Chasing the base deficit: hyperchloraemic acidosis following 0.9% saline fluid resuscitation

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Abstract

Base deficit is a parameter often used to guide further treatment in acidotic children and is taken as a measure of how "sick" they are. Five children with septic shock are presented who had persisting base deficit after large volume resuscitation with 0.9% saline. Stewart's strong ion theory of acid–base balance is able to quantify the causes of metabolic acidosis and is used to show that our patients had a hyperchloraemic metabolic acidosis. We show how the chloride content of the saline loads given to our patients caused this hyperchloraemia. It is concluded that 0.9% saline and other chloride rich fluids may not be ideal resuscitation fluids; if used, clinicians must be aware of their potential to cause a persistent base deficit.
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Keywords: base deficit; 0.9% saline; resuscitation; hyperchloraemic metabolic acidosis

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Base deficit (BD) is traditionally used as a marker for metabolic acidosis and as such has gained a wide variety of clinical uses including prognostication,[1 2] assessment of significant blunt trauma, shock, and regional hypoperfusion.[3–5]

It is therefore reasonable to assume that appropriate fluid resuscitation aimed at improving metabolic "well being", by restoring tissue oxygenation and perfusion, should decrease the BD. As the magnitude of the BD may be correlated with mortality, an important yet overlooked issue concerning the crystalloid–colloid controversy is that the type of fluid used for resuscitation may influence acid–base status directly. Chloride rich solutions, such as 0.9% saline, used in large volumes can potentiate metabolic acidosis regardless of the underlying disease process.[6–10] The mechanism for this chloride driven metabolic acidosis is easily explained by the strong ion theory of acid–base proposed by Stewart.[11]

In this report we briefly outline Stewart's theory and present clinical examples from five patients admitted to our paediatric intensive care unit, all with an appreciable base deficit due, in part, to large volume resuscitation (more than 40 ml/kg) with 0.9% saline.

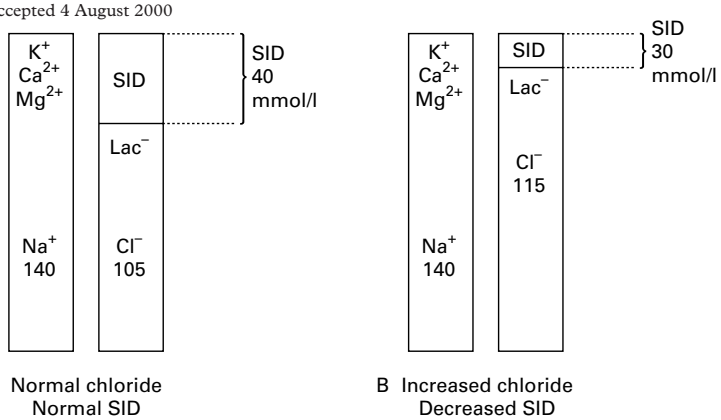

Figure 1 Simplified diagram showing SID in a patient with normal plasma Na^+ and Cl^- concentations (A) and in a patient with a hyperchloraemic metabolic acidosis (B).

The strong ion approach to acid–base balance

In contrast to the conventional Henderson–Hasselbalch approach, Stewart's theory states that three independent variables determine pH in plasma by changing the degree of water dissociation into hydrogen ions.[11] These three variables are the strong ion difference (SID), the pCO_2, and the charge from weak acids (A_{TOT}). For example, a decrease in the SID, an increase in the pCO_2 or A_{TOT} all have an acidifying effect on plasma.

The effect that plasma chloride has on pH can be assessed by analysing the SID, which is calculated as the charge difference between the sum of measured strong cations (Na^+, K^+, Ca^{2+}, and Mg^{2+}) and measured strong anions (Cl^-, lactate). A strong ion is defined as one that is almost completely dissociated at physiological pH. As both Na^+ and Cl^- are the major strong ions in plasma their ratio relative to one another largely determines the SID.

