CLINICAL SIGNIFICANCE OF P_aCO_2 DURING STATUS ASTHMA: THE CROSS-OVER POINT

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Hypercapnia with respiratory acidosis in status asthmaticus is a serious development. Clinical examples have been presented to stress the significance of the "cross-over" from the early hypocapnia of hyperventilation to normal range P_{aCO_2} (and pH) as an indicator of impending respiratory acidosis. In the clinical context, these indices should alert the physician to reassess the clinical course and to modify or intensify therapy.

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PHYSIOLOGIC GUIDELINES in the management of advanced or status bronchial asthmaticus have been limited by the extreme anxiety and poor cooperation of such patients. Serial measurements of lung mechanics, ventilation, lung volumes or airflow rates may be useful in conjunction with careful clinical observation.[1]

Some degree of hypoxemia is present in many if not all asthmatics during an acute attack of status asthmaticus. Such hypoxemia results from unequal ventilation-perfusion ($\dot{V}/Q$) relationships initiated by the acute airways obstruction. The early pulmonary response is often hyperventilation with varying degrees of hypocapnia and respiratory alkalosis.[2,3] Less commonly, hypoventilation with hypercapnia and respiratory acidosis may occur because of progressive disease or iatrogenic factors. This phase is critical and often precedes the death of the patient. Between these ventilatory extremes, serial changes in arterial P_aCO_2/pH may occur which may be of clinical value.

The purpose of this report is to stress the significance of relatively "normal" blood P_aCO_2 and pH values as a guideline to progressive respiratory failure. In the proper clinical context, the "cross-over" of P_aCO_2 and pH from hyperventilation blood values to normal range P_aCO_2 and pH may be the forerunner of severe hypoxemia, hypercapnia, and acidosis.

Patients and Methods

Four patients in status asthmaticus were admitted to the Boston City Hos-

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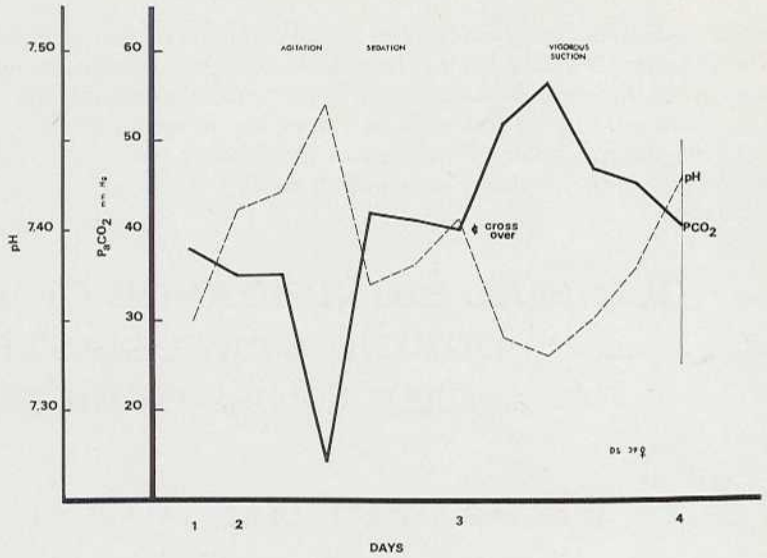

Figure 1.

pital. All were diagnosed as having bronchial asthma based upon clinical history, improvement in breathing mechanics following aerosol isoproterenol, positive skin tests, blood and sputum eosinophilia, and absence of conclusive findings of chronic bronchitis or emphysema. Full medical treatment was immediately instituted and modified as indicated clinically. None had complicating metabolic disorders.

Serial arterial bloods were drawn anaerobically from a permanently indwelling arterial cannula and analyzed immediately in the Instrumentation Laboratory Blood Gas Analyzer (Model No. 102), for P_aCO_2, P_aO_2, and pH at 37° C. Tonometered blood was employed for P_aO_2 calibration and dry gas for P_aCO_2 calibration. All samples were required to check within 5 mm. for P_aO_2 (50-100 mm. range), 2 mm. for P_aCO_2, and 0.005 units for pH. All blood analyses were correlated with the clinical state of the patient.

