Abstract  
Objective: To evaluate arterial lactate levels during treatment of acute severe asthma (ASA) and the prognostic value of arterial hyperlactatemia in ASA.

Design: Prospective study.
Setting: A respiratory intensive care unit (ICU) of a university hospital.
Patients: 29 consecutive patients admitted to the ICU for ASA not intubated on admission and with a peak expiratory flow (PEF) < 150 l/min or an arterial carbon dioxide tension (PaCO₂) > 40 mmHg. All patients received standardized treatment during the first 24 h including i.v. and nebulized salbutamol, i.v. theophylline, and dexamethasone.

Measurements and results: Arterial lactate levels were serially measured by an enzymatic method during the first 24 h following admission. On admission, the mean arterial lactate level was 3.1 ± 0.38 mmol/l (range 1.1-10.4); 17 patients (59%) had arterial hyperlactatemia with a lactate level > 2 mmol/l. No difference was found in lactate levels between patients with progressively worsening asthma and those with an acute onset of severe asthma. No correlation was found between arterial lactate levels on admission, on the one hand, and respiratory rate (RR), heart rate, PEF, pH, PaCO₂, arterial oxygen tension, potassium, phosphorus, creatine kinase, or transaminase values on admission, on the other hand. All patients developed an important but transient increase in arterial lactate levels during treatment, with a peak at 7.72 ± 0.46 mmol/l and a mean elevation of 4.62 ± 0.45 mmol/l (range 0.4-12.1), from the initial admission value contrasting with a significant clinical improvement assessed by RR, PEF, and arterial blood gas parameters.

Conclusion: This study suggests that, in ASA, arterial hyperlactatemia is frequently present on admission to the ICU. Delayed hyperlactatemia is a constant finding during treatment of ASA. Initial or delayed hyperlactatemia seems of no prognostic value because none of the patients required mechanical ventilation. The effects of therapy for acute asthma on lactate metabolism still need to be studied.

Key words  Acute severe asthma • Blood lactate • Bronchodilator therapy

Introduction

Acute asthma is usually associated with hyperventilation and respiratory alkalosis on blood gas analysis [1]. When airway obstruction is more severe or prolonged, respiratory acidosis may develop. Metabolic acidosis has been reported in acute severe asthma [2] and two types of metabolic acidosis have been described: renal loss of bicarbonate as a renal compensatory response to a preceding period of hypercapnia due to
a prolonged period of hyperventilation and lactic acidosis [3].

In critically ill patients, elevation of lactate levels usually reflects tissue hypoxemia and a predominant anaerobic metabolism [4]. Monitoring of lactate levels seems helpful for assessing the effectiveness of therapy and patient prognosis in several clinical situations, such as cardiogenic shock or septic shock [4–7]. A persistent elevated arterial lactate level is often associated with a poor prognosis [5].

An increase in arterial blood lactate has been noticed either on admission or during the course of acute severe asthma (ASA) [8–11]. Hyperlactatemia has been suggested to be a marker of severity of ASA, predicting respiratory failure and the requirement for mechanical ventilation [9]. However, hyperlactatemia in ASA has only been reported in retrospective studies [2, 8–10]. The incidence of arterial hyperlactatemia in ASA and its prognostic value are not well known.

The aim of our prospective study was to evaluate in patients with ASA arterial lactate levels on admission to the ICU and variations during treatment of ASA. Another aim of the study was to assess the prognostic value of hyperlactatemia in ASA by analysing the relationships between an elevated arterial lactate level and patient outcome, especially the occurrence of respiratory failure requiring mechanical ventilation.

**Patients and methods**

**Patients**

During a 6-month period all patients admitted to the ICU at Hôtel-Dieu Hospital for ASA were eligible for the study. The diagnosis of asthma was made according to the American Thoracic Society criteria [12]. A diagnosis of ASA was made according to the clinical indices of ASA given in the most recent guidelines for the diagnosis and management of asthma [13–15]. Admission to the ICU was decided on either because of a severe initial clinical status with a near-death state or because of failure of an initial emergency treatment including oxygen therapy, at least 10 mg of a nebulized beta 2 agonist (salbutamol), and i.v. corticosteroids. Failure of initial emergency treatment was determined 30 min after the patient had received the treatment by the presence of one or more of the following signs: respiratory rate above 30/min, heart rate above 120/min, severe dyspnea and difficulty speaking, intercostal or tracheosternal retraction, nasal flaring, cyanosis, inaudible breath sounds, pulsus paradoxus above 20 mm Hg, arterial carbon dioxide tension (PaCO₂) ≥ 40 mm Hg, or peak expiratory flow rate (PEF) ≤ 150 l/min.

