Life-Threatening Asthma in Children: Treatment With Sodium Bicarbonate Reduces PCO2

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Study Design: Retrospective study.

Setting: A pediatric ICU (PICU) of a tertiary care university hospital.

Patients: Seventeen children with LTA who received sodium bicarbonate.

Measurements and results: In January 1999, a new protocol for the treatment of LTA was initiated in our institution, incorporating the use of IV sodium bicarbonate in acidotic patients (pH < 7.15) with refractory status asthmaticus. Since January 1999, sodium bicarbonate was administered to 17 patients; 5 patients received two or three doses of sodium bicarbonate. In three patients, sodium bicarbonate was administered after intubation. Intubation and mechanical ventilation were performed in five patients before admission to the PICU, and in one patient during admission. There was a significant decrease of Pco_2 after sodium bicarbonate infusion ($p = 0.007$). An improvement of respiratory distress in all but one patient was seen as well.

Conclusions: Administration of sodium bicarbonate in 17 children with LTA was associated with a significant decrease in Pco_2 and an improvement of respiratory distress. The possible benefits of sodium bicarbonate in LTA deserve further study in a controlled, prospective design.

Acute severe asthma in children requires aggressive treatment with oxygen, bronchodilators, and corticosteroids. Life-threatening asthma (LTA) is defined as progressive respiratory failure due to asthma, refractory to treatment with inhaled bronchodilators and systemic corticosteroids.

Most children admitted to the hospital because of acute asthma do not require intensive care treatment. In those who are admitted to the ICU, approximately 10 to 33% need intubation and mechanical ventilation, with a risk of worsening bronchospasm and hyperinflation, barotrauma, and cardiovascular depression.[1,2] Mechanical ventilation compromises active expiration with increased air trapping and hypercapnia, and should therefore be delayed as long as possible by using medical therapy. LTA can be associated with metabolic acidosis, which reduces the effectiveness of ß-agonists.

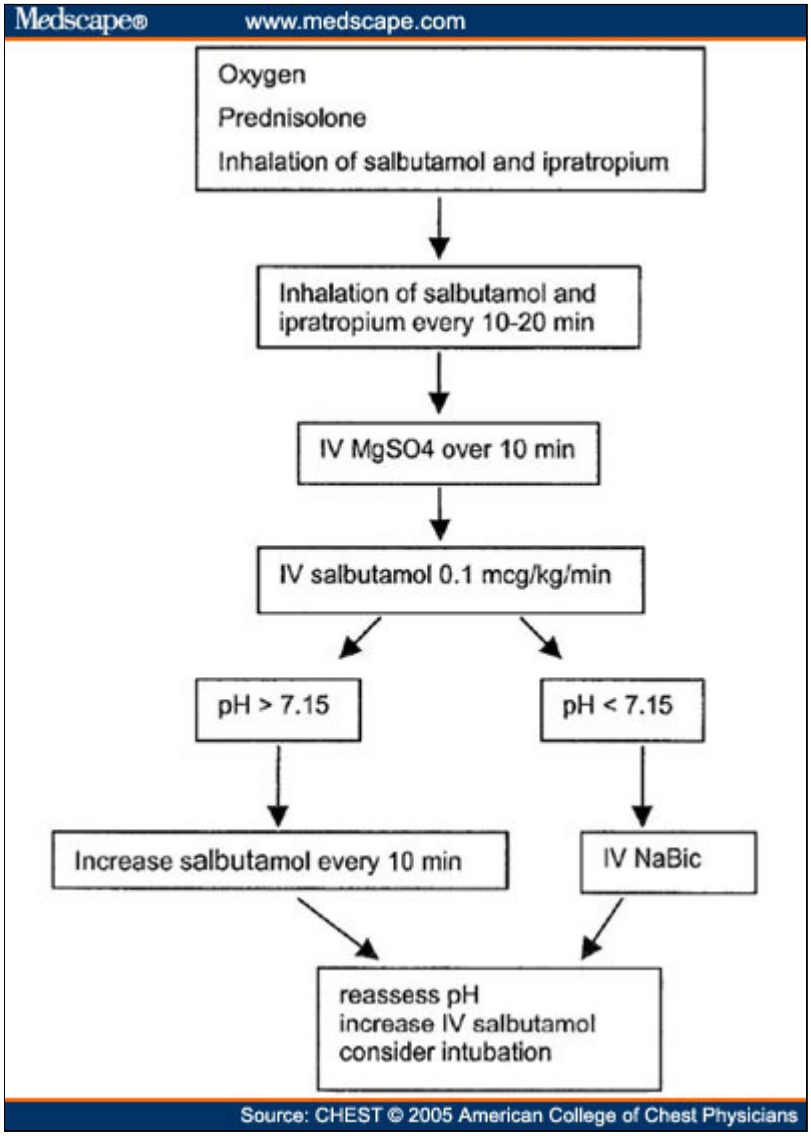
In January 1999, a new protocol for the treatment of LTA was initiated in the pediatric ICU (PICU) of the Erasmus MC-Sophia Children's Hospital. In this protocol, the use of IV sodium bicarbonate was added based on previous reports in the literature.[3-8] It was postulated that children with LTA could benefit from treating their acidosis, as this would lead to a better effect of ß-agonists. A potential risk of sodium bicarbonate infusion is a Pco_2 rise because of increased production, inadequate gas exchange, and hypoventilation. The aim of the present study was to observe the effect of administration of sodium bicarbonate on carbon dioxide levels in LTA and to evaluate the clinical effect of this treatment.

