UNIVERSIDAD SIMÓN BOLÍVAR | INSTITUTO DE POSGRADOS

APLICACIÓN MEDICA MEDICALAPIS

Castro ahumada Ronald
Garcerant campo Isaias
Perales Caballero Karen

Trabajo de Investigación o Tesis Doctoral como requisito para optar el título de:
Especialista en Medicina Critica y Cuidado Intensivo

Tutor de Contenido
Abul Ariza Algarín
Especialista en Medicina Critica y Cuidado Intensivo

Tutor Metodológico
Henry J. González Torres
Bio, Spcs App Stat, MSc Bio, DrSc (S) BioMed

Universidad Simón Bolívar
Barranquilla / Atlántico
2020

MEDICALAPIS

Antecedentes: Las alteraciones del equilibrio ácido-base son objeto de estudio de todas las especialidades médicas. Si bien la mayoría de los casos derivan de una patología preexistente, también pueden manifestarse en un contexto primario. La identificación adecuada del trastorno ácido-base permite caracterizar el proceso patológico causante. La correcta interpretación de la gasometría como técnica de monitoreo del estado ventilatorio, oxigenación y el equilibrio ácido-base de un paciente, requiere de la integración de diversos enfoques fisicoquímicos con el fin de precisar un diagnóstico, cuantificar una respuesta terapéutica, monitorizar la severidad o la progresión de un proceso patológico.

El Objetivo de esta aplicación medica es orientar la correlación clínica del paciente crítico con los parámetros de la gasometría sanguínea para caracterizar el trastorno ácido-base a través de la proposición de unas variables aplicadas a una aplicación que al introducir los datos desarrolla un algoritmo diagnostico en 1 minuto.

Materiales y Métodos: Se realizó una revisión de la literatura en las bases de datos PubMed, Scopus y Science Direct. Los artículos fueron seleccionados de acuerdo con el título y el resumen y ordenados por temas relevantes por fisiopatología, divergencias, enfoque clínico, diagnóstico y manejo, el cual se elaboró un artículo teórico y se presento a 2 revistas científicas a espera de aprobación, posterior se contacto con un diseñador de APP y se desarrolló una aplicación medica con el algoritmo del texto teórico, se incorporó a un hosting y se radico la aplicación en la página de dirección nacional de derechos de autor con Numero de registro **13-78-474 fecha del Registro 06-abr-2020.**

Resultados: Se realizo una guía de la correlación clínica del paciente crítico con los parámetros de gasometría de la sangre para caracterizar el trastorno ácido-base a través de la propuesta de un algoritmo de diagnóstico y una aplicación medica practica el cual fue validada y puesta a prueba de 24 personas al azar, el cual se les pidió una evaluación atraves de Google formulario con satisfacción del 100%.

Conclusiones: el uso de esta aplicación facilita la comprensión de los mecanismos fisiopatológicos del equilibrio acido básico en los pacientes permitiendonos identificar el objetivo terapéutico preciso y de esta manera corregir el trastorno subyacente en los diferentes contextos clínicos del paciente.

Palabras clave: Aplicación, equilibrio acido base, gases arteriales, diagnostico, algoritmo.

ABSTRACT

Background: The alterations of the acid-base balance are the object of study of all medical specialties. Although most cases derive from a pre-existing pathology, they can also manifest in a primary context. The proper identification of the acid-base disorder allows characterizing the pathological process that causes it. The correct interpretation of gasometry as a technique for monitoring the patient's ventilatory status, oxygenation and acid-base balance requires the integration of various physicochemical approaches in order to specify a diagnosis, quantify a therapeutic response, monitor the severity or the progression of a pathological process.

The objective of this medical application is to guide the clinical correlation of the critically ill patient with the parameters of blood gasometry to characterize the acid-base disorder through the proposition of variables applied to an application that, when entering the data, develops a diagnostic algorithm in 1 minute.