As shown in fig 1, an increase in the plasma Cl^- relative to Na^+ decreases the plasma SID (normal values 38–42 mmol/l), thereby increasing the dissociation of water into hydrogen ions. In other words, the smaller the SID, the lower the pH.

Using the above principles, normal saline 0.9% has equimolar concentrations of Na^+ and Cl^- (153 mmol/l) and therefore has an SID of 0. The administration of large quantities of normal saline will progressively lower the plasma SID, producing a hyperchloraemic metabolic acidosis. A solution of Ringer's lactate, which has an SID of 28 mmol/l, would decrease the pH to a lesser extent.

As the strong ion approach is based on the laws of mass conservation and electroneutrality, any discrepancy in the calculated SID from that directly measured allows for the detection of unmeasured anions in the form of a strong ion gap (SIG).[6 7 12 13] This quantitatively represents the concentration of unmeasured strong anions as a result of tissue metabolic acid production. The strong ion approach has been validated experimentally and clinically in both healthy and critically ill patients.[6 14 15]

Table 1 Patient demographic data, outcome, and haematological indices on admission in five patients with septic shock

	Patient 1	*Patient 2*	*Patient 3*	*Patient 4*	*Patient 5*
Organism	*Neisseria meningitidis* group B	*Neisseria meningitidis* group C	Streptococcus group B	*Neisseria meningitidis* group B	*Neisseria meningitidis* group B
Age	7 y	4 y	2 mth	4 mth	14 y
Wt (kg)	22	16.4	4.4	5	63
Inotropes (μg/kg/min)	Dopamine 5 Noradrenaline 0.13	Dopamine 5	Dopamine 7.5	Adrenaline 0.1 Noradrenaline 0.1	Dopamine 10 Adrenaline 0.2 Noradrenaline 1.0
PIM probability of death (%)	21.8	9.2	19.9	60.9	6.6
GMSPS score	11	5	Not applicable	12	9
Outcome	Alive	Alive	Dead	Dead	Alive
Hb (g/l)	111	101	92	92	131
WBC ($\times 10^9$/l)	35.3	15.6	1.3	9.1	3.9
Platelets ($\times 10^9$/l)	162	172	151	105	33

PIM, Paediatric Index of Mortality; GMSPS, Glasgow Meningococcal Septicaemia Prognostic Score.
GMPSP >8 gives mortality risk of ≥73.7% of death.[2]

Clinical examples

To illustrate, we present five septic patients who were admitted to our unit, having been retrieved from their local hospitals following initial resuscitation. All presented with the clinical picture of septic shock[16] and had been resuscitated with large volumes of normal saline. Blood samples were collected on admission from an indwelling arterial catheter and analysed for acid–base parameters (including lactate), electrolytes, and liver function tests; from these it was possible to calculate SID and SIG. Blood was also sent for microbiological culture and analysis for meningococcal PCR. Table 1 presents demographic data, including the Paediatric Index of Mortality and Glasgow Meningococcal Septicaemia Prognosis Score (GMSPS). Table 2 presents acid–base parameters taken on admission.

CALCULATING PLASMA CHLORIDE CHANGES FOLLOWING ADMINISTRATION OF NORMAL SALINE

In order to determine whether the chloride gain from normal saline administration was sufficient to explain the post-resuscitation hyperchloraemia observed in the five patients (table 3), we performed the following calculations, assuming that plasma Cl^- prior to normal saline treatment was normal and that chloride distributes throughout total body water:

(1) Total body chloride = total body water × plasma Cl^- concentration

(2) Chloride load from normal saline = volume normal saline given (litres) × 153 mmol/l (concentration of Cl^- in 0.9% saline)

(3) Calculated Cl^- concentration (Cl_{calc}) following normal saline load:

$$Cl_{calc}(mmol/l) = \frac{\text{initial total body } Cl^- + Cl^- \text{ load from normal saline}}{\text{total body water} + \text{volume normal saline given}}$$

From table 3, the Cl_{calc} closely approximated the measured plasma Cl^- following fluid resuscitation in all but one patient. This would imply that the relative hyperchloraemia could be largely explained by the chloride gain from normal saline administration. The measured Cl^- in patient 4, who received over twice as much volume per kg as the other patients, exceeded the Cl_{calc} by 7 mmol/l, indicating that either the plasma Cl^- was high prior to fluid resuscitation, or perhaps other mechanisms regarding chloride distribution are present following extremely large Cl^- loads.

