Using Quantitative Acid-Base Analysis in the ICU

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ABSTRACT

The quantitative acid-base ‘Strong Ion’ calculator is a practical application of quantitative acid-base chemistry, as developed by Peter Stewart and Peter Constable. It quantifies the three independent factors that control acidity, calculates the concentration and charge of unmeasured ions, produces a report based on these calculations and displays a Gamblegram depicting measured ionic species. Used together with the medical history, quantitative acid-base analysis has advantages over traditional approaches. (Critical Care and Resuscitation 2006; 8: 19-30)

Key words: Quantitative acid-base analysis, quantitative acid-base calculator, net unmeasured ions, strong ion gap, anion gap, base excess, standard base excess

With modern quantitative acid-base physiology theory based on the work of Peter Stewart1 and Peter Constable,2-5 it has been possible to develop a calculator that automatically fetches relevant results from the laboratory database and displays a report which quantifies the three independent parameters that are known to control acidity in arterial or venous plasma.6 These parameters are the strong ion difference (SID), which summarises the strong or fully-dissociated electrolytes, the total weak acid concentration (Atot), which summarises the nonvolatile weak or partially dissociated electrolytes, and the partial pressure of carbon dioxide (PCO2). (see Table 1).

In this paper the term ‘acidity’ refers to the activity of hydrogen ions as measured by a pH meter and quantified in nanomoles per litre: it is the exact counterpart of pH but expressed on a linear scale rather than a reversed-logarithmic scale. Acidity (in nmol/L) = 109*10pH. Acidity is related to the notional hydrogen ion concentration by the activity coefficient which varies nonlinearly with temperature, PCO2 and concentration of other ions.1 Because most hydrogen ions in plasma in fact combine with water to form hydronium ions (H3O+), use of the term ‘hydrogen ion concentration’ may be confusing and unhelpful.

Acidity varies almost linearly with PCO2 and with nonvolatile weak acid concentration. Nonvolatile weak acids normally present in plasma are albumin (75% of total buffering),5 globulins (20%), phosphate (about 5%) and uric acid (<1%).

The Strong Ion Difference = Σstrong cations - Σstrong anions and in plasma is approximately [Na+] - [Cl-]. Consider an experiment in which 105 mmol HCl in 499 mL of water is (carefully!) added to 140 mmol NaOH in 499 mL of water. The strong acid will neutralise 105 mmol of the strong base, with 35 mmol NaOH left over: 105 mmol H+ + 105 mmol OH- => 105 mmol H2O (= 2 mL water @ 55 mmol per mL).

The measurable remnant of strong acid is chloride (105 mEq/L) and of strong base is sodium (140 mEq/L). The SID = 140 - 105 = 35 mEq/L.

The SID represents the net excess of strong base over strong acid in plasma. Acidity bears an inverse relationship with SID: a reduced SID causes an increased acidity and vice versa.

The calculator itself can quantify the relative contributions of the three independent factors to the overall acid-base situation, but does not indicate whether a process is primary or compensatory. This often requires a medical history, examination, investiga-

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The main advantage of using the quantitative acid-base calculator is that it is exact and eliminates mental arithmetic errors associated with ‘rule-of-thumb’ based approaches.\textsuperscript{9,11} It also avoids the main weakness inherent in the Copenhagen base-excess approach, the Boston ‘rules’ approach, and the anion gap approach, all of which make varying assumptions about the normality of the protein, phosphate, chloride and other ionic concentrations. A patient with normal protein and electrolyte concentrations would be the exception rather than the rule in most Australasian ICUs.

