTRACT** Cardiac anaphylaxis was elicited in isolated working guinea pig hearts in the presence of the histamine receptor antagonists pyrilamine and cimetidine, adenosine or hydrocortisone. Histamine antagonists partially inhibited the occurrence of arrhythmias during cardiac anaphylaxis, but did not significantly antagonize the decrease in cardiac function. Adenosine used in combination with pyrilamine and cimetidine manifested an apparent anti-arrhythmic effect, however, the attenuation of cardiac function was still present. In the presence of hydrocortisone plus histamine antagonists, cardiac anaphylaxis, as expressed by arrhythmias and a decrease in cardiac function, was significantly inhibited. The results suggest that when histamine receptor antagonists are used in combination with hydrocortisone, a good protective effect on cardiac anaphylaxis can be achieved.

**KEY WORDS** cardiac anaphylaxis; isolated working heart; histamine; adenosine; glucocorticoids; arrhythmia; cardiac output

Heart is an important target organ in systemically immediate anaphylactic reaction<sup>(1)</sup>. "Cardiac anaphylaxis" is a term to express cardiac dysfunction in systemic anaphylaxis. We have produced cardiac anaphylaxis in isolated working guinea pig heart<sup>(2)</sup>. Three distinct phases of response were seen after antigen challenge in working heart sensitized with crystallized ovalbumin. Our previous results indicated that the sequence of events in cardiac anaphylaxis was the direct attack of the released

mediators on the heart, independent of pulmonary distress and peripheral vasomotor collapse. We also suggested that multiple mediators or autacoids, other than histamine, are involved in cardiac anaphylaxis. Because histamine is closely concerned with the cardiac dysfunction, the protective effects of the specific histamine H<sub>1</sub> and H<sub>2</sub> receptor antagonists, pyrilamine and cimetidine, on cardiac anaphylaxis have been observed. In addition, we observed the action of some non-specific antagonists. Adenosine inhibits the release of histamine by human basophils<sup>(3)</sup> and prevents the release of histamine and SRS-A induced by antigen in human lung<sup>(4)</sup>, but its action on cardiac anaphylaxis has not been reported. Hydrocortisone stabilizes the membrane of mast cells, then decreases the release of histamine. In this study, adenosine or hydrocortisone was used alone or in combination with histamine receptor antagonists to assess their protective effects.

### Materials and methods

The method of sensitization and experimental model used were the same as reference (2). Pyrilamine, cimetidine, adenosine each at 3 μmol/L, or hydrocortisone at 30 μmol/L were added to the perfusion solution 10 min before challenge. Antigen challenge was accomplished by a rapid intracardiac injection of 5 mg of ovalbumin dissolved in 0.1 ml warm oxygenated K-H solution.

Pyrilamine and cimetidine were purchased from Sigma Company. Adenosine was

Received 1987 Jul 27 Accepted 1988 Jun 22

<sup>1</sup> Project supported by the Science Fund of the Chinese Academy of Sciences, No 339

<sup>2</sup> To whom correspondence should be addressed

obtained from E Merck and hydrocortisone from An-yang Pharmaceutical Factory, China.

## Results

**Cardiac anaphylaxis in the presence of histamine  $H_1$  and  $H_2$  antagonists** Fourteen guinea pig hearts were used. Pyrilamine ( $3 \mu\text{mol/L}$ ) and cimetidine ( $3 \mu\text{mol/L}$ ) alone had inhibitory effects on cardiac function. In the presence of these two drugs, HR,  $+dP/dt_{\text{max}}$ ,  $-dP/dt_{\text{max}}$  declined by 13, 16 and 16% ( $P < 0.01$  or  $< 0.05$ ), respectively (Tab 1). Ten min after perfusion, HR and other parameters reached a steady state. When the heart was challenged at this time, the amplitude of augmentation in phase I was greatly reduced. Compared with the untreated hearts, the increases in LVP,  $\pm dP/dt_{\text{max}}$ , and ABF were abolished, but the increase in HR was not significantly affected (Fig 1). In phase II, arrhythmias, with an incidence of 8/14, including A-V block (8/14) and ventricular arrhythmia (5/14), occurred  $66 \pm 45$  s after challenge, and lasted for  $8 \pm 6$  min (Tab 2). Although the incidence of arrhythmias decreased in the presence of pyrilamine and cimetidine (from 80 to 57%) (Fig 2), it did not reach a level of statistical significance, and the onset and duration of arrhythmias were also not significantly changed. However, cardiac function