We retrospectively analyzed data from all children with LTA admitted to the PICU of the Erasmus MC-Sophia Children's Hospital, a tertiary care university hospital, during the period January 1999 until November 2003.

We reviewed the medical records of all patients, and the following data were collected: age, sex, duration of admission, treatment of the LTA, clinical condition, blood gases, the incidence of barotrauma, and outcome. Blood gas measurements were obtained by means of indwelling arterial catheters or by capillary punctures. The normal pH range in our laboratory is 7.35 to 7.45. For Pco_2 and base excess, the ranges are 30 to 42 mm Hg and - 3 to 3 mmol/L, respectively.

In January 1999, a new protocol for the treatment of LTA in our PICU was initiated (Figure 1). In this protocol, IV magnesium sulfate and IV sodium bicarbonate were added, and theophylline was no longer recommended. Patients

were managed with oxygen, frequent or continuous inhalation of nebulized salbutamol (2.5 to 5 mg), frequent inhalation of ipratropium bromide (0.25 to 0.5 mg), and parenteral corticosteroids (prednisolone, 1 mg/kg q12h for 5 to 7 days). If respiratory distress persisted, magnesium sulfate was administered at 25 mg/kg IV over 10 min.[9] IV salbutamol was started in patients unresponsive to treatment with continuous nebulization and IV magnesium sulfate.[10] The starting dose of IV salbutamol was 0.1 µg/kg/min. The infusion rate was increased by 0.1 µg/kg/min per 10 min if necessary. IV sodium bicarbonate (1 mmol/kg over 30 min) was administered if pH was < 7.15 and the patient remained in respiratory distress. Intubation and mechanical ventilation were initiated in case of progressive fatigue with a rapid decrease in level of consciousness and hypoxia despite the use of high-flow oxygen, IV salbutamol, and sodium bicarbonate.



Simplified flowchart for the treatment of LTA.

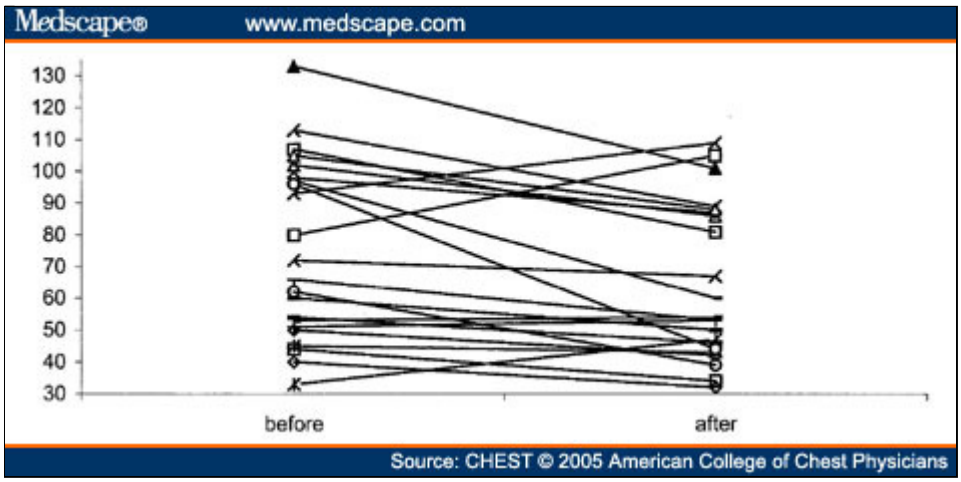
Pco_2 and pH before and after administration of sodium bicarbonate were compared with a paired-samples *t* test.

