Serum potassium responses to nebulized salbutamol administered during an acute asthmatic attack

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SUMMARY

A prospective study of 20 patients presenting to an accident and emergency department with an exacerbation of pre-existing reversible airways disease was undertaken in order to determine whether such patients incurred any changes in their serum potassium following administration of 5 mg of nebulized salbutamol.

Electrolytes were estimated before and 30 min after administration of nebulized salbutamol. No other drug was administered during this period.

Results indicate that nebulized salbutamol can cause a significant hypokalaemic response in such situations. Eight out of the 20 patients studied demonstrated falls in serum potassium of more than 0.3 mmol/l. Most of the falls in serum potassium occurred in patients with low pre-treatment PCO₂ values; a group of patients with less severe respiratory distress.

This preliminary study indicates that a further study aimed at elucidating the clinical significance of nebulized salbutamol-induced hypokalaemia is required.

INTRODUCTION

The administration of nebulized β_2 -adrenoceptor agonists is an established treatment for acute asthmatic attacks. Previous authors have shown that intravenous β_2 -adrenoceptor agonists are capable of producing a variety of biochemical responses, particularly hypokalaemia (Massara *et al.*, 1976; Jenkins & Marlin, 1981; Cheong *et al.*, 1988). Similar responses have been reported in healthy, non-asthmatic volunteers administered nebulized salbutamol (Monie *et al.*, 1980; Smith *et al.*, 1984) but there has to date

been no prospective clinical study of serum potassium changes induced by nebulized salbutamol administered during the course of an acute asthmatic attack.

If hypokalaemia is induced during an acute asthmatic attack, it probably ought to be corrected (Cheong *et al.*, 1988). A preliminary prospective study of 20 consecutive cases of acute asthma was undertaken in order to establish whether or not hypokalaemia occurred in response to nebulized salbutamol.

SUBJECTS AND METHODS

All patients presented directly to the Accident and Emergency Department, Leicester Royal Infirmary, where they were initially assessed by a senior house officer. If this doctor made a diagnosis of reversible airways disease and decided that nebulized salbutamol would be the appropriate clinical therapy, the patient was entered to the study.

Before administration of any drugs (excluding oxygen), patients had their peak expiratory flow rate recorded and venous and arterial blood samples were obtained for urgent analysis. Urea and electrolytes were either measured on a SMAC 2 or 508 multichannel analyser giving an intersample error of less than 1%. This reproducibility was confirmed by sampling normal subjects in tandem with the patients in the study. Arterial blood sample analysis was performed on an Instrumentation Lab System 1302 machine.

After blood letting, each patient received 5 mg of nebulized salbutamol diluted to a total volume of 5 ml in normal saline administered via a close-fitting Hudson mask driven by oxygen with a delivery time of 10 min. No other drugs were administered during the ensuing 30 min, after which peak expiratory flow rate and venous sampling for potassium and glucose were repeated. The timing of the repeat estimations (30 min) was based on the experience of Smith *et al.* (1984).

RESULTS

Twenty patients (12 male, 8 female) with a mean age of 39 years were studied. One of these patients was eliminated because pre-treatment blood samples were haemolysed. All patients improved subjectively following nebulized salbutamol and showed objective improvement with an increase in the peak expiratory flow rate. The average improvement was 60% over pre-treatment level (range 10–256%).

Arterial blood analysis showed that five patients had respiratory alkalosis ($\text{pH} \geq 7.45$, $\text{PCO}_2 \leq 4.7$) and 5 had an uncompensated respiratory acidosis ($\text{pH} \leq 7.35$, $\text{PCO}_2 \geq 5.5$).

Prior to treatment, all 19 patients studied had normal serum potassium levels. Thirty minutes after receiving nebulized salbutamol the following changes in potassium were observed.

(1) Eight patients (42%) sustained falls in serum potassium of > 0.3 mmol (Table 1). In this group the largest fall was 1.0 mmol with a mean fall of 0.54 mmol. Five of these patients had a corresponding rise in their serum glucose level.