### A quick tour

Arterial or venous blood is drawn into a heparinised blood gas syringe and a biochemistry tube and sent for analysis. A wide range of parameters can be accepted by the calculator. The minimum data set required is: pH,

### Table 1. The subdivision of ionic species present in plasma

<table>
<thead>
<tr>
<th>Strong Ions</th>
<th>Non-volatile weak acids</th>
<th>Volatile weak acids</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na\textsuperscript{+}, K\textsuperscript{+}, Ca\textsuperscript{2+}, Mg\textsuperscript{2+}, Cl\textsuperscript{-}, lactate, SO\textsubscript{4}\textsuperscript{2-}, NEFA, ketoacids, protein and phosphate</td>
<td>protein and phosphate, weak acid charge*, uric acid, (hydrogen ions, hydroxyl ions in nmol/L quantities)</td>
<td>CO\textsubscript{2}, carbonic acid, bicarbonate, (Henderson-Hasselbalch Equation), (carbonate in µmol/L quantities)</td>
</tr>
</tbody>
</table>

*Proteins and phosphate have a small acidity-independent (strong ion) negative charge and an additional acidity-dependent (weak acid) negative charge, NEFA = non-esterified fatty acids.

### Table 2. Traditional rules of thumb

<table>
<thead>
<tr>
<th>DISORDER</th>
<th>BOSTON RULES</th>
<th>COPENHAGEN RULES</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HCO\textsubscript{3} (mmol/L)</td>
<td>PCO\textsubscript{2} (kPa)</td>
</tr>
<tr>
<td>Metabolic acidosis</td>
<td>&lt; 22</td>
<td>HCO\textsubscript{3} /5 + 1</td>
</tr>
<tr>
<td>Metabolic alkalosis</td>
<td>&gt; 26</td>
<td>HCO\textsubscript{3} /10 + 2.6</td>
</tr>
<tr>
<td>Acute respiratory acidosis</td>
<td>= (PCO\textsubscript{2} - 5.3)\times 3/4 + 24 \textsuperscript{*}{\textit{up three-quarters per kPa}}</td>
<td>&gt; 6</td>
</tr>
<tr>
<td>Chronic respiratory acidosis</td>
<td>= (PCO\textsubscript{2} - 5.3)\times 3 + 24 \textsuperscript{*}{\textit{up three per kPa}}</td>
<td>&gt; 6</td>
</tr>
<tr>
<td>Acute respiratory alkalosis</td>
<td>= 24 - 1.5*(5.3 - PCO\textsubscript{2}) \textsuperscript{*}{\textit{down one-and-a-half per kPa}}</td>
<td>&lt; 4.7</td>
</tr>
<tr>
<td>Chronic respiratory alkalosis</td>
<td>= 24 - 4*(5.3 - PCO\textsubscript{2}) \textsuperscript{*}{\textit{down four per kPa}}</td>
<td>&lt; 4.7</td>
</tr>
</tbody>
</table>

SBE = Standard base excess

### Table 3. Traditional rules of thumb

<table>
<thead>
<tr>
<th>DISORDER</th>
<th>BOSTON RULES</th>
<th>COPENHAGEN RULES</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HCO\textsubscript{3} (mmol/L)</td>
<td>PCO\textsubscript{2} (mmHg)</td>
</tr>
<tr>
<td>Metabolic acidosis</td>
<td>&lt; 22</td>
<td>= 1.5 \times [HCO\textsubscript{3}] + 8</td>
</tr>
<tr>
<td>Metabolic alkalosis</td>
<td>&gt; 26</td>
<td>= 0.7 \times [HCO\textsubscript{3}] + 21</td>
</tr>
<tr>
<td>Acute respiratory acidosis</td>
<td>= (PCO\textsubscript{2} - 40)\times 1/10 + 24 \textsuperscript{*}{\textit{up one-for-ten}}</td>
<td>&gt; 45</td>
</tr>
<tr>
<td>Chronic respiratory acidosis</td>
<td>= (PCO\textsubscript{2} - 40)\times 4/10 + 24 \textsuperscript{*}{\textit{up four-for-ten}}</td>
<td>&gt; 45</td>
</tr>
<tr>
<td>Acute respiratory alkalosis</td>
<td>= 24 - (40 - PCO\textsubscript{2})\times 2/10 \textsuperscript{*}{\textit{down two-for-ten}}</td>
<td>&lt; 35</td>
</tr>
<tr>
<td>Chronic respiratory alkalosis</td>
<td>= 24 - (40 - PCO\textsubscript{2})\times 5/10 \textsuperscript{*}{\textit{down five-for-ten}}</td>
<td>&lt; 35</td>
</tr>
</tbody>
</table>
Critical Care and Resuscitation 2006; 8: 19-30

P. LLOYD & R. FREEBAIRN

Figure 1. Normal patient. SI = strong ion.