During the study period, 73 patients with LTA were admitted to the PICU. Four patients were admitted twice because of a recurrent episode of LTA. Indications for admission to the PICU were severe dyspnea, worsening or failure to improve on nebulized bronchodilators, and need for administration of IV salbutamol or mechanical ventilation. There were 43 boys and 30 girls (median age, 6.2 years; range, 0.6 to 16.4 years). The median duration

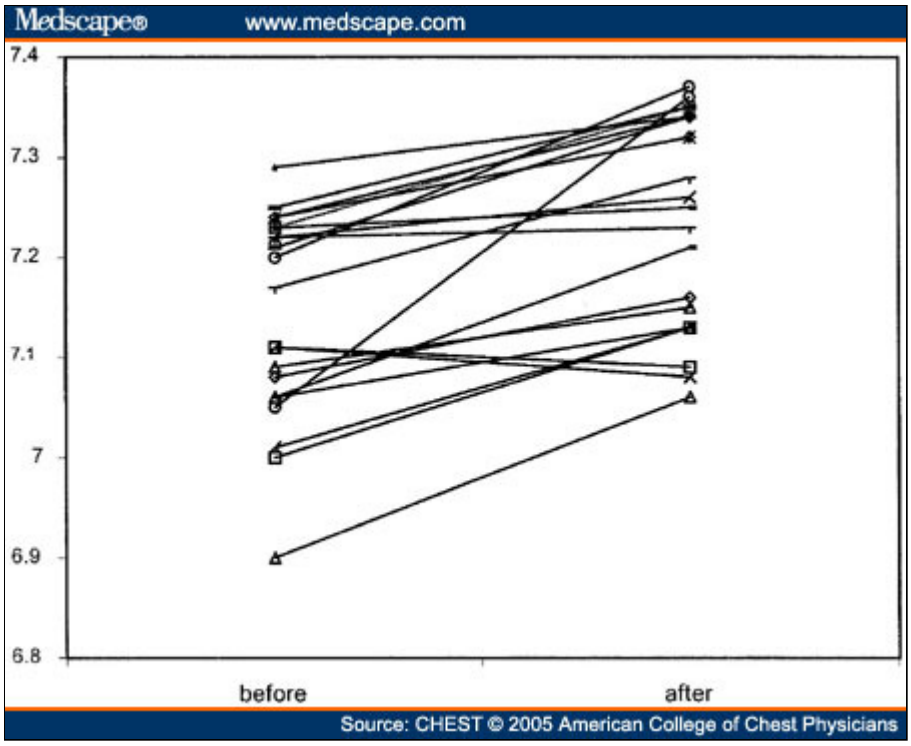
of admission in the PICU was 3 days (range, 1 to 12 days). All patients survived. Mechanical ventilation was required in six patients; intubation was performed in five patients at the referring regional hospital or by the paramedics at the scene prior to admission to our PICU. Barotrauma did not occur during mechanical ventilation. Table 1 summarizes these data.

Sodium bicarbonate was administrated to 17 patients, and 5 patients received two or three doses. The median dose of sodium bicarbonate was 0.9 mmol/kg (range, 0.5 to 4 mmol/kg). In three patients, sodium bicarbonate was administered after intubation because of persistent acidosis. In one patient, the respiratory distress worsened despite sodium bicarbonate, and intubation was needed subsequently. In two patients, sodium bicarbonate was already administrated in the referring regional hospital before transfer to our hospital after consultation by the physician of the regional hospital with a senior staff member of our PICU. Before administration of sodium bicarbonate, the acidosis was mixed respiratory and metabolic in 13 patients, the acidosis was predominantly respiratory in 1 patient, and was metabolic in 2 patients. In one patient, the initial blood gas values before administration of sodium bicarbonate in the referring hospital could not be traced. Paired blood gas values before and after administration of sodium bicarbonate were obtained 22 times in 16 patients. Table 2 summarizes these data.

