DISCUSSION

This otherwise healthy young female had asymptomatic thrombophlebitis with recurrent pulmonary emboli which caused her complaints of chest pain. This was confirmed by the presence of a proximal deep vein thrombosis in conjunction with abnormalities on the lung scan, both of which resolved under treatment.

Possible explanations for this negative angiogram include false positive lung scan, false negative angiogram, or recanalization. This last option seemed the easiest to accept until the second lung scan was performed and showed a persistent although resolving perfusion defect. It was our impression that this was a false negative pulmonary angiogram due to inadequate angiographic technique. The angiographic method used in this patient could exclude only large emboli. Since perfusion defects were demonstrated on the lung scan, the areas in question should have been studied by superselective catheter injections. Oblique views, as suggested by Bossart et al and Comes et al, may have shown a small right upper lobe artery embolism. In patients with a radioisotope perfusion defect, selective angiograms may be required to demonstrate pulmonary occlusions.

REFERENCES


Excess carbohydrate calories in total parenteral nutrition (TPN) solutions can precipitate acute hypercapnic respiratory failure in patients with chronic lung disease secondary to increased carbon dioxide (CO₂) production. Two young patients recovering from the adult respiratory distress syndrome experienced hypercapnia during weaning as a result of nutritionally related increased CO₂ production. As carbohydrate calories were decreased, CO₂ production diminished and hypercapnia resolved. Hypercapnia as a complication of nutritional support during weaning can occur in patients without chronic lung disease and is corrected by decreasing carbohydrate calories.

Nutritional support of intensive care unit patients is becoming widely practiced as malnutrition and multiple adverse effects of malnutrition are recognized. Multiple complications can occur when nutritional solutions are given as total parenteral nutrition (TPN). Metabolic complications of TPN include increased carbon dioxide (CO₂) production. Acute hypercapnic respiratory failure has been precipitated with the use of TPN in nonintubated patients with chronic lung disease. Excess carbohydrate (CHO) calories were associated with an increased carbon dioxide production resulting in hypercapnia and acute respiratory failure.

We describe a complication related to increased carbon dioxide production associated with TPN use that is clinically recognized, but to our knowledge, previously unreported and not clearly documented. Two previously healthy young patients recovering from the adult respiratory distress syndrome (ARDS) developed hypercapnia associated with increased CO₂ production which became clinically apparent during weaning from mechanical ventilation. Carbon dioxide production decreased concurrently with the PaCO₂ as total carbohydrate (glucose) calories were decreased. Both patients were subsequently weaned. Unexpected hypercapnia during weaning may be nutritionally related.

METHODS

Serial measurements of CO₂ production were performed in each patient in the following manner. After a washout time of approximately two minutes, a four-minute timed air collection was done using the exhalation port of the ventilator. The expired air was collected into a 120 L, nonporous bag; volumes were measured by a Wright respirometer. The collected air was analyzed for carbon dioxide fraction using Beckman infrared CO₂ analyzer. Carbon dioxide production was then calculated using the following equation:

\[ \dot{\text{V}}\text{CO}_{2} \text{ (ml)} = [\text{FE CO}_{2} - 0.0003] \times \dot{\text{V}}\text{E} \text{ (L) (STPD)} \times 10^{6}. \]

CASE 1

A 23-year-old white man was treated at the University of Kansas Medical Center for ARDS. After a long (three month) and complicated intensive care unit course, his respiratory status improved and weaning began. Preweaning arterial blood gas levels were a PaO₂ of 90 mm Hg, a PaCO₂ of 38 mm Hg, and pH of 7.43 on an FIO₂ of 0.3. Weaning parameters included a resting minute ventilation of 22.0 L, a negative inspiratory force of -58 cm H₂O, tidal volume of 611 ml, and a vital capacity of 1.0 L. During a short T-tube trial off the ventilator, hypercapnia (PaCO₂ 53 mm Hg), respiratory acidosis (pH 7.27), and respiratory distress were noted. At that time, he was
Table 1—Association Between Daily Carbohydrate (CHO) Calories, Carbon Dioxide (CO₂) Production and Arterial Carbon Dioxide Tension (PaCO₂)