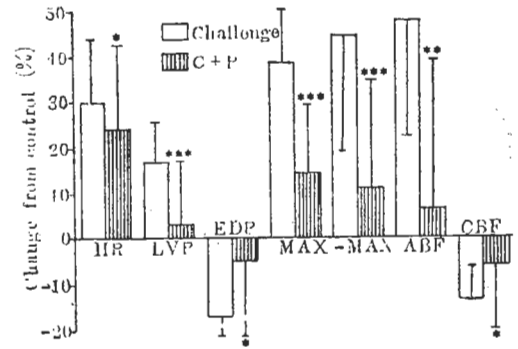


Fig 1. The changes in cardiac function parameters in the phase of augmentation (phase I) of cardiac anaphylaxis in the presence of cimetidine (C) and pyrilamine (P).  $\bar{x} \pm \text{SD}$ . \* $P > 0.05$ , \*\* $P < 0.05$ , \*\*\* $P < 0.01$  vs challenge. MAX;  $dP/dt_{\text{max}}$ , -MAX;  $-dP/dt_{\text{max}}$ . For details see text and Tab 3.

was reduced. LVP,  $+dP/dt_{\text{max}}$ , ABF and CBF were reduced by 5, 12, 19 and 16% ( $P < 0.05$  or  $< 0.01$ ), respectively, 5 min after challenge. Twenty min after challenge, arrhythmias ceased completely. Most of the cardiac parameters recovered to the level before challenge, however, ABF and CBF declined continuously (Tab 3).

**The influence of adenosine on cardiac anaphylaxis** Adenosine at  $3 \mu\text{mol/L}$  alone augmented cardiac function. LVP increased by 7% ( $P < 0.05$ ),  $+dP/dt_{\text{max}}$ ,  $-dP/dt_{\text{max}}$ , CBF increased by 14, 12 and 27% ( $P < 0.01$ ) respectively, while EDP decreased by 26% ( $P < 0.01$ ). No significant changes

Tab 1. Cardiac function parameters of sensitized isolated working guinea pig heart before and after administration of pyrilamine  $3 \mu\text{mol/L}$  and cimetidine  $3 \mu\text{mol/L}$ ,  $n = 14$ ; or adenosine  $3 \mu\text{mol/L}$ ,  $n = 5$ .  $\bar{x} \pm \text{SD}$ . \* $P > 0.05$ , \*\* $P < 0.05$ , \*\*\* $P < 0.01$

Parameter	Pyrilamine + Cimetidine			Adenosine		
	Before	After	% change	Before	After	% change
HR (bpm)	221 $\pm$ 22	192 $\pm$ 26	-13**	230 $\pm$ 27	249 $\pm$ 20	8*
LVP (kPa)	8.8 $\pm$ 0.7	8.2 $\pm$ 0.7	-7*	9.06 $\pm$ 0.9	9.7 $\pm$ 0.7	7**
EDP (kPa)	1.05 $\pm$ 0.2	1.09 $\pm$ 0.19	4*	0.82 $\pm$ 0.14	0.61 $\pm$ 0.11	-26***
$dP/dt_{\text{max}}$ (kPa/s)	310 $\pm$ 30	260 $\pm$ 37	-16***	350 $\pm$ 57	399 $\pm$ 60	14***
$-dP/dt_{\text{max}}$ (kPa/s)	230 $\pm$ 39	194 $\pm$ 39	-16***	260 $\pm$ 54	296 $\pm$ 61	12***
ABF (ml/min)	40 $\pm$ 10	31 $\pm$ 8	-22*	33 $\pm$ 12	35 $\pm$ 11	6*
CBF (ml/min)	7.0 $\pm$ 2.2	6.6 $\pm$ 2.5	-5*	9 $\pm$ 2	11.7 $\pm$ 2.3	27***

