Reminder of important clinical lesson

Salbutamol: beware of the paradox!

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Summary

A 7-year-old known asthmatic presented with an acute severe asthma attack to the Accident and Emergency department. Following a poor response to salbutamol and ipratropium nebulisers, he was given intravenous salbutamol and aminophylline. Over the course of the following 3 h, there was improvement in his bronchospasm with decreasing oxygen requirement, however, his respiratory rate showed an upward trend. Serial blood gas estimations showed a worsening metabolic acidosis unresponsive to two fluid boluses of 20 ml/kg of normal saline. Lactate levels were subsequently measured and found to be high, accounting for the metabolic acidosis. High lactate levels were attributed to intravenous salbutamol. His blood gases and lactate level returned to normal within 3 h after stopping intravenous salbutamol. He was recommended on salbutamol nebulisers while still continuing on intravenous aminophylline. He continued to improve and was discharged home after 4 days.

BACKGROUND

The case is an opportunity to remind doctors of an uncommon yet important adverse effect associated with salbutamol treatment during an acute asthma attack; that is, lactic acidosis. It has implications for complicating assessment, inappropriate intensification of bronchodilator treatment, as well as inappropriate fluid management.

CASE PRESENTATION

A 7-year-old known asthmatic presented to the Accident and Emergency department with coryzal symptoms for 2 days and difficulty in breathing for 1 day. His parents treated him at home with salbutamol inhalers with a poor response. He had never required Intensive Care Unit (ITU) admission in the past. His maintenance treatment was inhaled beclomethasone 100 µg twice daily and inhaled salbutamol 100–500 µg as required.

On presentation he had a respiratory rate of 35 breaths/min, nasal flaring, subcostal retractions and oxygen saturations of 88% in air. Chest auscultation revealed widespread expiratory wheeze. He was well perfused. He was treated immediately with salbutamol and ipratropium nebulisers and oral prednisolone. Response was poor and his respiratory distress worsened with his oxygen requirement increasing to 8 litres/min by facemask. Following this, he was given a bolus of intravenous salbutamol at 15 µg/kg followed by a continuous salbutamol infusion of 2 µg/kg/min. He was also given intravenous aminophylline with a loading dose of 5 mg/kg followed by a continuous infusion of

1 mg/kg/h. A capillary blood gas test 20 min later showed a metabolic acidosis with pH 7.28 and base excess (BE) –9 mmol/litre. He received a 20 ml/kg bolus of normal saline. His bronchospasm improved with his oxygen requirement reducing to 3 litres/min. His respiratory rate showed an upward trend to 45/min. A repeat capillary blood gas approx 90 min after the start of intravenous salbutamol showed a pH of 7.17, BE of –14 mmol/litre and pCO₂ of 4.82 kPa. He received another bolus of 20 ml/kg of normal saline. He was continued on intravenous salbutamol and aminophylline for a further 90 min. A discrepancy was emerging between worsening dyspnoeic symptoms and improving bronchospasm over the 3 h period. A repeat blood gas 3 h after the start of intravenous salbutamol showed a worsening metabolic acidosis with pH 7.13, BE –15.4 mmol/litre and a lactate of 9.2 mmol/litre (table 1). Blood sugar measured at this time was 12.6 mmol/litre, which gradually came down as salbutamol was weaned off and required no additional treatment. Because of his improvement in bronchospasm symptoms and decreasing oxygen requirement, his tachypnoea was attributed to the metabolic acidosis and high lactate levels, which in turn was attributed to intravenous salbutamol. A decision was made to gradually reduce and stop intravenous salbutamol and give salbutamol nebulisers with an aminophylline infusion on a continuous basis. His dyspnoea, blood gases and lactate improved within 3 h of stopping the salbutamol infusion (table 1). He continued to improve and treatment was gradually reduced until he was able to go home on his maintenance treatment 4 days later.

Table 1 Serial blood gas estimations

	20 min after intravenous salbutamol bolus	90 min after starting intravenous salbutamol	3 h after starting intravenous salbutamol	3 h after stopping intravenous salbutamol
pH	7.28	7.17	7.13	7.37
Partial pressure CO ₂ , kPa	4.79	4.82	5.2	5.06
HCO ₃ [–] , mmol/litre	16.8	12.9	12.7	19.8
Base excess, mmol/litre	–9	–14	–15.4	–2.7
Lactate, mmol/litre			9.2	2.2

INVESTIGATIONS

- ▶ Chest x-ray: bilateral hyperinflation, no evidence of consolidation
- ▶ Serial blood gas analyses.

OUTCOME AND FOLLOW-UP

The patient was discharged from the hospital after 4 days having made a full recovery.

DISCUSSION

There is paucity of literature reporting lactic acidosis after use of either inhaled or intravenous use of salbutamol in children. Interestingly, there have been various reports in the literature about metabolic effects of salbutamol in adults even as early as 1974. Kuo *et al*¹ and Phillips *et al*² reported increased glycogenolysis in the liver and skeletal muscles resulting in hyperglycaemia and hyperlactataemia. Hyperlactataemia was also reported by Chapman³ after the use of salbutamol. Hypokalaemia was reported by Smith and Thompson⁴ and Wang and Clausen⁵. Increased lipolysis in adipose tissues leading to increased plasma free fatty acids and ketone concentrations after its use was reported by Goldberg *et al*⁶.

There are also fairly recent reports of hyperlactataemia after inhaled⁷ and intravenous⁸ salbutamol treatment in adults. The mechanism for this has been poorly understood. Type B lactic acidosis (without hypoxia and hypoperfusion) may be caused by increased pyruvate and/or NADH⁺ secondary to over production or their underuse, or decreased lactate conversion to glucose.⁹ The reason why only a small number of patients experience this adverse effect is also unexplained and needs further evaluation.

Irrespective of the cause, this small group of patients with asthma manifesting this complication during their treatment with salbutamol remains a challenge to doctors as it frequently complicates assessment and may lead to unwarranted intensification of the bronchodilator treatment.

Learning points

- ▶ Any discrepancy between exacerbation of dyspnoea and improvement of bronchospasm when using intravenous salbutamol should alert the doctor to possible lactic acidosis.
- ▶ Serial blood gas analyses may be useful in detecting evolving lactic acidosis.
- ▶ Use of salbutamol is linked to other metabolic and cardiovascular derangements such as hyperglycaemia, hypokalaemia and hypotension.

Competing interests None.

Patient consent Obtained.

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