Acid-Base Assessment

When and How To Apply the Henderson-Hasselbalch Equation and Strong Ion Difference Theory

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KEYWORDS

• Acidosis • Alkalosis • Total CO_2 • Anion gap • Strong ion gap

KEY POINTS

- The Henderson-Hasselbalch equation is probably the most famous equation in biology but is more descriptive than mechanistic.
- The traditional approach to acid-base assessment using the Henderson-Hasselbalch equation provides a clinically useful and accurate method when plasma protein concentrations are within the reference range.
- The Henderson-Hasselbalch equation cannot explain why abnormal plasma protein concentrations change plasma pH, why ingestion of $CaCl_2$ is acidifying, and why the rapid intravenous administration of large volume 0.9% NaCl solution is acidifying.
- The Henderson-Hasselbalch equation is a simplified version of strong ion difference (SID) theory that assumes plasma protein concentration is fixed within the reference range.
- The simplified strong ion approach is a mechanistic acid-base model that can provide new insight into complicated acid-base disturbances.
- The simplified strong ion approach should be used to evaluate acid-base balance whenever plasma protein concentrations are abnormal.

A revolution is under way in the clinical assessment of acid-base status. All veterinarians are familiar with the Henderson-Hasselbalch equation, which was formulated in 1916.[1,2] Clinically important applications of the equation include development of the base excess (BE) concept by Astrup and colleagues in 1960[3,4] and introduction of the anion gap (AG) concept in the 1970s and 1980s.[5,6] Application of the Henderson-Hasselbalch equation has greatly facilitated the diagnosis and treatment of acid-base and electrolyte abnormalities in humans and domestic animals.

The author has nothing to disclose.

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Vet Clin Food Anim ■ (2014) ■–■

http://dx.doi.org/10.1016/j.cvfa.2014.03.001 vetfood.theclinics.com

Two quantitative mechanistic physicochemical approaches have been developed to describe acid-base balance in animals[7]: Stewart's strong ion model[8–10] and Constable's simplified strong ion model.[11] The 2 strong ion approaches use a systems approach that makes a clear conceptual distinction between dependent and independent variables. In this context, independent variables influence a system from the outside and cannot be affected by changes within the system or by changes in other independent variables. In contrast, dependent variables are influenced directly and predictably by changes in the independent variables.

The purpose of this brief review is to summarize the key concepts in the Henderson-Hasselbalch equation and SID approach, identify existing anomalies with the Henderson-Hasselbalch equation, demonstrate how the Henderson-Hasselbalch equation is a simplification of SID theory, and provide clinically relevant guidelines for the evaluation of acid-base balance in neonatal calves and adult cattle. Additional reviews can be consulted if more detailed information is required regarding acid-base assessment using the Henderson-Hasselbalch equation or SID approach in cattle.[12–16]

THE HENDERSON-HASSELBALCH EQUATION

The traditional approach for assessing acid-base balance in animals uses the Henderson-Hasselbalch equations and focuses on how plasma pH is determined by the interaction between carbon dioxide tension (P_{CO_2}), the bicarbonate concentration ($cHCO_3^-$), the negative logarithm of the apparent dissociation constant (pK_1') for carbonic acid (H_2CO_3), and the solubility coefficient for CO_2 in plasma (S). The dissociation equilibrium of carbonic acid can be represented by[1,2]

$$P_{CO_2} \leftrightarrow CO_2(aq) + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^- \quad (1)$$

where $CO_2(aq)$ is dissolved CO_2.

The equilibrium reaction of carbonic acid is most commonly expressed as the Henderson-Hasselbalch equation:

$$pH = pK_1' + \log_{10}\{cHCO_3^-/(S \cdot P_{CO_2})\} \quad (2)$$

with the recommended value for pK_1' in human blood at 37°C and an ionic strength of 0.16 mol/L (mammalian extracellular fluid) 6.105 and S 0.0307 [mmol/L]/mm Hg. The evaluation of acid-base balance using the Henderson-Hasselbalch equation uses pH as an overall measure of acid-base status, P_{CO_2} as an independent measure of the respiratory component of acid-base balance, and plasma $cHCO_3^-$ or BE as a measure of the metabolic (nonrespiratory) component of acid-base balance (**Fig. 1**).[13]

The actual $cHCO_3^-$ (in units of mmol/L) is calculated using the Henderson-Hasselbalch equation, measured values for pH and P_{CO_2}, and documented values for pK_1' and S for blood, whereby[17–19]

$$cHCO_3^- = S \times P_{CO_2} \times 10^{(pH - pK1')} = 0.0307 \times P_{CO_2} \times 10^{(pH - 6.105)} \quad (3)$$

This equation assumes a fixed and constant value for pK_1'; this assumption has been questioned when Equation (3) was applied to blood from critically ill patients with varying sodium and plasma protein concentrations.[20,21]

BE is calculated from the results of routine blood gas and pH analysis using the van Slyke equation with hemoglobin concentration ([Hb]) and $cHCO_3^-$ in mmol/L[22]:

$$BE = (1 - 0.023 \times [Hb]) \times \{cHCO_3^- - 24.4 + (7.7 + 2.3 \times [Hb]) \times (pH - 7.40)\} \quad (4)$$