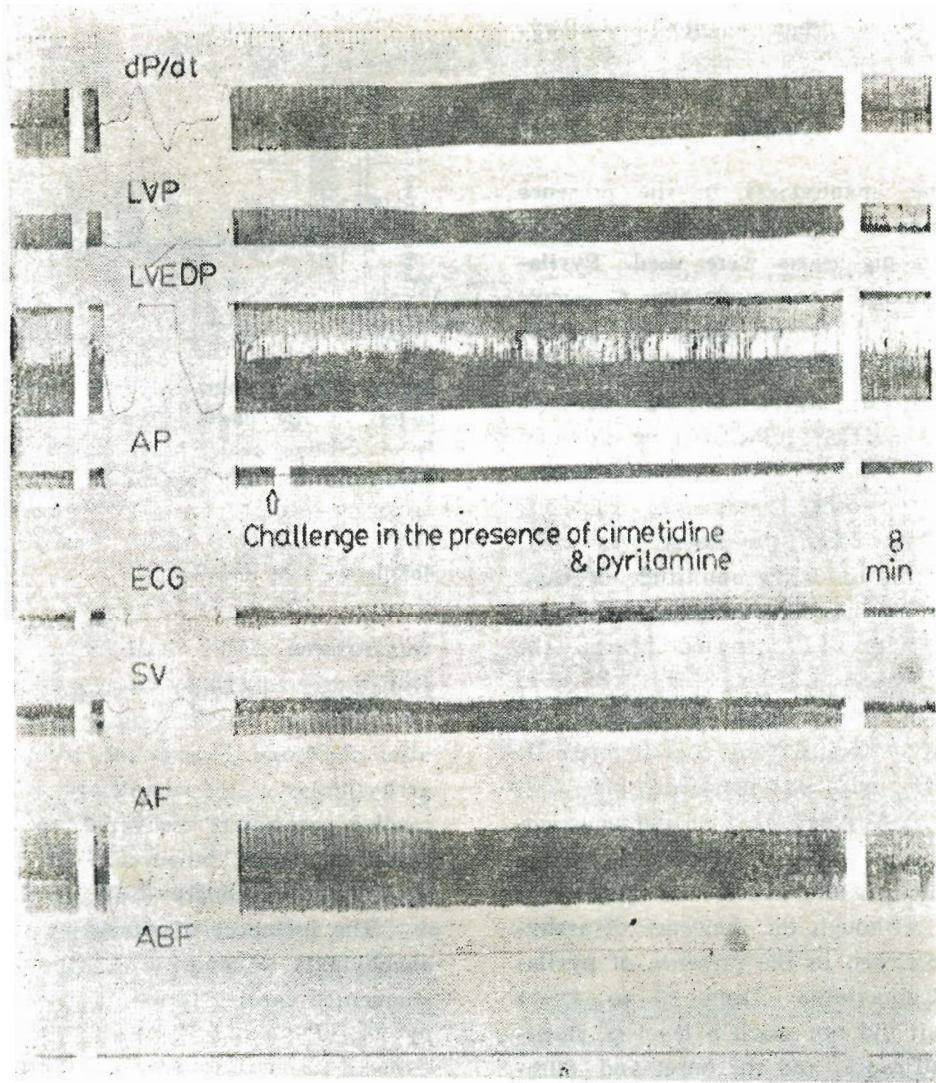


Fig 2. Response of sensitized, isolated working guinea pig hearts upon challenge in the presence of cimetidine ( $3\mu\text{mol/L}$ ) and pyrilamine ( $3\mu\text{mol/L}$ ). Note that arrhythmias were inhibited.

were seen in HR or ABF (Tab 1). When cardiac anaphylaxis was elicited in the presence of adenosine, cardiac function was enhanced  $21\pm 3$  s after challenge. HR, LVP,  $+dP/dt_{\text{max}}$ ,  $-dP/dt_{\text{max}}$  and ABF increased by 36, 16, 26, 36 and 19% ( $P < 0.05$  or  $< 0.01$ ) respectively, but the intensities of augmentation of  $\pm dP/dt_{\text{max}}$  and ABF in this phase were relatively suppressed compared with those of untreated hearts (control group), except for HR and EDP which increased remarkably (47%,  $P <$

0.01) (Tab 3). The onset of arrhythmias was delayed (from  $61 \pm 32$  to  $90 \pm 41$  s,  $P < 0.05$ ), while their duration (from  $8 \pm 4$  to  $7 \pm 7$  min,  $P > 0.05$ ) and incidence did not change significantly (Tab 2). In phase II, the declines of  $+dP/dt_{\text{max}}$  and  $-dP/dt_{\text{max}}$  were not very apparent, but ABF and CBF did decrease significantly (45 and 22% respectively,  $P < 0.05$ ). In the recovery phase, arrhythmia ceased and ABF remained at a low level, while EDP increased (Tab 3). After perfusing the sen-

