PAPERS AND ORIGINALS

Intravenous Salbutamol in Management of Status Asthmaticus

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Summary

After the administration of intravenous salbutamol (100-300 μ g) to 11 patients admitted to hospital with a severe exacerbation of asthma there was a mean increase in peak expiratory flow of 44% accompanied by a rise in pulse rate of 24 beats/min. Blood gas tensions showed a trend to improvement and there were no serious side effects.

It is concluded that intravenous salbutamol is an effective and apparently safe bronchodilator in the management of acutely ill patients with severe asthma.

Introduction

Though intravenous aminophylline is widely used as a bronchodilator in the management of severe attacks of asthma recent reports have drawn attention to its potential cardiotoxicity (*Lancet*, 1973). The specific β_2 -adrenergic agonist salbutamol has been shown to be effective and safe by both inhalation (Tattersfield and McNicol, 1969) and the oral route (Parker *et al.*, 1971). We report here an initial assessment of its use intravenously in severe acute asthma.

Patients and Methods

The observations were made on 11 patients who had been admitted to hospital with a severe acute exacerbation of asthma. Clinical details are given in table I. Patients who had received an intravenous bronchodilator within the preceding three hours

were excluded, but not those who had been treated with oral or inhaled bronchodilators or corticosteroids. Patients in whom there was evidence of particularly severe illness (a peak expiratory flow (PEF) <100 l/min, pulse rate than 130/min, or P_{CO_2} >5.3 kPa (40 mm Hg)) or who had previously received steroids were given concurrently intravenous hydrocortisone 200 mg.

Baseline observations of PEF (by Wright's peak flow meter) and pulse rate were made at five-minute intervals for 10 minutes before injection of intravenous salbutamol. A dose of 100-300 μ g was used. The injection was given over a period of up to one minute. Observations of PEF and pulse rate were then continued at five- and ten-minute intervals for 40 minutes. Blood gas tensions were analysed before injection and 60 minutes later. If there was a deterioration in symptoms, circulatory state, or blood gas tensions the observations were stopped and other therapy given. In five patients the effect of an additional dose of intravenous salbutamol was observed. The second dose was given at least 20 minutes after the first dose and only to patients in whom PEF and pulse rate had remained constant within the preceding 10 minutes.

Side effects were monitored by careful observation of the patient for a period of one hour. Any untoward symptoms experienced by the patients were noted.

Results

PEF.—Results are shown in fig. 1 expressed as percentage change from the final value of the baseline period. Mean readings throughout the baseline period showed no significant differences. The mean maximum rise in PEF with relief of symptoms occurred between five to 10 minutes in eight of the 11 patients. In the remaining three patients, all of whom were steroid-dependent and had severe asthma, the mean maximum response was achieved at about 30 minutes. At five minutes after intravenous salbutamol the mean increment ($\pm$ S.D.) in PEF was $44 \pm 23\%$ (range 4-78%; $P < 0.001$). In six of the patients there was some reduction in dyspnoea. The mean value of PEF for the group as a whole remained above pretreatment levels throughout the 40-minute period of observation. At 40 minutes the mean increment was $34 \pm 30\%$ (range -12 to +70%; $P < 0.05$). In the five patients given a second injection

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TABLE 1—Clinical Details of Patients and Summary of Results

Case No.	Age and Sex	Duration of Previous Asthma (Years)	Duration of Episode Studied	Maintenance Treatment	Pretreatment PEF (l./min)	Dose of Salbutamol (μ g)	Clinical Result	Maximum % Increase PEF	PEF at Discharge (l./min)	Side Effects
1	16 F.	None	3 days	Nil	130	100	Good	122	380	None
2	60 M.	20	4 hours	Prednisone	125	150 + 150	Poor	21	250	None
3	35 M.	6	7 days	theophylline	75	180	Poor	31	490	Tremor
4	39 F.	34	3 days	Oral salbutamol	110	150	Good	63	200	Tremor
5	63 M.	25	12 hours	Prednisone	130	200	Good	43	375	Tremor
6	30 F.	10	36 hours	oral salbutamol	130	200	Good	84	380	+ Tremor
7*	56 M.	5	48 hours	Franol isoprenaline inhaler	145	200	Poor	47	500	None
8	30 M.	23	4 days	Beclomethasone dipropionate inhaler	170	300	Good	76	580	None
9	53 F.	34	8 days	oral salbutamol	120	200	Good	25	225	Dizziness
10	58 F.	13	2 days	Isoprenaline inhaler	85	150	Poor	30	250	Tremor
11	55 F.	4	5 days	Prednisone	75	200 + 200	None (respiratory) failure	4	450	See text
				Franol Salbutamol inhaler	<60		None (respiratory) failure	10		

*This patient had a further episode of asthma 24 hours after first.