PCO₂, [Na⁺], [K⁺], [Cl⁻]. However, missing data decreases the accuracy (because a default value is substituted for an unmeasured parameter), so a suite of tests as complete as is practical including measurement of important electrolytes and proteins is recommended on admission to ICU.

Subsequent tests are performed according to the clinical situation. The online version of the calculator available in our hospital has rules allowing it to carry forward some recent results.

For example, if yesterday’s albumin was 30 g/L then the calculator will use yesterday’s albumin if it has not been remeasured. By not being required to do the whole gamut of tests every time one wants to perform quantitative acid-base analysis, using the calculator routinely has minimal impact on laboratory costs. Here is the report page of a normal patient with every parameter measured that the calculator can accept (Figure 1). The values of the three independent parameters are displayed at each corner of a triangle to draw the eye. In brackets is displayed the direction and degree to which variation of each parameter individually affects the acidity in the present clinical context. Nearby are tabulated the individual results that contributed to the calculation of the independent parameters. The normal arterial acidity is 40 mmol/L. Respiratory physiology calculations such as the arterial to inspired PO₂ ratio (PaO₂/PiO₂), the alveolar-arterial PO₂ gradient (A-a gradient) and the pulmonary admixture or shunt fraction (Qs/Qt), when available, are included for the convenience of the intensivists. The anion gap is also calculated.

CASE REPORTS

Patient 1

A 6-year-old boy admitted in diabetic ketoacidosis with a new diagnosis of diabetes mellitus (Figure 2).

Abnormal results are colour coded (inspired by litmus paper) according to the direction in which they influence acidity. For instance, the low sodium of 129 mmol/L contributed to the very low measured SID. Both factors were outside their normal range in the direction that increased the acidity, hence they are coloured red. In the context of the very low PCO₂ (reduced acidity - colour blue) and nearly normal protein concentrations, the deviation of measured SID from normal had an acidifying effect of +9 mmol/L. Some might argue that we should correct the sodium concentration for hyperglycaemia. Hyperglycaemia causes osmotic translocation of fluid from the intracellular to the extracellular space, reducing by dilution not only the sodium concentration but also the concentrations of all the other cations and anions in equal proportion. Because sodium is the most abundant
ion in plasma, its absolute reduction in concentration is greater than the absolute reduction of the other ions. In our opinion ‘pseudohyponatraemia’ is a misnomer because the plasma sodium concentration really is reduced, and quantitative analysis is appropriately performed with the plasma concentrations as they really are.

The PCO₂ was very significantly reduced, especially considering that this was a venous sample. In the context of the low measured SID, the calculated net unmeasured anion concentration, and the nearly normal protein concentration, this reduction in PCO₂ from the normal (arterial) value caused a massive reduction in acidity of 77 nmol/L.

The protein concentrations were nearly normal. The measured nonvolatile weak acid summarising factor A\textsubscript{tot} was 15 nmol/L compared to its normal value of 17. In the context of the highly abnormal measured SID and calculated net unmeasured anion concentration, despite the modulating influence of the low PCO₂, even this small deviation in measured A\textsubscript{tot} caused a reduction in acidity of 14 nmol/L (A\textsubscript{tot} coloured blue).

**Gamblegram**

Because we know in detail the acid-base behaviour of proteins, phosphate, carbonic acid and uric acid, we know their degree of dissociation and how much negative charge they carry for any combination of concentration and degree of prevailing acidity. We can therefore draw up a balance sheet of positive and negative charges must be in balance in aqueous solutions. In this case of diabetic ketoacidosis, we find that there was a net 18 mEq/L of negative anionic charge that was unaccounted for (Figure 3, coloured red). This is the net unmeasured ions (NUI).