**Tab 2.** Arrhythmias upon challenge on sensitized isolated working guinea pig hearts in the presence of drugs. P; pyrilamine 3  $\mu\text{mol/L}$ ; C; cimetidine 3  $\mu\text{mol/L}$ ; A; adenosine 3  $\mu\text{mol/L}$ ; HC; hydrocortisone 30  $\mu\text{mol/L}$ .  $\bar{x} \pm \text{SD}$ . \* $P > 0.05$ , \*\* $P < 0.05$ , \*\*\* $P < 0.01$  vs control group

Group	Incidence of severe arrhythmia	%	Onset of arrhythmia (s)	Duration of arrhythmia (min)
Control	8/10	80	61 $\pm$ 32	8 $\pm$ 4
P+C	8/14	57*	66 $\pm$ 45*	8 $\pm$ 6*
A	4/5	80*	90 $\pm$ 41**	7 $\pm$ 7*
P+C+A	5/12	42*	81 $\pm$ 22**	4.2 $\pm$ 2.2***
HC	6/7	85*	76 $\pm$ 28*	2.6 $\pm$ 1.5****
P+C+HC	4/6	67*	74 $\pm$ 16*	4 $\pm$ 3**

sitized heart with adenosine plus the histamine receptor antagonists pyrilamine and cimetidine, the brief stimulation in phase I was abolished, however, the increase in HR was not completely inhibited. These drugs reduced the incidence of arrhythmias (from 80 to 42%), delayed their onset (from 61  $\pm$  32 to 81  $\pm$  22 s,  $P < 0.05$ ), and remarkably shortened their duration (from 8  $\pm$  4 to 4.2  $\pm$  2.2 min,  $P < 0.05$ ) (Tab 2), but the inhibition of cardiac function was still apparent and was not completely recovered 20 min after challenge.

**The influence of hydrocortisone on cardiac anaphylaxis** Hydrocortisone at 30  $\mu\text{mol/L}$  alone exhibited some cardiotoxic effect on isolated working heart, although no significant differences were observed in the measured parameters compared with control values. When challenged in the presence of hydrocortisone, HR, LVP,  $+dP/dt_{\text{max}}$ ,  $-dP/dt_{\text{max}}$  and ABF in phase I increased by 38, 18, 20, 31 and 25% ( $P < 0.05$  or  $< 0.01$ ) respectively, but the intensities of augmentation of  $\pm dP/dt_{\text{max}}$  and ABF were relatively suppressed as compared with those of untreated heart (control group). The condition was the same as in the presence of adenosine. The onset of arrhythmias was slightly delayed (from 61  $\pm$  32 to 76  $\pm$  28 s,  $P > 0.05$ ), and their duration was

remarkably shortened (from 8  $\pm$  4 to 2.6  $\pm$  1.5 min,  $P < 0.01$ ) (Tab 2). The cardiac function parameters decreased obviously in phase II, with  $+dP/dt_{\text{max}}$ ,  $-dP/dt_{\text{max}}$ , ABF and CBF decreased by 25, 28, 53 and 22% ( $P < 0.01$  or 0.05) respectively, 5 min after challenge. In phase III, the attenuation of  $dP/dt_{\text{max}}$  returned to the level before challenge, while ABF, CBF and HR did not recover completely (Tab 3). When cardiac anaphylaxis was elicited in the presence of hydrocortisone plus pyrilamine and cimetidine, only an increase in HR in phase I was observed. The incidence of arrhythmia was 4/6 (67%), and its duration was shorter (from 8  $\pm$  4 to 4  $\pm$  3 min,  $P < 0.05$ ) (Tab 2). Cardiac function was less inhibited in phase II. Twenty min after challenge, cardiac function returned completely to the pre-challenge condition, except for the increase in HR.

## Discussion

As observed in our experiments, when the sensitized heart was challenged in the presence of pyrilamine and cimetidine, only the augmentation of contractility in phase I was abolished. Sinus tachycardia could not be completely inhibited. This dissociation of inhibition of the inotropic and chronotropic action was also seen in the presence of cimetidine alone, a detailed study on which has been reported in a separate paper<sup>(5)</sup>.