Table 2 Patient admission acid–base, blood lactate measurements, strong ion difference (SID), and strong ion gap (SIG) calculations

	Patient 1	*Patient 2*	*Patient 3*	*Patient 4*	*Patient 5*
pH	7.30	7.32	7.33	7.27	7.33
pCO_2 (kPa)	4.22	4.2	3.8	3.43	4.26
Base excess (mmol/l)	−8.5	−9	−8.3	−12.6	−7.2
Lactate (mmol/l)*	1.2	1.37	1.96	2.39	1.59
SID (mmol/l)†	35	29	29	28	34
SIG (mmol/l)‡	2	−1	0	0	−1
Urine ketones	Negative	Negative	Negative	Negative	Negative

*Normal lactate is defined as <2 mmol/l.
†The normal range for SID is 38–42 mmol/l.[10]
‡The normal range for SIG is −3 to +3 mmol/l.[10]

Table 3 Patient blood chemistry measurements and calculated variables (Cl^- load and Cl_{calc})

	Patient 1	*Patient 2*	*Patient 3*	*Patient 4*	*Patient 5*
Plasma Na (mmol/l)	135	138	132	149	141
Plasma Cl (mmol/l)	110	111	108	124	113
Normal saline given (ml/kg)	80	90	80	180	85
Volume normal saline given (l)	1.76	1.53	0.35	0.9	5.3
Cl^- load (mmol)	269	234	54	138	811
Cl_{calc} (mmol/l)	112	112	112	117	112

Discussion

Following the initial fluid resuscitation of the critically ill patient, clinicians are often faced with a grumbling, unexplained BD despite correction of hypoxia or hypovolaemia. In this situation it is tempting to chase the BD with further fluid boluses in order to improve metabolic "well being". The aetiology of the acidaemia cannot be further explored using the traditional Henderson–Hasselbalch approach.

Using Stewart's approach on our patient group, we could show that the BD was a result of hyperchloraemia alone (decreased SID in the absence of significant lactate or unmeasured anion (SIG) concentrations). This relative hyperchloraemia could be accounted for by the large chloride load secondary to the volume resuscitation with normal saline.

Although restoration of intravascular volume remains a crucial and necessary goal of fluid resuscitation, failure to recognise the contribution of hyperchloraemia could lead to the BD becoming unreliable as a marker for effective resuscitation when large volumes of normal saline are used.

This then raises an interesting angle to the debate concerning the ideal resuscitation fluid. Neither normal saline nor colloid preparations

such as 4.5% human albumin solution, which continue to be used,[17] are physiological in the sense that both have an acidifying effect on the plasma. According to the strong ion theory, albumin, being a weak acid, increases the A_{TOT}, therefore lowering pH.[14] In addition, the electrolyte solution accompanying the 4.5% albumin preparation has similar Na^+ and Cl^- concentrations (100–160 mmol/l), which will further acidify plasma by reducing SID. Solutions with multicarbon anions (Ringer's lactate, Hartmann's, and Plasmalyte), which contain Cl^- and Na^+ in concentrations similar to plasma, are more physiological and may be less likely to acidify plasma.

Although a persisting base deficit has been associated with increased mortality,[12 18] to what degree a chloride driven acidosis influences mortality remains an open question. With this in mind, all one can conclude at present is that the use of large volumes of "non-physiological" chloride rich solutions such as normal saline or albumin, may potentiate metabolic acidosis, making BD interpretation misleading. Clinicians should be aware of the concept of a chloride driven acidosis and when faced with a persisting base deficit, once hypotension or hypoxia has been corrected, think twice before prescribing yet another fluid bolus of normal saline or 4.5% albumin solution to "chase" the base deficit.

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