Case Reports

Case 1: D.S., a 39-year-old negro female, was admitted in status asthmaticus. (Figure 1).

With medical therapy including adrenal corticosteroids and penicillin she did well; an arterial blood revealed P_aCO_2 38 mmHg., pH 7.35, and P_aO_2 58 mmHg. (no O_2). On the next day, however, a severe asthmatic exacerbation developed with marked anxiety and agitation. A blood sample at this time showed a P_aCO_2 of 14 mmHg., pH of 7.47, and P_aO_2 of 77 mmHg. (on O_2). The reasons for this clinical change were not obvious, nevertheless, she was sedated with Chlordiazepoxide (Librium (R)) and barbiturates. It was reported that she spent a quiet evening, this supported by a P_aCO_2 of 40 mmHg., pH of 7.41, and P_aO_2 of 72 mmHg. (on O_2). On our visit early the next morning, she was lethargic, confused, and unable to cough properly; the P_aCO_2 was 56 mmHg., the pH 7.33, and P_aO_2 92 mmHg. (on O_2). It appeared the major problems were sedation and stasis of secretions, and with vigorous IPPB, suctioning, and encouragement to cough, she improved dramatically by clinical criteria; P_aCO_2 was 41 mmHg., and pH was 7.43 at this time. The remainder of the hospital course was uneventful.

Comment: The administration of sedatives in this patient reduced effective cough and resulted in stasis of secretions with hypoventilaton. The ap-

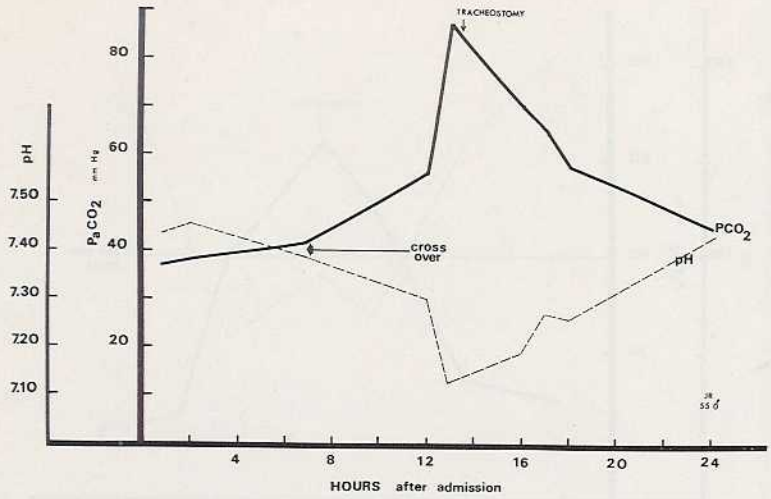

Figure 2.

parently "normal" P_aCO_2 and pH values obtained at night under sedation were misleading. In this instance, the P_aCO_2 of 40 mmHg. (and pH of 7.40) was most likely the cross-over from hyperventilation to progressive respiratory failure in an unagitated, sedated patient.

Case 2: J.R., a 55-year-old white male was admitted because of an infectious exacerbation of long standing asthma (Figure 2). Medical treatment was instituted including adrenal corticosteroids and penicillin. The patient was awake but mildly confused, and having difficulty in raising secretions. Initial arterial blood studies revealed: P_aCO_2 38 mmHg., pH 7.42, and P_aO_2 of 80 mmHg. (on nasal O_2 5L/min.).