Levi *et al* once reported that in the Langendorff heart, when cardiac anaphylaxis was elicited in the presence of both histamine  $H_1$  and  $H_2$  antagonists, the rhythm disturbances could be prevented<sup>(6)</sup>. We found this not to be the case in the working heart preparation. Arrhythmias which appeared in the working heart during cardiac anaphylaxis can not be completely reversed or abolished under the combined blockade of  $H_1$  and  $H_2$  receptors as shown

**Tab 3.** The changes in cardiac function parameters of isolated working guinea pig hearts during cardiac anaphylaxis. Control, n=10; P+C, in the presence of pyrilamine 3 μmol/L and cimetidine 3 μmol/L, n=6; A, in the presence of adenosine 3 μmol/L, n=5; P+C+A, in the presence of adenosine, cimetidine and pyrilamine, 3 μmol/L respectively, n=12; HC, in the presence of hydrocortisone 30 μmol/L, n=7; P+C+HC, in the presence of hydrocortisone (30 μmol/L), cimetidine (3 μmol/L) and pyrilamine (3 μmol/L), n=6,  $\bar{x} \pm SD$ . \*P>0.05, \*\*P<0.05, \*\*\*P<0.01 vs before challenge, ††P<0.05, †††P<0.01 vs control group.

Parameter	Group	Before	Phase-I (1 min)		Phase-II (5 min)		Phase-II (20 min)	
		challenge	Changes	%	Changes	%	Changes	%
HR (bpm)	Control	236±22	71±32	30***	-17±51	-7*	-4±19	-2*
	P+C	192±26	45±32	24***	-17±52	-9*	-6±38	-3*
	A	249±20	91±24	36***	34±64	13*	23±26	9†††
	P+C+A	231±24	34±28	14***††	15±50	6*	-0.5±17	-0.2*
	HC	246±19	92±12	38***	42±73	17*†††	31±18	12***†††
	P+C+HC	233±21	25±16	11***†††	-39±61	-17*	14±11	6**
LVP (kPa)	Control	8.2±0.7	1.5±0.7	18***	-0.3±0.7	-4*	-0.8±1.5	-10*
	P+C	8.2±0.7	0.3±1.1	3*†††	-0.5±0.8	-5**	-0.1±0.8	-3*
	A	9.7±0.7	1.6±0.5	16***	-0.9±0.5	-10**	-0.4±0.4	-4*
	P+C+A	10.1±1.1	-0.1±0.6	-1*†††	-1.5±0.9	-15***†††	-1.2±0.7	-12***
	HC	9.2±1.6	1.6±0.9	18**	-0.7±1.1	-7*	-0.1±0.7	-1*
	P+C+HC	7.4±0.5	0.4±0.7	6*†††	-0.4±0.3	-5**	-0.1±0.4	-2*
EDP (kPa)	Control	0.84±0.15	-0.15±0.19	-18**	-0.01±0.21	-1*	0.21±0.28	25**
	P+C	1.09±0.19	-0.05±0.23	-5*	0.004±0.19	0.5*	0.01±0.16	2*
	A	0.61±0.11	0.29±0.11	47***†††	0.25±0.23	42*††	0.25±0.16	41**
	P+C+A	0.98±0.24	0.15±0.24	15***†††	0.20±0.34	20*	0.15±0.23	16***
	HC	0.90±0.21	0.16±0.23	18*†††	0.30±0.47	34*	0.08±0.13	9*
	P+C+HC	0.86±0.20	0.05±0.29	7*	0.11±0.49	13*	0.03±0.29	4*
dP/dt <sub>max</sub> (kPa/s)	Control	311±30	120±36	38***	-22±32	-7*	-49±50	-16**
	P+C	260±37	37±44	14***†††	-31±46	-12**	-20±52	-8*
	A	399±60	103±80	26**	-39±53	-10*	-11±34	-3*
	P+C+A	347±61	0.4±28	0.1*†††	-73±78	-21***†††	-52±30	-15***
	HC	389±50	79±72	20**	-96±62	-25***	-20±39	-5*
	P+C+HC	268±39	21±33	8*†††	-46±60	-17*†††	-6±19	-2*
-dP/dt <sub>max</sub> (kPa/s)	Control	218±34	97±44	44***	-20±27	-9**	-38±38	-17**
	P+C	194±39	23±50	12*†††	-15±30	-8*	-16±36	-8*
	A	296±61	103±54	36**	-48±45	-16*	-8±38	-3*
	P+C+A	291±61	-8±42	-3*†††	-81±61	-28***†††	-63±39	-20***
	HC	296±38	91±59	31***	-84±48	-28***†††	-28±63	-9*
	P+C+HC	223±40	16±22	7*†††	-38±44	-17*	-20±20	-9*
ABF (ml/min)	Control	23±3	11±4	46***	-5±4	-23***	-9±10	-39**
	P+C	31±8	2±8	8*††	-5±8	-19**	-5±8	-19**
	A	35±11	7±1	19***†††	-16±8	-45***†††	-7±4	-19**
	P+C+A	37±14	1±6	4*†††	-13±15	-36***†††	-7±5	-19***
	HC	36±7	9±4	25***	-19±12	-53***†††	-8±8	-23**
	P+C+HC	24±8	4±5	18*†††	-7±10	-29*	-2±7	-11*
CBF (ml/min)	Control	6.6±1.3	-0.9±0.7	-14***	-1.0±0.6	-14***	-0.3±1.0	-5*
	P+C	6.6±2.5	-0.4±0.9	-4*	-1.1±0.8	-16***	-0.8±0.9	-13***
	A	11.7±2.3	-1.4±2.0	-12*	-2.6±1.9	-22***†††	-1.8±1.5	-15*††
	P+C+A	10.5±2.8	-1.2±1.4	-12**	-3.4±4.5	-32***†††	-3.3±2.3	-32***†††
	HC	13.0±4.0	-1.5±1.1	-11**	-2.9±2.3	-22**††	-1.7±1.7	-12***†††
	P+C+HC	9.1±2.2	-0.8±1.6	-9*	-1.6±2.1	-18*	-1.3±1.7	-14*