<table>
<thead>
<tr>
<th></th>
<th>Patient 1</th>
<th>Patient 2</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Day 1</td>
<td>Day 2</td>
</tr>
<tr>
<td>CHO Kcal/Day</td>
<td>4284</td>
<td>2595</td>
</tr>
<tr>
<td>CO₂ production ml/min</td>
<td>500</td>
<td>390</td>
</tr>
<tr>
<td>PaCO₂ (T-tube) mm Hg</td>
<td>53</td>
<td>39</td>
</tr>
<tr>
<td>Minute ventilation (L/min)</td>
<td>22.0</td>
<td>24.0</td>
</tr>
</tbody>
</table>

receiving a daily calorie intake of nearly 5,400 Kcal (4,284 carbohydrate Kcal) of TPN to correct a severely depleted nutritional status. Carbon dioxide production at that time was measured and was 500 ml/min (Table 1). Carbohydrate calories were decreased to 2,550 and 2,040 Kcal/day with resultant decreases in CO₂ production to 390 and 356 ml/min. The T-tube trials on those days did not result in hypercapnia. Weaning parameters and overall status remained stable, and with no other changes in therapy, weaning was successful within several days.

Case 2

A 26-year-old previously healthy white woman was admitted and treated at the University of Kansas Medical Center for ARDS secondary to cytomegalovirus infection. After a long (six weeks) and complicated course, she improved and weaning attempts began. Preweaning arterial blood gas levels were PaO₂ 63 mm Hg; PaCO₂ 42 mm Hg; and pH 7.43 (FIO₂ 0.4). Weaning parameters at that time included a resting minute ventilation of 16.3 L, a negative inspiratory force of −38 cm H₂O, tidal volume 500 ml, and a vital capacity of 650 ml. While breathing on a T-tube, she developed hypercapnia (PaCO₂ 52 mm Hg), a fall in pH (7.36), and respiratory distress. At that time, she was receiving 3,200 Kcal/day (2,550 CHO Kcal/day) of TPN. Daily serial measurements of total CO₂ production and PaCO₂ during spontaneous breathing on a T-tube were made as CHO calories were decreased (Table 1). Carbon dioxide production decreased from 378 ml/min to 258 ml/min resulting in a lowered PaCO₂ (52 mm Hg to 42 mm Hg) as CHO calories were decreased from 2,550 to 1,530/day. Weaning parameters, overall status, and therapy remained stable and weaning was accomplished within several days.

Discussion

Our report confirms the increased carbon dioxide production noted when large carbohydrate loads in TPN are given. Carbon dioxide production is increased in this patient population because calories in excess of energy needs result in lipogenesis and a markedly increased respiratory quotient (RQ). The RQ is defined as the ratio of carbon dioxide production to oxygen consumption during substrate utilization. For example, when one molecule of glucose is oxidized, six oxygen molecules are necessary for the oxidative process and six molecules of carbon dioxide are produced. Therefore, the RQ of glucose is 1.0. The RQ of lipogenesis is approximately 8.0, reflecting the much greater production of carbon dioxide relative to oxygen consumed.

Normal CO₂ production in a 70 kg man is approximately 200 ml/min. When carbohydrate (glucose) calories in TPN exceed a patient's metabolic demands, lipogenesis occurs with an increased CO₂ production. Our patients had a marked increase in CO₂ production at times of high carbohydrate intake; patient 1 initially had a greater than twofold increase over normal CO₂ production. Elevated CO₂ production in normal patients does not result in hypercapnia as normal patients respond by increasing minute ventilation. Patients who have chronic lung disease or a fixed minute ventilation from any cause will not be able to react to the elevated CO₂ production by an increase in minute ventilation. Hypercapnia results, and as demonstrated by our patients, leads to weaning difficulty and prolongation of weaning time.

With a decrease in carbohydrate calories, measured CO₂ production decreased and hypercapnia during weaning resolved. Covelli et al. first reported hypercapnia as a result of increased CO₂ production in three chronic lung disease patients, probably with chronic obstructive lung disease, who developed acute hypercapnic respiratory failure with excessive carbohydrate loads. Our patients did not have a history of chronic lung disease. However, their pulmonary disease was severe, protracted, and probably restrictive in nature, leaving them with markedly limited ventilatory reserve. Both patients were nutritionally depleted, and we speculate that nutritionally associated decreased respiratory muscle strength contributed to a relatively fixed minute ventilation. In the setting of compromised pulmonary and muscle status, our patients simply could not handle the increased CO₂ load. Hypercapnia during weaning developed, and the patients could not be weaned until carbohydrate calories were decreased.