Materials and Methods: A review of the literature was performed in the PubMed, Scopus and Science Direct databases. The articles were selected according to the title and abstract and ordered by relevant topics by pathophysiology, divergences, clinical approach, diagnosis and management, which was developed a theoretical article and submitted to 2 scientific journals pending approval, later I contacted an APP designer and a medical application was developed with the algorithm of the theoretical text and it was incorporated into a hosting and the application was based on the national copyright address page with **Registration number 13-78-474 Registration date Apr 6, 2020.**

Results: A guide of the clinical correlation of the critically ill patient with the blood gas parameters was carried out to characterize the acid-base disorder through the proposal of a diagnostic algorithm and a practical medical application which was valid and approved. of 24 random people, who were asked for an evaluation through the Google form with 100% satisfaction.

Conclusions: the incorporation of this practical theoretical material by applying the three theories in a diagnostic algorithm that takes time to understand through this application facilitates a better understanding of the pathophysiological mechanisms and allows us to identify a more precise therapeutic objective to correct the underlying disorder in the different clinical contexts of the patient.

Key words: Application, Acid-base imbalance; blood gases; diagnosis; algorithm

ANEXO I
REGISTRO DE LA APLICACIÓN


UNIDAD ADMINISTRATIVA ESPECIAL
DIRECCIÓN NACIONAL DE DERECHO DE AUTOR
MINISTERIO DEL INTERIOR Y DE JUSTICIA

TRAMITES
Obra Literaria Inédita
Obra Literaria Editada
Obra Artística
Obra Musical
Obra AudioVisual
Software
Actos y Contratos
Fonogramas
SESIÓN
Inicio
Actualizar Datos
Salida Segura
VIDEOTUTORIALES
Registre sus obras audiovisuales y sus fotografías a través de su

MINISTERIO DEL INTERIOR
DIRECCION NACIONAL DE DERECHO DE AUTOR
UNIDAD ADMINISTRATIVA ESPECIAL
OFICINA DE REGISTRO

Libro - Tomo - Partida
13-78-474
Fecha Registro
06-abr-2020

CERTIFICADO DE REGISTRO DE SOPORTE LOGICO - SOFTWARE

Página 1 de 2

1. DATOS DE LAS PERSONAS

AUTOR
Nombres y Apellidos: ISAIAS GARCERANT CAMPO — No de identificación CC: 1143226470
Nacional de: COLOMBIA
Dirección: CALLE 100 12 D 19 — Ciudad: BOGOTA D.C.

AUTOR
Nombres y Apellidos: KAREN PERALES CABALLERO — No de identificación CC: 55309006
Nacional de: COLOMBIA
Dirección: CARRERA 6 SUR NO 46B 95 — Ciudad: BARRANQUILLA

AUTOR
Nombres y Apellidos: RONALD CASTRO AHUMADA — No de identificación CC: 8647890
Nacional de: --
Dirección: CALLE 79 B N 42 - 322 — Ciudad: BARRANQUILLA

ANEXO II
IMÁGENES DE LA APLICACIÓN FUNCIONADO

ARTICULO EN FASE 2 A ESPERA DE PUBLICACION

Acid-base imbalance: a review with proposed unified diagnostic algorithm

Running head: Acid-base imbalance

Abul Ariza-Algarín[1 2], Henry J. G onzález-Torres[1 3], Isaías Garcenas-Campo[1], Ronald Castro-Ahumada[1], Karen Perales-Caballero[1], Alex Domínguez-Vargas[4], Carlos G. Musso[5].

[1] Universidad Simón Bolívar, Facultad de Ciencias de la Salud, Barranquilla, Atlántico, Colombia

[2] Clínica General del Norte, Unidad de Cuidados Intensivo, Barranquilla, Atlántico, Colombia

[3] Universidad del Valle, Doctorado en Ciencias Biomédicas, Cali, Valle del Cauca, Colombia

[4] División Ciencias de la Salud, Universidad del Norte, Barranquilla, Atlántico, Colombia.