We observed a significant mean decrease of Pco_2 after sodium bicarbonate infusion ($p = 0.007$) (Figure 2) together with a significant mean increase of pH ($p < 0.005$) (Figure 3). Sodium bicarbonate was administered 5 to 30 min after the blood gas analysis, and the second blood gas measurement was obtained 5 to 60 min after the administration of sodium bicarbonate. In the period between the two blood gas analyses, the other therapies remained unchanged. Improvement of respiratory distress and level of consciousness were reported after the administration of sodium bicarbonate in all but one patient.



Pco2 before and after sodium bicarbonate (NaBic).



pH before and after sodium bicarbonate.

The most common acid-base disturbance in patients with LTA is initial respiratory alkalosis, followed by metabolic acidosis, either alone or as part of a mixed acidosis. In 1976, Roncoroni et al[11] described a large group of patients with LTA who had lactic acidosis. Patients with LTA and metabolic acidosis are at increased risk for the development of respiratory failure.[12,13] The causes of metabolic acidosis in asthma are increased lactic acid production by respiratory muscles due to prolonged and increased work of breathing, tissue hypoxia secondary to reduced cardiac output and ventilation-perfusion mismatch, decreased lactate clearance due to hypoperfusion of the liver, and excessive renal bicarbonate loss due to compensation for a preceding period of hypocapnia and respiratory alkalosis.[12-14] Acidosis produces myocardial depression, reduces the effectiveness of ß-agonists, and may stimulate ineffective rapid, shallow ventilation. Therefore, it has been postulated in previous reports[3-8] that correction of acidemia by sodium bicarbonate can relieve bronchospasm and restore the response to bronchodilators in patients with LTA. In most reports[3,4,6-8] on the use of sodium bicarbonate in treatment of LTA, sodium bicarbonate is administered before intubation and mechanical ventilation. In these patients, sodium bicarbonate infusion did produce clinical improvement without a rise of Pco_2.

Despite these reports, the use of sodium bicarbonate in the treatment of LTA has not been generally accepted. This could partly be due to the risk of a Pco_2 rise after sodium bicarbonate infusion because of inadequate gas exchange and hypoventilation. In review articles,[15-17] sodium bicarbonate is not even mentioned in the treatment of LTA in both adults and children.

In our study, we retrospectively studied all children with LTA requiring intensive care treatment during the last 5 years. There was no mortality. Since January 1999, only one patient with LTA required mechanical ventilation after admission to our PICU. Sodium bicarbonate was administered to 17 patients. Sixteen patients were acidotic, which indicates the severity of the respiratory distress. In 14 patients, sodium bicarbonate was administered in a last attempt to avoid mechanical ventilation. Only one patient did not improve, and she required intubation subsequently. In three patients, sodium bicarbonate was administered after intubation and mechanical ventilation because of persistent acidosis. Eight patients received sodium bicarbonate despite a pH > 7.15 because of severe respiratory distress and ineffectiveness of ß-agonists. Not only was there a significant decrease of Pco_2 after sodium

bicarbonate infusion but also a prompt improvement of the clinical condition, especially the level of consciousness, in all but one patient.

Since treatment of asthma is directed at inflammation, bronchoconstriction, and mucus plugging, clinical improvement in our patients likely resulted from a combination of treatment, including IV salbutamol and IV magnesium sulfate. There are several factors that suggest an adjunctive role for sodium bicarbonate in treatment of patients in this study. Other therapies remained unchanged during the time period between the blood gas analysis before and after the administration of sodium bicarbonate. Since the dose of IV salbutamol remained unchanged during this time period and IV magnesium sulfate was administered before this time period, it is unlikely that this may have had a sudden significant impact on the degree of hypercapnia and respiratory distress. Available data on magnesium sulfate show a slow increase of lung function in contrast to the sudden improvement seen in our patients exposed to sodium bicarbonate.[18]