Over the next 7 hours, he exhibited increasing agitation and was unable to cooperate for IPPB. A repeat blood analysis revealed a P_aCO_2 41 mmHg., pH 7.39 and P_aO_2 52 mmHg. (on O_2); the P_aCO_2 and pH values were considered normal by the attending physicians. However, over the next 5 hours cyanosis, agitation, and severe confusion developed with an arterial P_aCO_2 of 57 mmHg., pH of 7.30, and P_aO_2 of 40 mmHg. (on nasal O_2). At this point, tracheostomy was performed during which the P_aCO_2 and pH deteriorated further (P_aCO_2 86 mmHg., pH 7.12). With controlled ventilation and adequate suctioning he was alert, cooperative and tolerated assisted IPPB by the following day. Arterial blood revealed P_aCO_2 45 mmHg., pH 7.45, and P_aO_2 90 mmHg. Complete recovery occurred thereafter.

Comment: From the "cross-over" point of P_aCO_2 40 mmHg., this patient rapidly deteriorated into respiratory acidosis necessitating tracheostomy. The "normal" P_aCO_2-pH data and the progressive hypoxemia were not fully appreciated during a period of clinical instability. Awareness of the cross-over period might have alerted the physicians to impending ventilatory failure and resulted in more vigorous therapy.

Case 3: E.J., a 46-year-old negro female was admitted in status asthmaticus. (Figure 3). On medical treatment including adrenal corticosteroids and tetracycline an arterial blood on the second day showed: P_aCO_2 25 mmHg., pH 7.51, and P_aO_2 74 mmHg. (on mask O_2).

Status asthmaticus persisted, and on the third hospital day the P_aCO_2 was 27 mmHg., pH 7.47, and P_aO_2 80 mmHg. (on O_2). Severe fatigue and clinical deterioration ensued but repeat blood analysis was not obtained until noon of the fourth hospital day: P_aCO_2 46 mmHg., pH 7.37, and P_aO_2 48 mmHg. (on O_2). Despite renewed intensive treatment, a rapid downhill course developed over the next 7 hours necessitating a tracheostomy (P_aCO_2 52 mmHg., pH 7.31). The patient was placed on assisted ventilation

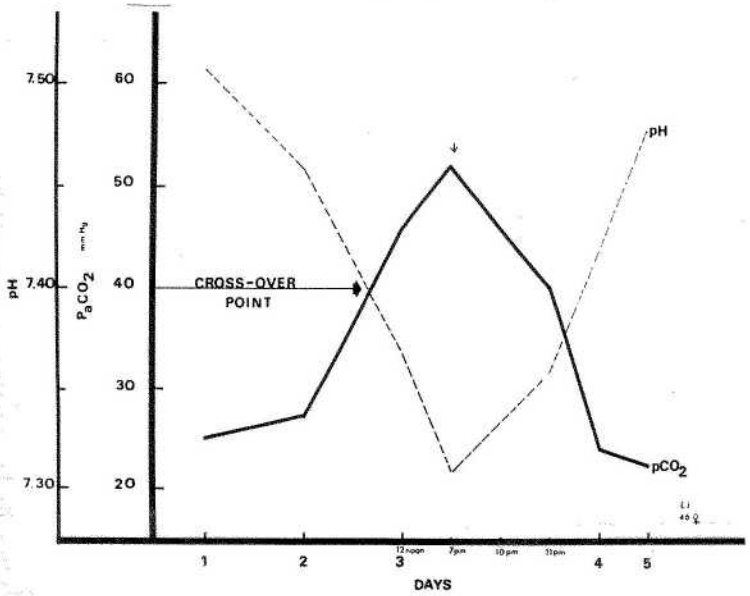

Figure 3.

and 4 hours later was clinically improved (P_aCO_2 40 mmHg., pH 7.36, and P_aO_2 120 mmHg.). Thereafter, she recovered manifesting hyperventilation until the tracheostomy was removed one week prior to discharge.

Comment: This case emphasized the need for frequent arterial blood determinations during the course of status asthmaticus particularly if clinical improvement fails to occur. The cross-over phase (Figure 3) might have been appreciated by additional serial P_aCO_2 and pH observations reflecting progressive $\dot{V}/Q$ disturbances or reduced effective alveolar ventilation, and earlier attempts to reverse her course may have been successful. Thus, further medical observation and vigorous treatment are clearly indicated at this potentially critical point in an asthmatic's course.