Table 1 Patients with a hypokalaemic response of ≥ 0.3 mmol/l

	Patient no.							
	2	3	6	8	9	12	18	20
Potassium (pre-treatment)**	3.2	4.2	4.5	4.9	4.5	4.2	4.2	4.5
Potassium (post-treatment)**	2.7	3.6	4.2	4.2	4.1	3.2	3.9	4.0
PEFR (pre-treatment)*	100	250	150	250	370	275	125	110
PEFR (post-treatment)*	125	350	320	420	550	350	220	140
Glucose (pre-treatment)**	6.0	5.7	6.1	4.6	4.8	6.5	5.1	7.8
Glucose (post-treatment)**	5.3	6.2	6.8	4.9	5.1	7.9	4.9	6.8
Blood Gases (pre-treatment)								
PCO ₂ (kPa)	3.3	3.5	3.6	3.8	4.2	3.8	3.6	6.50
pH	7.49	7.40	7.56	7.42	7.45	7.41	7.52	7.32

* Peak expiratory flow rate (l/min).

** mmol/l.

- (2) In nine patients the serum potassium altered by < 0.3 mmol/l. These alterations could be explained by the normal 1% error margin allowed by the equipment used.
- (3) Two patients had increases in their serum potassium, one of 0.3 mmol and one of 1.3 mmol (Table 2).

DISCUSSION

There is considerable controversy concerning serum potassium responses to therapeutic doses of nebulized salbutamol. There has been no prospective study of this response in patients actually suffering an acute exacerbation of asthma, though there have

Table 2 Patients not exhibiting a substantial hypokalaemic response

	Patient no.										
	1	4	5	7	11	13	14	15	16	17	19
Potassium (pre-treatment)**	4.1	3.7	3.8	3.9	4.0	4.3	4.6	4.1	4.8	4.1	4.6
Potassium (post-treatment)**	3.9	3.8	3.9	4.1	5.3	4.2	4.9	4.1	4.7	3.9	4.5
PEFR (pre-treatment)*	70	90	170	50	90	90	90	100	125	220	150
PEFR (post-treatment)*	130	150	260	150	110	150	100	170	320	260	180
Glucose (pre-treatment)**	23.6	6.1	4.9	4.7	5.4	4.3	11.3	5.4	5.4	5.8	6.3
Glucose (post-treatment)**	NA	7.0	5.0	5.3	6.6	4.5	11.7	6.6	5.6	6.0	8.8
PCO ₂ (kPa)	5.8	4.2	5.21	5.0	7.2	5.05	6.76	3.7	4.7	5.7	4.7
pH	7.23	7.45	7.40	7.38	7.2	7.32	7.22	7.40	7.51	7.34	7.38

* Peak expiratory flow rate (l/min).

** mmol/l

recently been a number of people expressing differing opinions on the subject in stable asthmatics and in patients who have received a number of anti-asthma drugs (Ebden *et al.*, 1987; Sears, 1987). What is not in doubt is that were hypokalaemia to be induced by therapeutic dose of nebulized salbutamol in an already stressed patient it could lead to serious cardiovascular side-effects. Indeed, a recent report on asthmatics from New Zealand (Godden & Symon, 1987) has implied that hypokalaemia may have been the cause of some of their deaths whilst on nebulizer treatment.

As no other drug was administered between blood sample estimations during the course of this study, it appears reasonable to link the administration of nebulized salbutamol to the resulting hypokalaemia. Most of the large falls in serum potassium occurred in patients with low pre-treatment PCO₂ values—patients with less severe respiratory disease. A possible explanation for this phenomenon is that an already maximally stressed patient may be incapable of responding metabolically to the adrenalin-mediated side-effects of salbutamol.

Whilst we cannot correlate the changes in serum potassium to any specific factors in the history or drug therapy, this study shows that it is possible to induce substantial changes in serum potassium in submaximally stressed patients using nebulized salbutamol.

A larger study must be undertaken if the clinical significance of such changes is to be substantiated and risk groups identified. It is possible that patients who are hypoxic, those already on diuretics and/or steroids, and those who require additional bronchodilator therapy with intravenous aminophylline may be at risk.

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