FIG. 1—Mean % change (± 2 S.E.) in peak expiratory flow in 11 patients with status asthmaticus after intravenous salbutamol 100-300 μ g.

of salbutamol (100-300 μ g) there was a further increase in PEF at five minutes after the injection ($23 \pm 15\%$; range 8-48%) to levels significantly higher than those immediately before the second injection ($P < 0.005$). There was no significant difference, however, between the highest PEF achieved after the first and second injections.

Pulse Rate.—There was a mean peak increase in pulse rate of 22 beats/min 10 minutes after injection from a pretreatment mean of 117 beats/min (fig. 2). The pulse rate fell rapidly during

FIG. 2—Mean change (± 2 S.E.) in pulse rates in 11 patients with status asthmaticus after intravenous salbutamol 100-300 μ g.

the next five minutes to 125 beats/min and at 40 minutes after injection had returned to the pretreatment level.

Arterial Blood Gas Tensions.—In the 10 patients in whom blood gas tension was measured there was an increase in mean P_{aO_2} ($\pm$ S.D.) from 9.2 ± 2.4 kPa (69 ± 18 mm Hg) to 9.9 ± 3.5 kPa (74 ± 26 mm Hg) and no change in mean P_{aCO_2} (5.2 ± 0.8 to 5.2 ± 1.5 kPa (39 ± 6 to 39 ± 11 mm Hg)) at one hour after intravenous salbutamol (fig. 3). These differences did not reach conventional levels of significance.

FIG. 3—Individual and mean (± 2 S.E.) changes in arterial blood gas tensions in 10 patients with severe asthma after intravenous salbutamol 100-300 μ g.

★ = Mean.
Conversion: SI to Traditional Units—Blood gas: 1 kPa = 7.5 mm Hg.

Clinical Response.—In six patients there was a good clinical response with considerable relief of dyspnoea. In one patient (case 7) who was initially a poor responder there was a good clinical response when he had a further episode of asthma 24 hours later. Four patients had a poor response with little relief, and two patients had no response. These were the two who later required mechanical ventilation.

Side Effects.—A transient tremor was seen in six patients and

was troublesome in one. This did not seem to be dose dependent. One patient (case 8) reported a transient sensation of warmth, and another sweated profusely and became giddy though there was no change in blood pressure. Continuous electrocardiographic monitoring in three patients did not show any evidence of an arrhythmia. Two patients continued to deteriorate after injection and required artificial ventilation for progressive respiratory failure.

Case 10.—This 58-year-old woman who had a 13-year history of asthma was admitted with a severe episode of two days' duration. She was extremely distressed, cyanosed, and exhausted with a pulse rate of 120 beats/min and respiratory rate of 42 breaths/min. Blood gas measurements were: P_{aO_2} 6.7 kPa (50 mm Hg); P_{aCO_2} 5.7 kPa (43 mm Hg); pH 7.34. Treatment was begun with hydrocortisone 400 mg intravenously, salbutamol 200 μ g intravenously, and 28% oxygen. The pulse rate rose to 150 beats/min and the PEF from 70 l./min to 83 l./min, but there was no symptomatic relief. After 30 minutes the P_{aCO_2} had risen to 7.1 kPa (53 mm Hg) and intravenous aminophylline 500 mg was given with no effect. One hour later the patient was noticeably drowsy with a P_{aCO_2} of 10.4 kPa (78 mm Hg). Mechanical ventilation was started via an endotracheal tube. Ventilation was continued for 48 hours and after extubation she made an uncomplicated recovery. PEF at time of discharge was 250 l./min.