Case 4: This 61-year-old white male, M.M., entered the Boston City Hospital with status asthmaticus.

Arterial blood gases on admission revealed a P_aCO_2 of 34 mmHg., pH of 7.52, and P_aO_2 of 64 mmHg.; the Peak Expiratory Flow Rate (Wright meter) (PEFR) was 200 L/min. (60% of predicted) and Forced Vital Capacity (FVC) was 1.8 L (50% of predicted). (Figure 4).

Despite medical treatment including high doses of adrenal corticosteroids, clinical decline continued during the first hospital day. The FVC fell to 1.47 L., the PEFR to 140 L/min., with the P_aCO_2 rising to 39 mmHg., and a pH of 7.40. This clinical and physiologic deterioration was treated more aggressively with IPPB, bronchodilators, sputum evacuation etc., and by late that evening he improved clinically, with the P_aCO_2 falling to 34 mmHg. Significant clinical progress continued over the next 2 days. Concurrently, spirometric and blood gas data improved: (FVC 3.0 L, PEFR 350 L/min., P_aCO_2 39 mmHg., and pH 7.45).

Comment: This case demonstrates the value of serial data as an indicator of possible ventilatory failure which may be therapeutically altered. In the clinical context, the rise in P_aCO_2 from 34 to 39 mmHg. (also corroborated by simple mechanics testing) was interpreted as approaching the cross-over phase. More intensive treatment at this point was associated with clinical and blood gas improvement. Of course, a

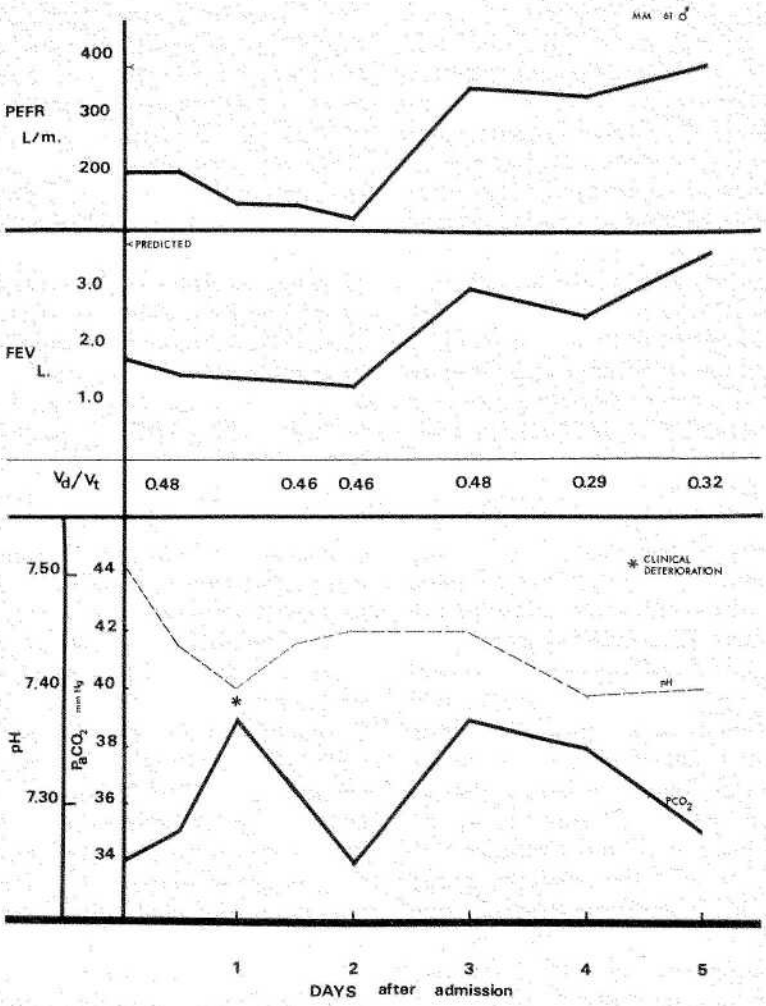

Figure 4.

spontaneous remission may have occurred, but in view of the clinical course we feel that the serial rise in P_aCO_2 alerted us and may have prevented gross respiratory failure.