The NUI was formerly known as the strong ion gap (SIG). The term ‘Strong Ion Gap’ was coined by John Kellum in 1995. Unfortunately, when there are unmeasured anions present, some authors report a positive SIG (i.e. it behaves like the anion gap) but others report a negative SIG (i.e. it behaves like base excess); one is -1 times the other. Rather than get mired in an argument, after discussion with John Kellum (personal communication), it was felt to be more descriptive to define the term NUI as:

\[
\text{NUI} = [\text{unmeasured cations}] - [\text{unmeasured anions}]
\]

This mirrors the term SID which is the measured strong cations - measured strong anions. It also reflects the fact that unmeasured anions are not necessarily strong. Kellum describes the use of gelatins in resuscitation.
tion as being associated with unmeasured anions, and gelatins are weak acids. A negative NUI means that unmeasured anions outnumber unmeasured cations; the normal NUI is close to zero.

The normal range for the NUI in the calculator was estimated from the normal range for relevant parameters such as pH, PCO₂, electrolyte and protein concentrations as specified by our local laboratory, using a Monte Carlo simulation similar to the one outlined in a previous paper published in this Journal. The resulting estimated range for NUI seems to be wider than what is encountered in practice: further work is necessary. The standard deviation of SID and Atot were calculated in a similar manner. Mild, moderate and severe deviations were defined as more than 1, 2 and 3 standard deviations from the mean.

A complete analysis of the patient’s acid-base status requires measurement of the PCO₂, SID, Atot and NUI. The NUI represents the unmeasured component. It is not uncommon to encounter a mixed picture in which, for example, there is simultaneously present in a patient a measured strong ion alkalosis and a metabolic acidosis due to unmeasured anions (see Table 4).

Returning to the child in Figure 2, the report box indicates severe measured strong ion acidosis and severe additional metabolic acidosis due to unmeasured anions (likely to be ketoacids in this case).

After resuscitation and insulin treatment overnight the child’s acid-base derangement had improved to the following (Figure 4). The report box indicates a combination of severe respiratory alkalosis, severe measured strong ion acidosis, severe measured weak acid alkalosis and moderate additional metabolic acidosis due to unmeasured anions. The Gamblegram shows the overnight reduction in the concentration of unmeasured anions (Figure 5).

Table 4. Classification of acid-base disturbances

<table>
<thead>
<tr>
<th>Disturbance</th>
<th>SID</th>
<th>Atot</th>
<th>PCO₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>↑ SI alkalosis</td>
<td>WA acidosis</td>
<td>Respiratory acidosis</td>
<td></td>
</tr>
<tr>
<td>↓ SI acidosis</td>
<td>WA alkalosis</td>
<td>Respiratory alkalosis</td>
<td></td>
</tr>
<tr>
<td>NUI &lt; -5 mEq/L</td>
<td>Metabolic acidosis due to unmeasured anions (SI or WA)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SI = strong ion, WA = weak acid, NUI = net unmeasured ions

**Patient 2**

**Status asthmaticus: Arterial sample**

This illustrates an advantage of the quantitative
Figure 4. Diabetic ketoacidosis after overnight resuscitation and insulin

Figure 5. Gamblegram of diabetic ketoacidosis after overnight resuscitation and insulin.
Figure 6. Status asthmaticus

The patient, a young woman, was in extreme respiratory distress at the time this blood sample was taken. The base excess was -11 mmol/L and the anion gap was 15 mmol/L (Figure 6). It should be added that our laboratory does not report standard base excess, so this is not shown in the figures. However, for the purpose of comparison in this paper, standard base excess has been calculated manually using the Van Slyke equation; in the present case the standard base excess was also -11 mmol/L.

Unfortunately the standard base excess cannot be used directly to interpret the metabolic component of an acid-base disturbance without first applying the Copenhagen set of rules (similar to the Boston rules), (set out in Tables 2 and 3). Finally one must rule out ‘concealed metabolic acidosis’ by calculating the anion gap, in the present case the standard base excess was also -11 mmol/L.

Unfortunately the standard base excess cannot be used directly to interpret the metabolic component of an acid-base disturbance without first applying the Copenhagen set of rules (similar to the Boston rules), (set out in Tables 2 and 3). Finally one must rule out ‘concealed metabolic acidosis’ by calculating the anion gap, in the present case the standard base excess was also -11 mmol/L.

