DEMONSTRATIONS

Enhanced effect of isoprenaline after chronic administration in microanaphylactic shock of guinea-pigs

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Microanaphylactic shock can be produced in guinea-pigs, sensitized to egg albumen, by inhalation of antigen aerosol (Herxheimer, 1952). We have investigated the protective effect of acute and chronic administration of isoprenaline on the micro-anaphylactic shock and on the response to a mediator of anaphylaxis, histamine, given by aerosol.

Male guinea-pigs (Dunkin-Hartley, 200 g) were sensitized to egg albumen. They were then exposed individually in a perspex chamber (20 × 10 × 12 cm) to an aerosol of egg albumin (1 g/100 ml) produced by a Wright's nebulizer (air pressure 69 kPa). Preconvulsion times were measured following a procedure similar to that developed by Herxheimer (1952). The animals were exposed to the antigen at weekly intervals to avoid desensitization (Hicks & Okpako, 1968). Histamine shocks were given using an aerosol of the drug (5–10 mg/ml). Isoprenaline was given by aerosol for 2 min prior to antigen or histamine challenge–acute dosing. Chronic dosage meant a 2 min exposure three times daily for 1–3 weeks.

Acute dosing with isoprenaline protected guinea-pigs against microanaphylactic and histamine shock by increasing the preconvulsion time. The effect of isoprenaline lasted up to 15 minutes. Chronic dosing with isoprenaline progressively and reversibly increased the degree of protection obtained each week against microanaphylactic shock without a similar effect on histamine shock. The duration of action of isoprenaline was unaffected. Table 1 summarises the results of one such experiment on microanaphylactic shock.

β-Adrenoceptor agonists act not only as bronchodilators but also reduce the release of mediators of anaphylaxis (Assem & Schild, 1971). Perhaps the latter mechanism becomes more effective with chronic administration of isoprenaline.

References

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Table 1 Preconvulsion times (mean ± s.e. mean) of guinea-pigs caused by egg albumen before (control) and after inhalation of isoprenaline given by aerosol

Isoprenaline concentration in aerosol (mg/ml)	*Isoprenaline concentration in chamber (μg/l)*	*Control Preconvulsion Time (s)*	*Preconvulsion times after isoprenaline*			
			Acute dosage	*Chronic dosage*		
				1 week	*2 weeks*	*3weeks*
0.33	6	50 ± 2.9 (6)	85 ± 5.5	112 ± 8.5	178 ± 4.3	213 ± 11.0
1	18	49 ± 4.1 (6)	140 ± 7.9	184 ± 8.1	223 ± 9.2	258 ± 19.0
10	180	55 ± 5.4 (4)	210 ± 14.8	280 ± 14.1	280 ± 12.1	—

Figures in brackets are the number of animals. The progressive increase in preconvulsion times after chronic dosage was significant ($P < 0.05$) as shown by the Friedman two-day analysis of variance by ranks (Siegel, 1956)