[5] Instituto Universitario Hospital Italiano, Departamento de Fisiología Humana, Buenos Aires, Buenos Aires, Argentina

Corresponding Author:

Email address: carlos.musso@hospitalitaliano.org.ar

Abstract

Background: Alterations in the acid-base balance are studied in all medical specialties. Although most cases derive from a preexisting pathology, they can also manifest themselves in a primary context. The proper identification of the acid-base disorder allows the pathological process to be characterized. The correct interpretation of the blood gasometry as a technique for monitoring the ventilatory status, oxygenation and acid-base balance of a patient requires the integration of various physicochemical approaches in order to specify a diagnosis, quantify a therapeutic response, and monitor the severity or the progression of a pathological process.

Material & Method: A literature review was conducted in the PubMed, Scopus and Science Direct databases. The articles were selected according to the title and the abstract and sorted by topics relevant by pathophysiology, divergences, clinical approach, diagnosis, and management. **Results:** A guide the clinical correlation of the critical patient with the blood gasometry parameters to characterize the acid-base disorder through the proposition of a diagnostic algorithm. **Conclusion:** The incorporation of the three theories in a diagnostic algorithm facilitates a greater understanding of the pathophysiological mechanisms and allows us to identify a more precise therapeutic objective to correct the underlying disorder in the different clinical contexts of the patient.

Keywords: Acid-base imbalance; blood gases; diagnosis; algorithm

Introduction

Acid-base disorders are frequent, especially in the critical patient. Although most of the cases derive from a preexisting pathology, they can also manifest themselves in a primary context[1,2]. The proper identification of the acid-base disorder allows to characterize the causative pathological process[1-4].

Classically, different authors: Siggard, Andersen, Henderson, Emmett, Hasselbalch and Stewart have contributed to the understanding of the acid-base balance[3–6]. In clinical practice, three models are currently used:

(A) The Henderson-Hasselbalch equation to classify the acid-base disorders. [6]

(B) The base excess concept by Siggaard-Andersen[7] as a parameter to assess the magnitude of the metabolic abnormality [6].

(C) The strong ion difference proposed by Stewart,[8,9] which offers more information about extreme acid-base conditions observed in the critical patient[4].

The correct interpretation of the blood gasometry requires the integration of the above mentioned three models in order to specify a diagnosis, quantify a therapeutic response and monitor the severity or the progression of a pathological process[3–5].

The aim of this article is to originally propose a diagnostic algorithm for guiding physicians to perform an adequate correlation between the clinical condition of critical patients and their acid-base parameters, in order to achieve an accurate characterization of the patients´ acid-base disorders.

Material & Method

A review of the literature was performed in the PubMed, Scopus and Science Direct databases. The following MESH terms were used for the advanced search, such as “acid-base equilibrium” or “acid-base imbalance” or “acidosis “or “ alkalosis”, which were included in the articles title,

abstract or key words. The search was restricted to articles published after 2000, although some previous articles were reviewed in order to describe traditional approaches.

The articles were selected according to the title and the abstract and sorted by topics considered relevant by the authors for performing a detailed review, including pathophysiology, divergences, clinical approach (according to different authors), diagnosis, and management.

Blood gasometry

The blood gasometric study is indicated when there is the need to evaluate the ventilatory status, the oxygenation and the acid-base balance in order to establish a diagnosis, measure the therapeutic response to oxygen-therapy and monitor the severity of a pathological process[10].

The blood gas analyzers use three types of electrodes for the direct measurement of the hydrogen-ion potential (pH), the partial pressure of oxygen (pO_2) and the partial pressure of carbon dioxide (pCO_2), from these measurements it is possible to mathematically calculate other parameters such as the bicarbonate ion (HCO_3^-), the base excess (BE), and the oxygen saturation (SaO_2)[6,11,12] **(Table 1).**

Importance of pH regulation

The hydrogen-ion (H^+) is one of the most important parameters in the acid-base balance and its concentration depends on the interaction between the pCO_2, the plasma concentration of HCO_3^- and the dissociation constant of H_2CO_3[12–14]. The pH at physiological levels is essential for biological processes, including the supply of oxygen to the tissues, the correct structure of the proteins and countless biochemical reactions that depend on a neutral pH to be in equilibrium[12,15,16]. In addition, cell functions such as glycolysis, gluconeogenesis, mitosis, DNA synthesis, among others, are altered by acute changes in pH. Therefore, a series of compensatory mechanisms is

required to respond quickly to the changes in the concentration of H^+ in all cellular compartments[12,16,17].