Returning to the patient, a key management decision hinged on, ‘Were there unmeasured anions present that might belie further unsuspected diagnoses?’ Quantitative acid-base analysis shows that her low PCO2 biased the acidity down by 14 mmol/L. The reduced measured SID (mostly caused by increased chloride and lactate concentrations) biased the acidity upward by 14 mmol/L. There was in addition a moderate hypoproteinaemia. Taking all three factors into consideration simultaneously the predicted acidity (assuming no unmeasured ions) was 41 mmol/L, the measured acidity was 48 mmol/L, and the discrepancy between the two was caused by a net concentration of unmeasured anions of 2 mEq/L (NUI = -2 mEq/L), which is within normal limits. Mixed strong ion (hyperchloremic and lactic) acidosis and respiratory alkalosis collectively accounted for her acid-base status.

The report box indicates a combination of severe respiratory alkalosis, moderate measured strong ion acidosis, and severe measured weak acid alkalosis.

Patient 3

Acute renal failure: rhabdomyolysis

This was 38-year-old man with a mild intellectual impairment and bipolar disorder who lived alone. He was found by his caregiver in the morning, having spent the night on the kitchen floor in a collapsed state. He was admitted at 0900 but the first full set of blood tests allowing quantitative acid-base analysis were not done until 2315. By this time he had already received significant resuscitation with normal saline: his chloride had been 105 mmol/L in the morning but was now 119 mmol/L (Figure 7). His creatine kinase level exceeded our laboratory’s maximum reading of 42 670 U/L for > 24 hours.

The Report box indicates a combination of severe respiratory alkalosis and severe metabolic acidosis due
to unmeasured anions.

In this case, the measured SID and Atot parameters were almost normal (although it is unusual to encounter a patient with ‘normal’ proteins in ICU, and we suspect the increased globulin fraction in this patient was due to his rhabdomyolysis). The base excess (-14 mmol/L), standard base excess (-15 mmol/L), anion gap (22 mmol/L) and NUI (-11 mEq/L) calculations were all in agreement that there was a severe primary metabolic acidosis with respiratory compensation. Usually, when the assumptions of normal electrolytes, normal proteins and phosphate are fulfilled, there is good agreement between traditional base excess, anion gap and the quantitative acid-base calculator.

The anion gap is the difference in concentration between the principal cations (Na\(^+\) and K\(^+\)) and the principal anions (Cl\(^-\) and HCO\(_3\)-) present in plasma. This ‘space’ is normally occupied by the weak acid anions of proteins. When there is hypoproteinaemia, the anionic charge on proteins is proportionately reduced. To adjust for this, the expected anion gap in mmol/L should equal the albumin concentration in g/L divided by 4.\(^{14}\) In the present case the measured anion gap was 22 mmol/L, the expected anion gap was 45/4 = 11 mmol/L, a difference (observed minus expected) of +11 mmol/L. Because this difference increases in the presence of unmeasured ions whereas the NUI becomes more negative, and because the normal value of both is zero, we convert from one to the other by multiplying by -1.\(^{14}\) A difference (observed minus expected) of +11 mEq/L is therefore in perfect agreement with a NUI of -11 mEq/L. Speaking about patients more generally, the observed minus expected anion gap and the NUI usually agree, with the NUI being the more rigorously correct parameter because it also adjusts to the acidity-dependent shift in the dissociation of proteins (and phosphate and uric acid), whereas the observed minus expected anion gap does not.\(^{14}\)

Forty-eight hours after admission, haemodialysis with Baxter Haemofiltration Replacement had started (Figure 8). This dialysate contains: sodium 140, potassium 1.0, calcium 1.6, magnesium 0.8, chloride 100, lactate 46 and glucose 10.8 mmol/L. The base excess was + 5 mmol/L and the standard base excess was + 3 mmol/L. It is difficult to decide how the Copenhagen rules\(^{11,16}\) for interpreting standard base excess should be applied in this mixed acid-base disorder.

The report box indicates a combination of mild respiratory alkalosis, severe measured strong ion alkalosis, severe measured weak acid alkalosis and severe additional metabolic acidosis due to the presence of 10 mEq/L of unmeasured anions (almost certainly lactate in view of the dialysate fluid being used unfortunately his lactate was not measured at this time).

