TOPICAL ANTI-INFLAMMATORY ACTIVITY OF SALBUTAMOL IN MICE

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Various mechanisms may be involved in the anti-inflammatory activity of β-adrenoceptor agonists, including functional antagonism of endothelial cell contraction induced by inflammatory mediators, inhibition of mast cell disruption and suppression of leucocyte activity. We have investigated the topical anti-inflammatory activity of the selective β_2 agonist salbutamol by measuring its effects on oedema, plasma protein exudation and intravascular blood volume.

Inflammation was induced in Schofield mice (25-30g) by applying croton oil (5µl 2.5% w/v in chloroform) to the inner surface of one ear. Maximal oedema developed 4-5hr later. Drugs were applied to the ear in 5µl ethanol 1h prior to croton oil. The mice were killed 4h after application of croton oil and both control and inflamed ears amputated. A 4 or 5mm disc was cut out of each ear with a steel punch and the difference in weight of the discs taken as a measure of oedema. The plasma volume of the ear discs and plasma protein extravasation were assessed by injecting ^{125}I-human serum albumin (^{125}I-HSA) i.v. and comparing the accumulation of ^{125}I in the ear discs with levels of ^{125}I in blood plasma collected by cardiac puncture. Similarly, intravascular volume of the ear discs was assessed by injecting ^{51}Cr-labelled erythrocytes i.v. and comparing the ^{51}Cr content of the ear discs with ^{51}Cr in the blood (Green, 1978).

There was excellent correlation between the accumulation of ^{125}I and the increase in weight of ears inflamed by croton oil. Inflamed ears contained up to 55 fold more ^{125}I than contralateral non-inflamed ears (Table 1), indicating a dramatic increase in the permeability of the local blood vessels to plasma proteins. Indeed, the increase in weight of the ears appeared to be essentially due to the accumulation of undiluted plasma in the extravascular space. For example, an increase in ear disc weight of 23.0±1.2mg was associated with an increase in the ^{125}I content equivalent to 22.3±1.2µl of plasma. Intravascular volume of inflamed ear discs as assessed by the accumulation of ^{51}Cr-erythrocytes was only increased approx 2 fold ($P < 0.05$). Thus, the additional ^{125}I-HSA in inflamed ears appeared to be mainly extravascular. Salbutamol was effective in inhibiting oedema and plasma protein exudation (Table 1), being approx 2-4 times more potent than hydrocortisone. Neither salbutamol nor hydrocortisone had a significant effect on the ^{125}I or ^{51}Cr content of non-inflamed ears.

These results show that salbutamol has significant topical anti-inflammatory activity. In view of its effectiveness in inhibiting mast cell disruption salbutamol might be particularly useful in the treatment of inflammatory skin conditions.

Table 1. Effect of salbutamol on the oedema and accumulation of ^{125}I-HSA or ^{51}Cr-erythrocytes in inflamed mouse ears. (mean ± SEM, n = 6)

Concentration of salbutamol applied	Ear wt (mg)	% oedema inhibition	% increase in ^{125}I content	% increase in ^{51}Cr content
Control	38.0 ± 1.2	-	5544 ± 272	239 ± 98
0.01% w/v	31.1 ± 2.3*	29 ± 10	3231 ± 681*	143 ± 36
0.1 "	23.4 ± 2.0**	62 ± 9	1830 ± 438**	116 ± 40
0.25 "	22.1 ± 1.2**	69 ± 6	1161 ± 282**	71 ± 15
1.0 "	21.5 ± 1.1**	73 ± 5	1067 ± 308**	120 ± 43

* $P < 0.05$; ** $P < 0.001$ unpaired t-test

We thank the Psoriasis Association for financial support.

Green, K.L. (1978) Br.J.exp.Path. 59, 38-47.