Comparison of intravenous and aerosol salbutamol

Aerosol salbutamol has a prolonged bronchodilator effect[1] and is more potent than an equal intravenous dose.[2] We have studied both routes of administration in asthmatic patients to compare their length of action.

Patients, methods, and results

Five patients with well controlled asthma were studied. Their asthma showed no significant diurnal variation. All were being treated with salbutamol by regular inhalation, and three took prednisone. They were studied on two consecutive mornings, having stopped bronchodilator drugs for 12 hours.

Recordings were made of FEV_1 and forced vital capacity (FVC) with a Vitalograph dry spirometer. Peak expiratory flow rate (PEFR) was measured with a Wright peak flow meter. Radial pulse rate was measured manually.

On the first day, after consistent baseline readings were obtained, all patients received 250 μg salbutamol intravenously over 3 minutes. Pulse rate was recorded immediately and all measurements were made 5, 10, and 15 minutes following intravenous injection and then repeated at 15-minute intervals to 90 minutes and at 30-minute intervals to 240 minutes. Aerosol salbutamol was then given from a pressurised aerosol in 100 μg doses at 5-minute intervals to estimate the cumulative dose required to produce an equivalent increase in FEV_1 to the intravenous dose.

On the second day this equivalent dose of aerosol salbutamol was given in 100 μg increments over 3 minutes followed by the same protocol of measurements.

Four patients required 200 μg aerosol salbutamol and one needed 100 μg to produce the same immediate increase in FEV_1 as 250 μg intravenous salbutamol. The table shows the mean increases ($\pm$standard error) in FEV_1 for the two preparations; curves drawn for individual patients conformed to the mean pattern. Similar curves were obtained for PEFR and FVC. The peak response was not significantly different, but the aerosol bronchodilatation declined more slowly. Student's paired t test showed a significant difference between the means from 45 to 210 minutes ($P < 0.05$), which was more significant at 120 minutes ($P < 0.01$). The differences were not significant ($P < 0.1$) for PEFR over similar periods or for FVC. Pulse rate increased by a mean 20 beats min^{-1} after intravenous salbutamol; no increase was detected after the aerosol.

Mean ($\pm$standard error) percentage changes in FEV_1 in five patients after 250 μg salbutamol intravenously and 100-200 μg by aerosol observed over 240 minutes

Time (minutes)	Intravenous		Aerosol	
	Mean % change FEV_1	Standard error	Mean % change FEV_1	Standard error
0	0		0	
5	44·8	10·2	44·6	15·4
10	47·0	9·7	47·4	14·3
15	43·8	10·8	51·5	12·9
30	32·6	8·8	48·4	12·0
45	33·8	11·3	48·4	13·8
60	32·2	14·0	43·5	14·8
75	23·1	9·4	43·7	14·3
90	26·9	8·9	41·0	9·3
120	18·6	4·9	34·9	5·5
150	15·8	5·8	33·5	7·1
180	9·4	2·7	21·9	5·6
210	4·5	2·0	20·1	5·9
240	1·3	1·3	7·6	2·2

Discussion

Aerosol salbutamol might be expected to achieve higher surface concentrations in bronchial mucosa and smooth muscle than an equal intravenous dose and thus have a greater bronchodilator effect.[2] However, when we deliberately lowered the aerosol dose to produce an equivalent increase in FEV_1 and, therefore, presumably an equivalent stimulation of $beta_2$-receptors, the aerosol showed a more prolonged bronchodilator effect. The discrepancy between these two routes is even greater when one appreciates that only a fraction of an inhaled aerosol reaches the bronchi.[3,4] This suggests that a very small dose is required for bronchodilator activity, which is most economically achieved by the aerosol route.

The prolonged bronchodilatation provided by very small doses of aerosol salbutamol was also a striking finding and may result either from its slow removal from bronchial epithelium or because inhibition of mediator release[5] augments its bronchodilator effect by this route. Further studies of the rate of removal of salbutamol from the human lung should resolve this question.

The results also have a clinical message. For ambulant patients the aerosol route is very potent, minimises side effects, and lasts longer than intravenous injection. It is important to see if this also applies to acute severe asthma, when parenteral bronchodilators are often used in preference to the aerosol route. It needs to be established which route is best for this common medical emergency.

[1] Kennedy, M C S, and Simpson, W T, *British Journal of Diseases of the Chest*, 1969, **63**, 165.
[2] Spiro, S G, *et al*, *Thorax*, 1975, **30**, 236.
[3] Palmes, E D, *et al*, *Journal of Applied Physiology*, 1973, **34**, 356.
[4] Symposium on isoproterenol therapy in asthma, *Annals of Allergy*, 1973, **31**, 1.
[5] Assem, E S K, and Schild, M O, *Nature*, 1969, **224**, 1028.

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Hypertransaminasaemia with heparin treatment: effect of regular haemodialysis

Sonnenblick *et al*[1] reported that chronic heparin treatment (10 000 units intravenously every six hours for 10-21 days) increased serum aspartate aminotransferase (SGOT) and alanine aminotransferase (SGPT) activities by about 500%. This might cause confusion in the differential diagnosis of pulmonary infarction, myocardial infarction, or liver disease in patients treated with heparin. Since this confusion might also extend to patients undergoing regular haemodialysis, where heparin treatment is routine, it is important to know whether heparin will induce an increase in the serum activities of these enzymes in such patients. An increase in SGPT activity may be an early sign of hepatitis and so the action of heparin on this enzyme's activity must be closely defined in all patients undergoing regular haemodialysis.

Patients, methods, and results

SGPT was measured by the Technicon SMA 12/60 method in 19 patients with chronic renal failure before, during, and at the end of routine haemodialysis. Patients had been maintained on either a Meltec 1·5 m^2 multipoint four hours three times a week or a Meltec 1·0 m^2 multipoint six hours three times a week for one to 41 months. The heparin regimen (Heparin BP) was either a bolus of 5000 units with supplementary infusions of 1000 units hourly (total dose 10 000 units) or simply 9000 units at the beginning of dialysis.

The results are shown in the table. The normal range for our laboratory is 8-47 IU/l. There were no significant differences (on the paired t test) between the values at different times.

Mean SGPT values at various stages during haemodialysis

	Before dialysis	2 hours	4 hours	6 hours
No of patients	19	19	19	10
Geometric mean (IU/l)	22·9	21·9	22·3	20·6
95% confidence limits (IU/l)	10–53	10–50	10–52	10–42

Comment

These results indicate that routine heparin treatment during standard haemodialysis three times a week caused no significant acute change in the SGPT activity. Moreover, the range of SGPT values was not significantly different from that of the normal population, suggesting that chronic, intermittent heparin treatment does not cause