

Beta Agonist-Induced Lactic Acidosis in Asthma

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Citation

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Abstract

Patients admitted to the hospital with an asthma exacerbation will on occasion develop an elevated lactate. This immediately triggers increased patient surveillance due to the possibility that the lactate may signify inadequate delivery of oxygen to the tissues that results in a lactic acidosis type A. Type A lactic acidosis may be related to septicemia or heart failure as very common factors and intensive care unit management would be a consideration. Alternatively, it may simply be due to the more benign type B₂ lactic acidosis that is now commonly seen in asthma (1,2,3,4). The onus is on the clinician to make this distinction.

CASE REPORT

A 32-year-old slim black female (BMI = 23) with moderate persistent asthma on fluticasone 500 ug/salmeterol 50 ug inhaler, montelukast 10 mg daily, and albuterol as needed was seen in the emergency department (ED) for worsening dyspnea unrelieved by home treatment in January of 2012. The home treatment included nebulized albuterol at 2.5 mg given three times that day, use of an albuterol inhaler at least 5 times that day with two (90 ug/puff) or more puffs each time, and an albuterol nebulization of 2.5 mg in the ambulance. In the ED she was noted to be in respiratory distress with a blood pressure of 151/80 mm Hg++, heart rate (HR) at 110 beats/min, and respiratory rate of 30 breaths/min with a pulse oximeter saturation of 100% while receiving intermittent bronchodilator nebulizations. She had bilateral diffuse wheezing. She was given nebulized albuterol 2.5 mg with ipratropium bromide three times, terbutaline 0.25 mg subcutaneously twice, magnesium sulfate 2 grams intravenously, and intravenous methylprednisolone 125 mg intravenously. During the second ED hour, she received three more albuterol 2.5 mg nebulizations and was admitted to the medical ward with a diagnosis of an asthma exacerbation. An initial arterial blood gas as seen in the table was noteworthy for an elevated lactate of 5.8 mmol/L (normal lactate is 2 mmol/L or less).

She said her asthma was triggered by a change in the weather and she denied yellow or green sputum production. There was no history of cigarette smoking or drug abuse and she had been admitted to the hospital in August of 2011 for

an asthma exacerbation. She had never been intubated for asthma. She had an influenza vaccine in the fall of 2011. She had no other illnesses except asthma. Pulmonary function in 2011 showed mild obstruction. She had a family history of asthma.

The laboratory values include the following Na 141 mmole/L, K 3.8 mmole/L, Cl 104 mmole/L, HCO₃ 28 mmole/L, BUN 12 mg/dL, Cr 0.8 mg/dL, Ca 8.9 mg/dL, Glucose 126 mg/dL. The hemogram and hepatic panel were normal as was the chest roentgenogram.

Figure 1

Table 1. Serial arterial blood gas analysis

Time since admission	Blood Pressure (mmHg)	Heart Rate (beats/min)	pH	PaCO ₂ (mm Hg)	PaO ₂ (mmHg)	Lactate (mmol/L)
ER 00:00	151/80	110	7.38	34.7	78.5	5.8
09:00	102/53	92	7.39	31.1	101	3.3
28:00	130/59	66	7.43	32.5	89.0	1.7

Hospital Course: She was treated overnight with intravenous methylprednisolone 125 mg every eight hours and less frequent doses of albuterol with resolution of the elevated lactate level within twenty eight hours. No antibiotics were given for the asthma exacerbation. She was discharged on a short course of oral prednisone in addition to her regular asthma medications.

DISCUSSION

With the advent of routine lactate levels on arterial blood gas analysis in the last decade, the finding of an elevated lactic acid level in patients admitted to the medical ward with

asthma is a common finding (1,2,3,4). On acutely ill patients, it is important to consider that the lactic acidosis is secondary to aggressive beta-2 agonist therapy and not due to more life-threatening asthma that may require more aggressive support or even intubation (5,6).

Our patient was given over 20 mg of albuterol plus terbutaline in less than one day and clearly had beta-2 agonist induced elevated lactic acidosis. She had no infection, no hemodynamic instability, and no history of liver disease or any other health problem except asthma. Beta-2 agonist-induced lactic acidosis was very clearly described and elegantly induced by Rodrigo and Rodrigo (2). They studied 18 asthmatic patients who came to the ED with an asthma exacerbation, obtained a baseline normal lactate level, and then treated them with 4800 ug of albuterol by metered dose inhaler over 2 hours. Four of eighteen subjects developed a lactic acid level greater than 4 mmol/L (2). All of their patients remained hemodynamically stable and did well clinically with traditional treatment for asthma that included systemic steroids (2). Like our patient, none of their patients developed a severe metabolic acidosis and no one was admitted to the intensive care unit (2).

The mechanism of the beta-2-agonist-induced elevated lactate is unclear but has been seen with intravenous infusion of beta-2 agonists in normal volunteers (7,8,9), in women who undergo infusions for premature labor (10), and in severe asthmatics who were intubated, the latter due to the overuse of salbutamol (albuterol) itself (11,12). The elevated lactate levels in these reports are generated prospectively after beta-2 agonist use, clearly indicating that the beta-2 agonists are in some way stimulating the increase in lactic acid. The mechanism is unclear but presumably is related to increased production of lactate and/or decreased clearance. Most likely, the beta-2 agonists produce an increased lactate production since the subjects studied are known to have normal liver and renal function suggesting that lactate clearance should not be impaired. Definitive studies are needed to determine the exact mechanism of the transient elevation in lactate that occurs in the minority of asthmatics treated aggressively with beta-2 agonist therapy. The elevated lactate levels start to drop several hours after albuterol treatments are discontinued.

Mild elevation in lactic acid levels without a severe

metabolic acidosis is now a common finding in acute asthma exacerbations. The lactic acid levels rise as high as 7 or 8 mmol/L but are usually lower and resolve quickly with reduction in inhalational albuterol treatments. Only some asthmatics develop elevated lactic acid with inhalational beta-agonist treatment and it is important to ascertain whether there is a type B lactic acidosis and not the more serious type A lactic acidosis. All of reported type B lactic acidosis asthmatics have been hemodynamically stable, have a normal or near normal anion gap, have been hypocarbic, and had a near normal pH.

Now routine lactic acid level determinations with arterial blood gas measurements have identified a drug-induced metabolic alteration in asthmatics, that may not have been recognized in the past. Recognition of this alteration will help in directing therapy and even help prevent unnecessary intubations (11,12).

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