Compensation systems

The concentration of H^+ within the plasma and other aqueous solutions is tightly regulated. The cell metabolism produces about 70 mmol/day of H^+, but under physiological conditions, the concentration remains balanced between 36-43 nmol/L,[9,17] due to the following regulation systems:

• Buffering: It is a rapid physicochemical response. A buffer is a solution that resists the changes in pH when acids or alkalis are added. The buffers that regulate the pH in intracellular and extracellular fluids include sodium bicarbonate ($NaHCO_3$), carbonic acid (H_2CO_3), phosphates, proteins (albumin, globulins), hemoglobin and oxyhemoglobin.[12,16–18] The dynamics of the system is predominantly of HCO_3^-/ H_2CO_3 as follows:

$$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^- + (Na^+) \leftrightarrow NaHCO_3$$

Le Chatelier principle establishes that when the concentration, pressure or temperature variables change, the systems in equilibrium react accordingly to reestablish a new equilibrium state, which indicates that if more H^+ are produced, the equation will shift to the left so that more reagents are formed and the system remains in equilibrium[12,17]. The conversion of CO_2 into H_2CO_3 is slowly catalyzed by the carbonic anhydrase present in the pulmonary and renal tissues. The H_2CO_3 is slowly ionized to produce H^+ and HCO_3^-, while the $NaHCO_3$ is completely ionized to produce HCO_3^- [4,5,14].

- The *respiratory system*, increases or reduces the concentration of H+ or CO2, through changes in alveolar ventilation (hypoventilation or hyperventilation, respectively)

mediated by chemoreceptors. From the quantitative point of view, it is the predominant system and depends on the complete oxidation of the anions during the Krebs cycle[3,16,19,20].

- The *renal system*, eliminates the H^+ produced in the amino acids metabolism, through the formation of urea or ammonium ion, at the same time that the secretion of H^+ in the proximal tubule increases or decreases; in addition, it reabsorbs around 80% of the HCO_3^-. There is an important relationship between the transport of HCO3- and the excretion of acid because during acidosis, the excretion of titratable acid (phosphate buffer) is modified inversely with the administered amount of $HCO3^-$. The distal acidification is constituted not only by the titratable acidity, but fundamentally by the ammoniacal acidity, which is regulable as it can be induced by aldosterone[3,12,13,18,21].

Therefore, the acid-base balance disorders will have a compensatory response: renal, mediated by HCO_3^- in respiratory disorders, and respiratory, mediated by CO_2 in metabolic disorders **(Table 2).**

In addition, acid base disorders can be characterized according to the increase or decrease of the pH/HCO_3^-/pCO_2 variables in order to identify the evolution time as acute, subacute and chronic. (i.e., if a metabolic alkalosis have increased pH, HCO_3^- and pCO_2 it indicates a subacute metabolic alkalosis)[4,6,16] **(Table 3).**

In the table 4, useful formulas are provided for acid-base interpretation that allow to calculate the compensatory response of the renal and respiratory systems. (i.e., if a metabolic acidosis produces HCO_3^- of 15 mEq/L, the expected pCO_2 is (1.5 x 15 + 8) ± 2 = 30.5 ± 2 mmHg). If the measured pCO_2 is equivalent to the expected pCO_2, the respiratory compensation is adequate and the condition is called compensated metabolic acidosis[12,18,22].