Lactate is an interesting ion. As lactate it is a strong anion and causes a strong ion acidosis. When it has been metabolised by the liver the SID increases, and provided the resulting CO\(_2\) can be eliminated by the lungs, the acidity decreases.

The creatine kinase was 42 439 U/L. The anion gap was 15 mmol/L, the expected anion gap = 28/4 = 7 mmol/L. Therefore the observed minus expected anion gap was + 8 mmol/L, in good agreement with the NUI (-10 mEq/L). Both the increased measured SID and the reduced measured Atot were acting in concert to decrease the acidity. Had there been no unmeasured anions present, the acidity would have been 24 mmol/L.

An acidity of 32 mmol/L, although it was still alkalae-mic (< 36 mmol/L), betrayed the presence of unmeasured anions.

**Patient 4**

**Non-ST-elevation myocardial infarction and bradyarrhythmic collapse**

This is a 50-yr-old woman with a history of systemic lupus erythematosis and Type II diabetes. She was admitted to the Coronary Care Unit with a non-ST-elevation myocardial infarction where she suffered a near-arrest with severe bradycardia and hypotension. Her quantitative acid-base analysis is shown (Figure 9).

The report box indicates a combination of severe respiratory acidosis, moderate measured strong ion alkalosis, and severe measured weak acid alkalosis.

If we consider the arterial blood gas only, there was a discrepancy between the measured pH (7.42 = normal) on the one hand and the PCO\(_2\) (7.2 kPa) and bicarbonate concentration (33 mmol/L) on the other. Applying the Boston rule for acute respiratory acidosis we would have expected the bicarbonate to be about 26 mmol/L. The calculated bicarbonate was 33, so both Boston and Copenhagen interpretations were in agreement with the calculated base excess and standard base excess (both +8 mEq/L), consistent with a metabolic alkalosis.

The anion gap was 7 mmol/L. The expected anion gap = 30/4 = 7, so the observed minus expected anion gap (7 - 7 = 0 mmol/L) and the NUI (0) agree that there were no unmeasured anions present.

Applying quantitative acid-base analysis, we see there was a respiratory acidosis, biasing the acidity up by 9 mmol/L, opposed by a moderate measured strong ion alkalosis (SID 42 mEq/L), biasing the acidity down by 9 mmol/L, combined with a severe hypoproteinaemic nonvolatile weak acid alkalosis (Atot 12 mmol/L), biasing acidity down by 4 mmol/L. Taking all three independent factors into consideration at once, the expected acidity would have been 37 mmol/L. The measured acidity was 38 mmol/L and the net unmeasur-
Figure 7. Acute renal failure, rhabdomyolysis, 14 hours after admission.

Figure 8. Acute renal failure, rhabdomyolysis after resuscitation, on haemodialysis and mechanical ventilation.
ed ions was zero. Our interpretation of this case by all three methods (Boston, Copenhagen and Quantitative) is that she had a chronic respiratory acidosis with renal compensation, and that the bradyarrhythmia did not result in acute circulatory shock with lactic acidosis at the time the blood gas/electrolytes specimens were taken.

**Patient 5**

**Acute exacerbation of chronic obstructive respiratory disease**

This is a 65-yr-old woman with acute exacerbation of severe chronic obstructive respiratory disease. She was admitted to the ICU and was receiving physiotherapy and periods of CPAP. Quantitative acid-base analysis of arterial blood drawn soon after admission is shown (Figure 10).

The interesting features were a raised PCO2, which biased her acidity up by 25 mmol/L which was opposed by a raised SID which biased her acidity down by 25 mmol/L. Her protein and phosphate concentrations were normal. This is interpreted as chronic respiratory acidosis with renal compensation (the kidneys regulate the SID, mainly by adjusting the chloride concentration).

However we can go further. Her NUI was -5 mEq/L, which is a borderline mild unmeasured component of metabolic acidosis (possibly lactic acid, which had not been measured, but also other acids that accumulate as a result of her renal impairment: urea 17.2, creatinine 0.13 mmol/L). Applying the Boston rule for chronic respiratory acidosis (Table 2), we would expect her bicarbonate concentration to be increased by 16 mmol/L to 40 mmol/L. Her bicarbonate concentration was calculated to be 36 mmol/L, which is in keeping with an acute-metabolic on chronic-respiratory acidosis with 4 mmol/L of unmeasured metabolic acids neutralising 4 mmol/L of bicarbonate: very good agreement with the NUI of -5 mEq/L.