Discussion

The initial pathophysiological disturbance in bronchial asthma arises from airways obstruction as the result of bronchospasm, mucosal edema and inflammation, mucus secretion and effort-related expiratory airways collapse. A greater transpulmonary pressure is thereby required to overcome increased inspiratory and expiratory resistances. Hyperinflation with increases in residual air and a reduction in vital capacity may follow.[4] Concurrently, nonuniform gas distribution with inequalities in regional ventilation and/or perfusion ($\dot{V}/Q$) are manifested as arterial hypoxemia. Both this hypoxemia and psychological factors may contribute to

the ensuing hyperventilation. The presence of hypocapnia at this point indicates that alveolar hypoventilation is not the cause of the hypoxemia.

In chronically stable asthma, mild hypoxemia may occur at frequencies not previously appreciated,[5,6,7] since hemoglobin saturations are normal or minimally reduced. However, in severe or status asthmaticus, advanced hypoxemia develops. This may be intensified by the therapeutic use of isoproterenol, aminophylline or adrenaline as emphasized by the recent literature.[6,8,9]

The arterial P_aCO_2 in status asthmaticus may initially reveal normocapnia or hypocapnia with or without respiratory alkalosis. With progressive disease, further inequalities in $\dot{V}/Q$ develop and initial compensatory increases in effective alveolar ventilation subsequently fail because of increased airway resistances and associated excessive work of breathing. Thus, some patients with status asthmaticus will progress to gross hypercapnia and respiratory acidosis.[10] This form of "hypoventilation" may be intensified by the administration of sedative drugs. Palmer and Diament have clearly stressed the serious consequences of respiratory acidosis, and have concluded that acute hypercapnia is an important sign of impending deterioration in status asthmaticus.[6] Our cases suggest that this deterioration can occur rapidly and may be implicated in those patients who die suddenly.[11] Such demise may be related to limited CSF buffering during acute hypercapnia affecting respiratory or vasomotor centers.[12]

The patients presented in this paper illustrate the value of *serial* arterial P_aCO_2 and pH data as indicators of the transition from hyperventilation to alveolar hypoventilation in conjunction with progressive $\dot{V}/Q$ inequalities. In particular, the shift of P_aCO_2 from hypocapnia to *normocapnia* may herald the "cross-over" into hypercapnia and respiratory acidosis. It has been suggested that P_aCO_2 is not a reliable estimate of respiratory failure in asthma until late in the course of the disease.[7] However, this objection is minimized by our emphasis on serial changes in P_aCO_2 as an indicator of progressive respiratory failure, not on the result of one or two isolated samples. Furthermore, hypoxemia may be corrected by the administration of oxygen and the parameter of severe hypoxemia reflecting progressive $\dot{V}/Q$ abnormalities may be lost. The approach of P_aCO_2-pH data to the "cross-over" range of normal values should alert the physician to reassess the entire clinical picture and to modify or intensify therapy. Obviously, this concept will not apply to improved patients who attain normal P_aCO_2 and pH relationships. Cases 1, 2, and 3 illustrate this point of frank deterioration once the cross-over point is reached. Case 4 qualifies the concept by indicating that a patient receiving intensified treatment may recover without progressing to hypercapnia and respiratory failure. Further studies are underway to delineate the frequency and possibility of reversibility once this phase is reached. It should be clear that each patient's P_aCO_2 and pH data must be interpreted in the proper clinical context, and coexisting metabolic acid-base disorders defined, so that these indices may be of value in the management of status asthmaticus.

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