Acid-Base Interpretation Models

(A) Henderson-Hasselbalch equation

The traditional Henderson-Hasselbalch approach defines the pH in its non-logarithmic variant as $[H^+] = 24 + pCO_2/HCO_3^-$. The model is based on the application of the mass action law in equilibrium of CO_2 and the existing relationship between the plasma HCO_3^- and the concentration of strong acids,[20,23] through the following formula:

$$\mathbf{pH} = pKa + \log_{10} [HCO_3^-] / (0.03 \times pCO_2)$$

In this equation, pKa is the negative logarithm of the acid dissociation constant of the weak acid. The equation allows to infer that the CO_2 and the HCO_3^- are variables that determine the system that corrects the alterations of the H^+, which allows to classify the acid-base disorders according to the primary type of acid that is increased or decreased[16,24].

Although it is mathematically accurate, it does not consider aspects such as the presence of buffers other than HCO_3^- (plasma proteins), the intervention of weak acids such as phosphates and the directly proportional correlation that exists between HCO_3^- and pCO_2[8,22,24].

Metabolic acidosis can be induced by two main mechanisms: bicarbonate consumption secondary to buffer activity, or body bicarbonate loss. Both conditions can be distinguished by evaluating the patient´s anion gap (AG) value.

Anion gap

The AG is the difference between plasma anions and cations, based on the electroneutrality principle. The resulting value is usually positive (12 ± 2 mEq/l), and reflects anions such as proteins, phosphates and sulfates[20,23,25].

The mnemonic to remember the causes of metabolic acidosis with increased AG is ***"MUDPILES":*** **M**ethanol, **U**remia, **D**iabetic ketoacidosis (DKA), **P**araldehyde, **I**soniazid and **I**ron, **L**actic acid, **E**thylene glycol and **E**thanol induced ketoacidosis, **S**alicylates.

It is used to establish the differential diagnosis of the metabolic acidosis because it allows to distinguish the causes[5,25]. For the metabolic acidosis with normal AG is used the mnemonic ***"ACCRUED":*** **A**ldosterone inhibitors, **C**ompensation for respiratory alkalosis, **C**arbonic anhydrase inhibitors (acetazolamide), **R**enal tubular acidosis (RTA), **U**reteral diversion, **E**xtra alimentation and **D**iarrhea[4].

Regarding the limitations of the AG, they include: assumption of normal concentrations of albumin and phosphates, exclusion of unmeasured ions, therefore, in the critical patient[26] the corrected AG must be used:

$$(Na^+ + K^+) - (Cl^- + HCO_3^-) + 2.5\ (\text{Normal albumin} - \text{Measured albumin})$$

A corrected AG value above 12 indicates metabolic acidosis with increased AG, and a corrected AG value under 12 indicates metabolic acidosis with normal-decreased AG. There may be situations where concurrent metabolic disorders exist. To identify if mixed metabolic disorders are present, the delta Gap should be calculated (Δ Gap = Corrected AG – Calculated AG).

An AG delta ≥6 is a metabolic acidosis with increased AG and an AG delta <6 is a metabolic acidosis with normal AG.

When there is a suspicion that the origin of the metabolic acidosis is a toxic agent, it will be indispensable to calculate the osmolar gap (OG) by applying the following equation [4,5,25]:

$$OG = \text{measured serum osmolarity} - \text{calculated serum osmolarity}$$

In a case of increased AG metabolic acidosis secondary to intoxication, the OG value would be higher than 10. In case of a normal AG metabolic acidosis, the urinary AG should be obtained by applying the following equation [5,25]:

$$\text{Urinary AG} = (\text{urinary sodium} + \text{urinary potassium}) - \text{urinary chloride}$$

A positive urinary AG value (> -20) suggests a normal AG metabolic acidosis secondary to distal renal tubular acidosis, while a negative urinary AG value (≤ -20) suggests a normal AG metabolic acidosis secondary to proximal tubular acidosis or bicarbonate loss due to diarrhea.

(B) Base Excess

In order to understand how the pH and the concentration of HCO_3^- are altered independently of the pCO_2, Siggard-Andersen proposed the concept of base excess (BE) as the amount of acid-base or strong base required to maintain the pH in 7.4 and a temperature of 37 °C with a pCO_2 of 40 mmHg[3,15,27]. The BE normal value is -2 to +2.