We considered it useful to evaluate our recent experiences, especially regarding possible adverse effects of sodium bicarbonate in LTA, and we feel that our data, although collected in retrospect, are convincing evidence that Pco_2 decreases after sodium bicarbonate administration to children with LTA. Other limitations of this study should also be acknowledged. We did not use lung function tests or a scoring system to assess the severity of asthma before and after the administration of sodium bicarbonate. Lung function is, of course, unreliable in acute severe asthma and not feasible in intubated asthmatics. Moreover, we had information from blood gas analysis which indirectly reflects lung function. The time period between the administration of sodium bicarbonate and the second blood gas differed between patients. However, this time period was sufficiently long to show possible carbon dioxide retention. Therefore, our clinical observations do support a possible benefit of sodium bicarbonate in the treatment of LTA in children. A prospective study to evaluate the use of sodium bicarbonate is now in progress in our unit, using objective scoring systems for the evaluation of the severity of asthma and level of consciousness, and standardized time intervals between the blood gases and the administration of sodium bicarbonate.

Administration of sodium bicarbonate was associated with a significant decrease in Pco_2 in 17 children with LTA. Improvement of respiratory distress was observed as well. On the basis of this observation, we believe that sodium bicarbonate might be useful as an adjunctive treatment in patients with LTA and acidosis in whom mechanical ventilation is considered. The fear for an increase in Pco_2 is unsubstantiated. Further prospective randomized trials with sodium bicarbonate in this setting are warranted.

References

1. Dworkin G, Kattan M. Mechanical ventilation for status asthmaticus in children. J Pediatr 1989; 114:545-549
2. Stein R, Canny GJ, Bohn DJ. Severe acute asthma in a pediatric intensive care unit six years of experience. Pediatrics 1989; 83:1023-1028
3. Mithoefer JC, Runser RH, Karetzky MS. The use of sodium bicarbonate in the treatment of acute bronchial asthma. N Engl J Med 1965; 272:1200-1203
4. Mithoefer JC, Porter WF, Karetzky MS. Indications for the use of sodium bicarbonate in the treatment of intractable asthma. Respiration 1968; 25:201-215
5. Menitove SM, Goldring RM. Combined ventilator and bicarbonate strategy in the management of status asthmaticus. Am J Med 1983; 74:898-901
6. Mansmann HC Jr. A 29-year perspective of status asthmaticus in children. N Engl Reg Allergy Proc 1987; 8:327-334

7. Mansmann HC Jr, Abboud EM, McGeady SJ. Treatment of severe respiratory failure during status asthmaticus in children and adolescents using high flow oxygen and sodium bicarbonate. Ann Allergy Asthma Immunol 1997; 78:69-73

8. Bouachour G, Tirot P, Varache N. Acidose metabolique de l'asthme aigu grave effet de l'alcalinisation. Rev Pneumol Clin 1992; 48:115-119

9. Rowe BH, Bretzlaff JA, Bourdon C. Magnesium sulfate for treating exacerbations of acute asthma in the emergency department. Cochrane Database Syst Rev 2000; 2

10. Browne GJ, Trieu L, Van Asperen P. Randomized, double-blind, placebo-controlled trial of intravenous salbutamol and nebulized ipratropium bromide in early management of severe acute asthma in children presenting to an emergency department. Crit Care Med 2002; 30:448-453

11. Roncoroni AJ, Adrougue HJ, De Obrutsky CW. Metabolic acidosis in status asthmaticus. Respiration 1976; 33:85-94

12. Mountain RD, Heffner JE, Brackett NC. Acid-base disturbances in acute asthma. Chest 1990; 98:651-655

13. Appel D, Rubenstein R, Schrager K. Lactic acidosis in severe asthma. Am J Med 1983; 75:580-584

14. Okrent DG, Tessler S, Twersky RA. Metabolic acidosis not due to lactic acidosis in patients with severe acute asthma. Crit Care Med 1987; 15:1098-1101

15. Heinrich AW. Status asthmaticus in children. Chest 2001; 19:1913-1929

16. Marik PE, Varon J, Fromm R Jr. The management of acute severe asthma. J Emerg Med 2002; 23:257-268

17. Biarent D. Therapeutic strategies in near fatal asthma in children. Pediatr Pulmonol Suppl 2001; 23:90-93

18. Ciarallo L, Sauer AH, Shannon MW. Intravenous magnesium therapy for moderate to severe pediatric asthma results of a randomized, placebo-controlled trial. J Pediatr 1996; 129:809-814

Abbreviation Notes

LTA = life-threatening asthma; PICU = pediatric ICU

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