vitamin D in patients with COPD beyond this and in the absence of data cannot be supported at this time.

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Serum Lactate Increase During Acute Asthma Treatment

A New Piece of the Puzzle

The occurrence of a transient increase in serum lactate level (hyperlactatemia) with or without lactic acidosis during short-term asthma treatment has been a well-known event for several decades. Although initially observed in patients with asthma and respiratory failure,[2-4] there are now data on its occurrence in patients with less severe conditions and in patients receiving IV or nebulized salbutamol.[5-8] Far from being an exceptional phenomenon, the prevalence of hyperlactatemia is much more frequent than previously estimated. Thus, two prospective observational studies involving adults and children with acute asthma in the emergency setting found that between 50% and 80% of patients presented with hyperlactatemia (serum lactate level >2.2 mmol/L).[6,8] Despite these findings, the pathophysiology and clinical significance of this phenomenon remains controversial.

From a pathophysiologic perspective, type A lactic acidosis occurs with tissue hypoperfusion (systemic shock, carbon monoxide poisoning, or even intense exercise), and type B is associated with an altered cellular metabolism (in the absence of hypoperfusion or hypoxia), with either decreased lactate metabolism or increased flux of pyruvate to lactate rather than into the Krebs cycle (inborn errors of metabolism, liver failure, or metabolic changes induced by medications or toxins). Most of the evidence supports the notion that in acute asthma, lactic acidosis is type B and arises in the presence of normal oxygen delivery.[4-9] The aggressive administration of β_2-agonists during the treatment of acute asthma is considered the most likely cause of the abrupt increase of lactate concentration. In addition, it has been postulated that endogenous catecholamine levels related to marked respiratory distress may be associated with or predisposes an increase in the conversion of pyruvate to lactate.[3,6] Finally, it has been proposed that hyperlactatemia occurs secondary to increased respiratory muscle workload, leading to increased oxygen demands and lactic acidosis. However, the fact that lactic acidosis was shown to occur in patients with asthma receiving mechanical ventilation or who are paralyzed makes this scenario less likely.[4,10]

In this issue of *CHEST* (see page 53), Lewis and colleagues[11] bring a new piece of evidence that helps us to understand this phenomenon. They performed a subanalysis of subjects receiving placebo in a phase 2, prospective, randomized trial evaluating the safety and efficacy of an IV β_2-adrenergic agonist as an adjunct to standard therapy in adults with acute asthma. The

study population comprised adult patients with asthma who presented to the ED with severe asthma exacerbation ($FEV_1 < 50\%$ predicted after a therapeutic trial of 5-15 mg nebulized albuterol, 0.5-1 mg nebulized ipratropium, and at least 50 mg oral prednisone). The distinguishing feature of this study was that the authors not only measured serum lactate, electrolytes, and other variables but also evaluated plasma albuterol levels. Plasma albuterol, serum lactate, and bicarbonate concentrations were measured at baseline and 1.25 h, and dyspnea score and spirometry were measured at baseline and hourly for 3 h. The authors found 45 subjects (69.2% of the sample) with at least one serum lactate value greater than the upper limit of normal (2.2 mmol/L) and 10 subjects (15.4%) with at least one serum lactate level ≥ 4.49 mmol/L. After correcting for baseline lactate levels and using multiple regression to adjust for dyspnea and FEV_1, total albuterol plasma concentration was the only significant predictor of the 1.25-h serum lactate concentration. Additionally, hyperlactatemia did not increase the risk of hospitalization or relapse and was not associated with a lower FEV_1 at 3 h.

Even with acknowledging that the design cannot determine causality, data from this study support the following facts: (1) Hyperlactatemia developing during the first hours of treatment for acute asthma has a high prevalence, (2) hyperlactatemia associated with treatment for acute asthma is most often not accompanied by a metabolic acidosis, (3) the administration of β-adrenergic agonists seems to be the dominant cause of elevated serum lactate levels, (4) there are no clinical or laboratory indications of any alternative cause of hyperlactatemia (eg, hypoxemia, hypoperfusion, sepsis), and (5) hyperlactatemia does not appear to affect the effectiveness of bronchodilator therapy and had no clinical consequences in these patients.

It should be noted that patients in whom lactic acidosis develops present a paradoxical situation in which, despite improvement in bronchospasm, they look more dyspneic as a compensatory mechanism for metabolic acidosis. This may be mistaken for worsening respiratory distress due to asthma and lead to unnecessary intensification of β_2-agonist therapy, ultimately resulting in respiratory failure. The best way to recognize this situation is with serial peak flow measurements. Thus, the measurement of lung function provides a more objective assessment of airway obstruction and constitutes an integral part of the assessment of disease severity (static) and response to therapy (dynamic).[12]

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ROSEs Are Read

The use of rapid on-site cytologic evaluation (ROSE) of a fine needle aspiration specimen has been carried out for many years.[1] The purported advantages of ROSE include improving sample adequacy, diagnostic accuracy, and efficient triaging of the specimens for postprocessing testing.[2,3] Improving sample adequacy has an added benefit of decreasing the number of needle aspirates required to establish the diagnosis, which, in turn, can reduce both cost and procedure duration. This is especially important in mediastinal staging of lung cancer, where the finding of metastasis to a N3 lymph node would obviate the need for further sampling, even from the primary lesion.[4] The efficient triaging of the specimens based on preliminary