by the fact that about 50% of the hearts still exhibited the same typical arrhythmias in time of onset and duration. A possible explanation is that we induced cardiac anaphylaxis in the working heart preparation. The working and energy consuming heart is much more sensitive to myocardial ischemia. In addition to histamine, other substances, such as leukotrienes (LTs), prostaglandins (PGs) and platelet-activating factor (PAF) are released from sensitized heart after challenge<sup>(7,8)</sup>. The potent coronary constriction action mediated by LTs and PAF was usually an important cause of arrhythmias<sup>(9,10)</sup> and progressive decrease in cardiac function. Thus, when systemic anaphylaxis takes place, by using only histamine antagonists to treat the cardiac dysfunction, the protective effect is doubtful.

It has been reported that adenosine diminishes the immunological release of histamine and SRS-A via stimulating  $A_2$  receptors of the basophil membrane<sup>(4)</sup>, and inhibiting the action of cAMP via inhibiting adenylate cyclase, and then decrease the  $H_2$  receptor activity<sup>(11)</sup>. In addition, adenosine may also decrease the automaticity of the sinus node and dilate coronary vessels<sup>(12)</sup>. According to our results, adenosine 3  $\mu\text{mol/L}$  used alone can only delay the onset of arrhythmia in cardiac anaphylaxis, neither the incidence nor duration of the arrhythmia was significantly reduced. When it was used in combination with histamine antagonists, arrhythmias occurred less frequently and their durations was shortened remarkably. It is worth pointing out that adenosine alone can antagonize the attenuation of  $dP/dt_{\text{max}}$  and ABF as seen in the recovery phase of cardiac anaphylaxis, however, EDP, one of the important parameters for interpreting cardiac function, consistently increased concomitant with a decrease in CBF throughout the entire course of cardiac anaphy-

laxis, indicating that cardiac function had worsened. This condition did not improve when adenosine was used in combination with pyrilamine and cimetidine.

Hydrocortisone is a classic anti-inflammatory and anti-immunological agent. It stabilizes the granules of mast cells, inhibits the influx of  $\text{IgE-Ca}^{2+}$  and then interferes with immunological histamine release<sup>(13)</sup>. In the presence of hydrocortisone alone, the shortening of arrhythmic duration can be explained by its inhibitory action on the release of histamine and other mediators and its direct improvement of A-V conduction. When it was used in combination with histamine antagonists, arrhythmias occurred less frequently and pump function was less inhibited in phase II and recovered more quickly in phase III in the presence of these drugs, suggesting that a satisfactory protective effect was achieved.