We excluded from the study all patients with one of the following conditions: shock or systolic arterial pressure lower than 80 mm Hg, renal failure (creatinine level above 150 μmol/l), severe sepis, or liver dysfunction [bilirubin > 30 μmol/l]. Alanine amino-transferase (ALT) or aspartate aminotransferase (AST) exceeding five times the normal value) on admission to the ICU, retrospective diagnosis of chronic obstructive pulmonary disease (after review of clinical history and respiratory function evaluation), previously known endocrine disease (diabetes mellitus, pan-creatric or thyroid gland dysfunction), previous severe liver disease (cirrhosis), and pregnancy. We also excluded patients under mechanical ventilation, before ICU admission, as one of the study aims was to evaluate patient outcome and occurrence of respiratory failure with regard to lactate level.

**Treatment**

During the first 24 h in the ICU, all patients were treated according to a standard protocol, which included oxygen therapy to maintain arterial oxygen saturation (SaO₂) above 92%, intravenous hydration with 4 l per day of 5% dextrose in water with sodium, potassium, and phosphorus according to serum levels, intravenous β₂ agonist (salbutamol 1 mg/h) nebulized β₂ agonist (10 mg salbutamol nebulized on admission, repeated 20 min later and every hour during the first 6 h and then every 4 h), corticosteroids (i.v. dexamethasone, 20-μg bolus followed by 0.15 mg/kg i.v. 4-hourly) and continuous intravenous theophylline infusion adjusted to the individual theophylline clearance [16] in order to obtain a serum concentration of 12 mg/l. In the case of clinical worsening despite medical treatment, intravenous β₂ agonist infusion was progressively increased up to 5 mg per h. If bronchial obstruction still did not improve, intravenous epinephrine 0.1 mg up to 1 mg per h was infused. In the case of refractory bronchial obstruction, a decision to mechanically ventilate could be made. After 24 h, intravenous drugs were progressively withdrawn if clinical status, arterial blood gases, and PEF had improved.

Clinical improvement was assessed by hourly recording of respiratory rate, heart rate, and PEF during the first 24 h (Miniwright Peakflowmeter).

**Measurements of arterial blood lactate, serum electrolyte determination, and arterial blood gas analysis**

All specimens for blood gas analysis, lactate, electrolytes, creatine kinase (CK), ALAT and ASAT determination, and theophylline blood levels were obtained by collecting blood samples via an arterial catheter aseptically inserted on admission.

A 5-ml sample of arterial blood was obtained anaerobically via the arterial catheter for lactate determination. The specimens were placed on ice and immediately transported and analyzed within 5 min. The lactate level was determined by enzyme assay (Kodak Ektachem 700 Analyzer C series, Rochester, N.Y., USA). Normal arterial lactate values using this technique in resting normal volunteers have been reported to be less than 2 mmol/l. Another 3 ml of arterial blood was drawn anaerobically into a heparinized syringe and placed immediately on ice for arterial blood gas analysis. Arterial blood pH, PaCO₂, base excess, arterial oxygen tension (PaO₂), and SaO₂ were determined using an automated blood gas analyzer (Blood Gas Analyzer 1306, Instrumentation Laboratory, Milano, Italy). An additional 10 ml of arterial blood was collected into a non-heparinized syringe and placed immediately on ice for arterial blood gas analysis. Arterial blood pH, PaCO₂, base excess, arterial oxygen tension (PaO₂), and SaO₂ were determined using an automated blood gas analyzer (Blood Gas Analyzer 1306, Instrumentation Laboratory, Milano, Italy). An additional 10 ml of arterial blood was collected into a non-heparinized syringe and placed immediately on ice for arterial blood gas analysis. Arterial blood pH, PaCO₂, base excess, arterial oxygen tension (PaO₂), and SaO₂ were determined with an electrochemical method (Beckman, Brea, Calif., USA). Serum phosphorus levels were determined by a colorimetric method (Kodak Ektachem 700 Analyzer C series, Rochester, N.Y., USA), and CK, ALAT, and ASAT by enzyme assay (Kodak Ektachem 700 Analyzer C series, Rochester, N.Y., USA).

Arterial blood samples for determination of lactate, blood gas analysis, potassium, phosphorus, and CK concentrations were obtained on admission to the ICU (H0) and 3 h (H+3), 6 h (H+6), 14 h (H+14), and 24 h (H+24) after admission. ASAT and ALAT were determined only at H0 and at H+14 and H+24. Theophylline