Case 11.—This 49-year-old woman who had an 18-month history of asthma was admitted with a six-day history of increasing dyspnoea and productive cough. She was given intravenous aminophylline and hydrocortisone, with some symptomatic relief. Over the next 36 hours she had recurrent episodes of bronchospasm followed by a severe episode of dyspnoea. This responded transiently to intravenous aminophylline. Twelve hours later she was extremely distressed and exhausted with a pulse of 135 beats/min and early signs of peripheral circulatory failure. Blood gas measurements were P_{aO_2} 9.5 kPa (71 mm Hg); P_{aCO_2} 6.7 kPa (50 mm Hg). Intravenous salbutamol 200 μ g and hydrocortisone 300 mg produced no relief. One hour later, because of increasing exhaustion and rising P_{aCO_2} (7.6 kPa (57 mm Hg)) she was intubated and artificially ventilated. She required ventilation for five days as bronchodilation did not begin for 36-72 hours after the start of ventilation. She made a complete recovery apart from an unexplained lower motor neuron lesion of the right hand. PEF on discharge was 410 l./min.

Dose Response.—Dose responses were assessed in two patients (case 7 on day 2 and case 9) by the administration of consecutive intravenous doses of salbutamol 100 μ g, 300 μ g, and 500 μ g at 30-minute intervals (table II). In both patients the maximal

TABLE II—Maximal Increases in Peak Expiratory Flow (PEF) and Pulse Rate after increasing Salbutamol Doses

Salbutamol dose:		0	100 μ g	300 μ g	500 μ g
Case 7	PEF (l./min) ..	180	220	300	300
	Pulse rate/min ..	115	130	145	160
Case 9	PEF (l./min) ..	80	105	115	110
	Pulse rate/min ..	100	135	125	135

increase in PEF was seen after the 300 μ g dose with no further increase after 500 μ g. In case 7 salbutamol 500 μ g produced a further increase in pulse rate to 160 beats/min with no change in PEF.

Discussion

The assessment of a bronchodilator in severely ill asthmatic patients is not easy and we decided not to attempt any form of

blind trial but only to document the result of therapy under conditions in which little spontaneous variation would be expected. At the start of the trial we were uncertain about the optimum dose and duration of effect. Varying doses were therefore used and the total period of observation was limited to one hour so that other conventional therapy could be given as soon as possible if the patient did not respond. Ideally, treatment given in the period preceding the intravenous salbutamol should have been strictly controlled but this would have posed great problems, and we felt that to assess efficacy of salbutamol against this mixed background, excluding only recently administered intravenous aminophylline, would be useful. Corticosteroids were given when indicated but the responses we observed occurred earlier than could be attributed to steroid therapy (*British Medical Journal*, 1972; Collins *et al.*, 1970).

Intravenous salbutamol produced a good bronchodilator response. There was a trend towards not only a better response in the less severely ill patients but also an earlier response. In this group the optimum response was usually apparent at 10 minutes. There was on average a 44% increase in PEF and a significant improvement persisted for up to 40 minutes when the trial was ended in the six patients in whom observations were continued for that period. Side effects were not severe. The greatest rise in pulse rate was from 24 beats/min to a maximum of 141 beats/min at 10 minutes, and in all patients the pulse rate had returned to pretreatment levels by 40 minutes. The only other consistently noted side effect was tremor in six patients, which was severe in only one. No arrhythmias were observed in the three patients who were monitored electrocardiographically. The trend of arterial blood gas tensions was towards improvement though in the absence of controlled observations it is difficult to assess the significance of this increase. The progression of respiratory failure in two patients (cases 10 and 11) was a reflection of the severity of the asthma and was likely to have occurred whether or not a bronchodilator had been given.

Though the dose response studies were limited they suggest that an optimal effect may be achieved with an intravenous dose of salbutamol 300 μ g. Any further increase in dosage has no therapeutic advantage and may increase the incidence of side effects. For an initial therapeutic intravenous dose of salbutamol we suggest 100 μ g, which may be followed 15 minutes later by 300 μ g if there is an inadequate response.

Despite the limitations of design this trial has shown that intravenous salbutamol in a dose of 100-300 μ g is an effective and apparently safe bronchodilator with few side effects in the acutely ill patient admitted to hospital with severe asthma. Controlled trials against the established agent aminophylline seem to be justified.

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