Finally the anion gap was 13 mmol/L, the expected anion gap was 36/4 = 9 mmol/L, so the observed minus expected anion gap was +4 mmol/L. This is in good agreement with the NUI (-5 mEq/L). The base excess was +8 mmol/L and the standard base excess was +10 mmol/L. Applying the rule11,16 for chronic respiratory acidosis the expected standard base excess was +16 mmol/L the calculated standard base excess was 10, so approximately 6 mmol/L of buffer base has reacted with 6 mmol/L of unmeasured acids, consistent with the NUI of -5 but only after a lot of rule-of-thumb application.

**Other reports of using quantitative acid-base methods**

Several other teams have reported the usefulness of
Critical Care and Resuscitation 2006; 8: 19-30

P. LLOYD & R. FREEBAIRN

Figure 10. Acute exacerbation of chronic obstructive respiratory disease

The quantitative approach to acid base.\textsuperscript{18-20} Most have used the Figge-Mydosh-Fencl method\textsuperscript{21} to convert protein and phosphate data into a weak acid concentration in mmol/L. The quantitative acid-base calculator discussed here takes advantage of the subsequent work of Watson\textsuperscript{22} and Constable\textsuperscript{3,4} which is more precise than the old methodology.\textsuperscript{14} However the conclusions are the same:

- quantitative methods are useful and add insight into the processes underlying the patient’s acid-base status.\textsuperscript{10,17}
- unmeasured anions and hyperphosphataemia are the main causes of acidosis in acute renal failure.
- unmeasured anions are also associated with sepsis, hepatic failure.
- hypoproteinaemia is almost universal in critically ill patients.\textsuperscript{17}
- hypoproteinaemia causes a metabolic alkalosis that attenuates the acidifying effects of chloride, lactate and unmeasured anions.\textsuperscript{17}
- anion gap and base excess calculations work better when adjusted for hypoproteinaemia.\textsuperscript{14}

One other difference between the quantitative acid-base calculator discussed here and older methods is due to Constable’s work on human proteins.\textsuperscript{4} The normal SID is now 35 mEq/L but older reports put it at about 40 mEq/L. The reason is that both phosphate and proteins contain a component of permanent negative charge (about 1 mEq/L for phosphate and 4 mEq/L for proteins) in addition to their variable charge. When this permanent anion charge component is included in the SID calculation,\textsuperscript{8,14} the normal SID is reduced to 35.

CONCLUSION

In an ideal world the PCO\textsubscript{2} should represent the respiratory component of the patient’s acid base status and another number should represent the metabolic component. Unfortunately neither the bicarbonate concentration nor the base excess nor the standard base excess fulfill that role and an elaborate set of rules is necessary to interpret blood gases in the traditional way, irrespective of which side of the Atlantic you follow.

The quantitative acid-base calculator does achieve the ideal goal. We get one number each for:

- the respiratory component of the patient’s acid-base status (PCO\textsubscript{2})
- the measured strong ion metabolic component (SID) = net excess of strong base over strong acid
- the measured nonvolatile weak acid metabolic component (A\textsubscript{tot})
- the unmeasured metabolic component (NUI).
This information completely summarises the acid-base status of the patient’s plasma and no elaborate rules are necessary for interpretation. Acid-base physiology does not have to be difficult. With computerised laboratory information systems, it is now possible to bring together all the individual factors that influence acidity into one quantitative synthesis. This, together with the history, examination and ongoing care of patients allows us to have a much clearer, more accurate and consistent picture of the acid-base aspects of their illness.

A standalone version of the quantitative acid-base calculator is available free of charge at: http://homepage.mac.com/peterlloyd1/FileSharing8.html or, peterlloydnz@gmail.com or from: peterlloyd@orcon.net.nz.

However, the calculator really comes into its own when it is built into the laboratory information system, which spares the user of the tedium of manually entering data.6

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