EFFECT OF SOME β–ADRENOCEPTOR BLOCKERS AND OF (+) PROPRANOLOL ON ADRENALINE-INDUCED PULMONARY EDEMA IN MICE

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Summary : (+) Propranolol is considered to prevent adrenaline–induced pulmonary edema (A.P.E.) due to the β–adrenoceptor blockade. However, local anaesthetics also are known to prevent pulmonary edema. To assess the role of β–adrenergic blockade in A.P.E., the effect of a β_1–blocker possessing local anaesthetic action (± Metaprolol) and a β_1-blocker possessing no local anaesthetic action (± practolol) was studied along with propranolol derivatives. The study revealed that (+), (—), (±) propranolol and (±) metaprolol completely prevented A.P.E. whereas (±) practolol did not. This shows that local anaesthetic action but not the β–adrenergic blockade may be responsible for prevention of A.P.E.

Key words : β–blocker local anaesthetics pulmonary edema

INTRODUCTION

± Propranolol, a β-blocker was found to protect adrenaline-induced pulmonary edema (A.P.E.) in mice (6) and in rabbits (1). In rabbits, the effect is attributed to prevention of adrenaline-induced myocardial changes, since (±) propranolol is a potent β-adrenoceptor blocker. It is known that iv injection of local anaesthetics also prevent experimental pulmonary edema induced by various methods (4,7). To test whether the β-blocking effect or local anaesthetic effect of (±) propranolol underlines prevention of A.P.E., several β-blockers and (+) propranolol, an isomer without much β-blocking activity, but with a potent local anaesthetic action was studied in A.P.E.

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MATERIAL AND METHODS

Adult albino mice of either sex (17-26 g) were divided into various group (Table I). After 20 to 30 min of drug treatment, L-adrenaline (2 *mg/kg*; 1:10,000 w/v solution) was injected via tail vein (8). Untreated mice were also used and were given either saline or adrenaline (control groups). After 1 hr of injection of saline/L-adrenaline, the surviving animals were killed with ether. Pulmonary edema was assessed in all the animals in different groups from :

(1) haemorrhage in the lung as assessed by haemorrhagic patches and spots by macroscopic observation (qualitative) and

(2) lung body weight index (L.B.I.)— $\frac{\text{weight of lung}}{\text{body weight}} \times 100$

Results were analysed using 't' test (L.B.I) or 'Chi square test with Yate's correction' (haemorrhagic lungs).

RESULTS

Adrenaline in the dose of 2 *mg/kg*, iv was found to induce considerable pulmanary edema (Table I) as judged from haemorrhage in lung and LBI.

TABLE I : Effect of some β–adrenoceptor blockers and of (+) propranolol on pulmonary edema-induced by L–adrenaline (2 *mg/kg, iv*) in mice.

Pretreatment		*(a)*		*(b)*	
		L.B.I.$\pm$*S.E.*	*P value*	*% Haemorrhagic lung*	*P value*
Nil	(n=10)	1.33$\pm$0.11	—	90	—
(+) Propranolol	(n=10)	0.82$\pm$0.09	$<$0.005	20	$<$0.001
(—) Propranolol	(n=10)	0.79$\pm$0.10	$<$0.005	10	$<$0.001
($\pm$) Propranolol	(n=10)	0.74$\pm$0.08	$<$0.001	10	$<$0.001
($\pm$) Practolol	(n=10)	1.21$\pm$0.15	$>$0.05	80	$>$0.05
($\pm$) Metaprolol	(n=10)	0.87$\pm$0.07	$<$0.005	30	$<$0.001

(a) L.B.I. = lung body weight index (see Methods).

(b) A lung was considered 'haemorragic' if haemorrage was seen in at least one lobe of a lung. Adrenaline-induced a significant ($P<0.001$) rise in L.B.I. and proportion of haemorrhagic lungs (value in saline control: L.B.I. 0.71; % haemorrhagic lung 0; n=10).

Pretreatment with (+), (—) or (±) propranolol or (±) metaprolol completely prevented A.P.E. However, (±) practolol was unable to prevent A.P.E.

DISCUSSION

The observations in the present study with (±) propranolol and (—) propranolol (possessing β-adrenoceptor blocking action), (+) propranolol (possessing minimal β-blocking action), (±) practolol (a β_1-blocker possessing no local anaesthetic action) and (±) metaprolol (a β_1-blocker possessing local anaesthetic action) point out that β-blocking effect, particularly β_1-blocking effect may not be essential for prevention of A.P.E. It seems that local anaesthetic action may explain the prevention of A.P.E. observed by us. since iv injection of a local anaesthetic (procaine) prevents experimental pulmonary edema induced by various methods (4,7).

The site of action of these drugs however, is not clarified by our work. Adrenaline induced pulmonary edema has been shown to be mediated via the CNS (3,5) and "neuroedematogenic centre" responsible for pulmonary edema has been proposed (2,9). It is possible that drugs-effect observed in our work may be centrally mediated.

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