## References

- 1 Capurro N, Levi R. The heart as a target organ in systemic allergic reactions: comparison of cardiac anaphylaxis *in vivo* and *in vitro*. *Circ Res* 1975; 36 : 520
- 2 Qiu R, Guo ZG. Cardiac anaphylaxis in isolated working guinea pig heart. *Acta Pharmacol Sin* 1988; 9 : 143
- 3 Church MK, Holgate ST, Hughes PJ. Adenosine inhibits and potentiates IgE-dependent histamine release from human basophils by an  $A_2$ -receptor mediated mechanism. *Br J Pharmacol* 1983; 80 : 719
- 4 Hillyard PA, Nials AT, Skidmore IF, Varday CJ. Characterization of the adenosine receptor responsible for the inhibition of histamine and SRS-A release from human lung fragments. *Ibid* 1984; 83 : 337
- 5 Guo ZG, Qiu R. Dissociation of cimetidine effect on inotropic and chronotropic action in cardiac anaphylaxis. *Acta Pharmacol Sin* 1989; 10 (2) : (in press)
- 6 Levi R, Allan G. Histamine-mediated cardiac effects. In: Bristow MR, ed. *Drug-induced heart diseases*. Amsterdam: Elsevier, 1980 : 377-95

- 7 Engineer DM, Niederhauser U, Piper PJ, Sirois P. Release of mediators of anaphylaxis: inhibition of prostaglandin synthesis and the modification of release of slow reacting substance of anaphylaxis and histamine. *Br J Pharmacol* 1978; 62 : 61
- 8 Levi R, Burke JA, Guo ZG, *et al.* Acetyl glyceryl ether phosphorylcholine (AGEPC) : A putative mediator of cardiac anaphylaxis in the guinea pig. *Circ Res* 1984; 54 : 117
- 9 Roth DM, Lefer DJ, Hock CE, Lefer AM. Effects of peptide leukotrienes on cardiac dynamics in rat, cat, and guinea pig hearts. *Am J Physiol* 1985; 249 : H 477
- 10 Aehringhaus U, Peskar BA, Wittenberg HR, Wolbling RH. Effect of inhibition of synthesis and receptor antagonism of SRS-A in cardiac anaphylaxis. *Br J Pharmacol* 1983; 80 : 73
- 11 Hattori Y, Levi R. Adenosine selectively attenuates  $H_2$ - and *Beta*-mediated cardiac responses to histamine and norepinephrine: an unmasking of  $H_1$ - and *alpha*-mediated responses. *J Pharmacol Exp Ther* 1984; 231 : 215
- 12 Merrill G, Young M, Dorell S, Krieger L. Coronary interactions between nifedipine and adenosine in the intact dog heart. *Eur J Phamacol* 1982; 81 : 543
- 13 Heiman AS, Crews FT. Inhibition of immunoglobulin, but not polypeptide base-stimulated release of histamine and arachidonic acid by anti-inflammatory steroids. *J Pharmacol Exp Ther* 1984; 230 : 175

中国药理学报 1989年1月; 10(1): 34-40

## 组胺 $H_1$ , $H_2$ 受体拮抗剂, 腺苷及氩可的松对心性变态反应的保护作用<sup>1</sup>

丘容、郭兆贵 (湖南医科大学药理研究室, 长沙 410078)

**提要** 本文观察了组胺  $H_1$  受体拮抗剂美吡拉敏(P)和  $H_2$  受体拮抗剂西咪替丁(C), 以及非特异性拮抗剂腺苷(A)和氩可的松(HC)对豚鼠离体工作心脏心性变态反应三个时相变化的影响。P+C能明显减弱时相I的心功能增强, 但对心率增快无明显影响; 能部分抑制心性变态反应时心律失常的发生, 对心功能减弱无明显对抗作用。A与P+C合用时有较好的抗心律失常效应, 但心功能抑制仍较明显。HC与P+C合用能

明显抑制心性变态反应时的心律失常和心功能降低。结果提示特异性组胺拮抗剂与氩可的松药物合用对心性变态反应有较好的保护作用。

**关键词** 心性变态反应; 离体工作心脏; 组胺; 腺苷; 糖皮质激素; 心律失常; 心排出量

<sup>1</sup> 中国科学院科学基金资助的课题 № 339