Reasonable nutritional care requires knowledge not only of the potential benefits of nutrition, but also of the hazards associated with its use. Nutritional support should provide only what is needed; providing excess calories not only increases the potential for complications, but also the expense. Clinicians involved in the weaning of mechanically-ventilated patients receiving TPN should recognize that hypercapnia during weaning may be nutritionally related. In this setting, measurement of CO₂ production and correlation with total calories will allow the physician to determine if hypercapnia is related to nutrition. If confirmed, physicians should limit the total number or alter the percentage of carbohydrate calories in total parenteral nutrition solutions.

References

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Amiodarone Pulmonary Toxicity

Chest Radiography and CT in Asymptomatic Patients

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Two asymptomatic patients from a group of 30 being treated with the antiarrhythmic drug amiodarone developed roentgenographic pulmonary and pleural reactions. Computed tomography in one patient with an uncommon radiographic pattern of fuzzy nodules showed the spatial distribution of the parenchymal changes, as well as unrecognized pleural thickening. The disease in these asymptomatic patients was presumably detected on the periodic chest roentgenogram at an early stage because the changes disappeared after withdrawal of the drug. Periodic chest radiographs are recommended during amiodarone therapy and CT may be useful in evaluation of patients with unusual chest radiographic findings.

Amiodarone (Cordarone) is an antiarrhythmic drug which has recently undergone clinical testing in the United States and has shown good potential to become a commonly used cardiac drug. Similar studies of clinical use of this drug have taken place in Europe for more than 15 years.¹ Association of the use of this drug have been reports of side-effects and toxic reactions, including corneal microdeposits, thyroid dysfunction, neurotoxicity, photosensitivity, skin discoloration, elevated hepatic enzymes and bone marrow depression.² Clinical pulmonary reactions occasionally associated with the use of amiodarone therapy have been presented,³ with roentgenographic findings described as diffuse interstitial and patchy alveolar disease which predominantly involves the upper lobes. The pattern of pulmonary reaction in four patients has recently been described in the radiologic literature.⁷ There has been no report on the computed tomographic (CT) appearance of these pulmonary changes. In a series of 30 patients treated with amiodarone for cardiac arrhythmias at the University of Rochester Medical Center, two asymptomatic patients developed radiographic pulmonary changes. One case studied in detail with CT is reported herein.

Case Report

A 78-year-old white woman with a past history of myocardial infarction, chronic congestive heart failure, coronary artery bypass graft surgery, and mitral valve replacement presented with recurrent ventricular tachycardia. Since treatment with all conventional and one investigational antiarrhythmic drug was ineffective, the patient was started on therapy with amiodarone at a dose of 800 mg per day for one month, then which was tapered to 500 mg per day. This resulted in good control of the arrhythmia. Chest roentgenograms were obtained routinely every three months. Ten months after the initiation of amiodarone therapy, the chest roentgenogram demonstrated an increase in interstitial markings with ill-defined nodular shadows in the right upper zone and a larger lesion in the upper left zone. There was no roentgenographic sign of congestive heart failure. Several days later, a follow-up roentgenogram showed progression of the pulmonary disease despite the absence of respiratory complaints, so amiodarone was discontinued (Fig 1).

Computed tomography (CT) of the chest was performed to assess the unusual nodular shadows in the upper zones of the chest. The findings were diffuse interstitial reaction, especially at the lung bases posteriorly, in addition to the irregularly margined pulmonary nodules in the upper lobes. Also, pleural thickening was noted posteriorly on the left (Fig 2).

Pulmonary examination at the time of admission revealed inspiratory rales at the bases bilaterally. Cardiac auscultation revealed a grade 2/4 holosystolic murmur. An electrocardiogram showed normal sinus rhythm with 1° atrioventricular block, left axis deviation, and evidence of old diaphragmatic and anterior myocardial...