The BE limitation is that it does not allow to determine the metabolic acidosis cause and assumes that patient´s serum albumin and phosphate levels are normal. Since serum albumin and phosphate levels in the critical patient are frequently decreased, thus the corrected BE equation should be used[27].

$$BE = (HCO_3^- - 24.4) + (8.3 \times \text{albumin} \times 0.15) + (0.29 \times \text{phosphate} \times 0.32) \times (pH - 7.4)$$

(C) Peter-Stewart model

The Stewart model[7] includes the analysis and the relationship of the components of human fluids (water, strong ions in water, weak acids in water and CO_2) through the following

fundamental physicochemical principles: electroneutrality principle, conservation of mass law, and equilibrium of electrochemical dissociation. In addition, it adds the HCO_3 as a dependent variable, establishing that the changes in the H^+ and therefore, in the pH, can only occur through the modification of three independent factors: (¡) pCO_2, (ii) strong ion difference (SID) and (iii) total weak acid concentration (A_{TOT})[2,7,9,22].

(i) The pCO_2 is defined as the pressure exerted by the CO_2 in the arterial blood, independently from each arterial gas.

(ii) The SID is the difference between the sum of the plasma concentrations of cations and anions; the normal value is 36 to 40 mEq/L and it has a great electrochemical value on the dissociation of water: as the SID increases, the H+ decreases and consequently the pH increases to balance the electroneutrality.

(iii) A_{TOT}: body fluid compartments have varying concentrations of non-volatile weak acids. The most important weak acids in plasma are proteins and phosphates. The same applies to interstitial fluid, although total concentrations here are very small. In red cells the predominant source is hemoglobin[28].

The A_{TOT} represents the total amount of weak acids other than CO_2 in plasma. Albumin (normal value: 3.5 to 5 g/dl) is the most important protein that acts as a weak acid. Organic phosphates (normal value: 2.5 to 4 mg/dl) represent 5% when their levels are normal. Therefore, albumin concentrations can be used to estimate plasma A_{TOT}[2,29,30].

.The non-dissociated acids are described as [HA] and the dissociated acids as [A^-]. Then the weak acid dissociation reaction is:

$$HA \leftrightarrow H^+ + A^-$$

Based on the law of conservation of matter, if HA and A^- do not participate in other reactions in the solution, the sum of [HA] and $[A^-]$ will remain constant, then:

$$[A_{TOT}] = [HA] + [A^-]$$

Although $[A^-]$ varies with pH, A_{TOT} does not, and as such it is an independent variable[28,29].

From Peter-Stewart model, it can be concluded that the pH variations depend on the degree of dissociation of the plasma water (H^+, OH^-) as a source for H^+ production and in turn, this dissociation depends on the three independent factors (pCO_2, SID, and A_{TOT})[30,31].

Clinical application: Diagnosis of the acid-base disorders in 7 steps

The approach to the acid-base disorders, requires to establish a clinical correlation between the medical record of the patient (anamnesis and physical examination) and the gasometric parameters[3,14]. In this review, we recommend the use of a systematic approach to problem solving through a diagnostic algorithm (Figure 1 and Figure 1.1), in order to guide the correct interpretation and the diagnosis of the acid-base disorders through the following analytical sequence:

Step 1. Identify the type of gas: the correct reading of the blood gasometry requires the verification of the arterial gas, through the ratio between the formula (80 – Mantissa pH) and the calculation of hydrogen ions (H^+= 24 (pCO_2)/HCO_3^-), where the mantissa refers to the decimal fraction of a logarithm that follows the characteristic or whole part (example. 7.34, the whole part is 7 and the mantissa is 0.34). If the result is <2, then we confirm arterial gas and the analytical sequence is continued.

Step 2. Degree of Oxygenation: the Pa/Fi index, which relates the arterial oxygen pressure and the fraction of inspired oxygen (pO_2/FiO_2) is assessed, the alteration in gas exchange is measured as mild (200 - 300), moderate (<200 - >100) and severe (**≤**100) respiratory distress. The **Pa/Fi** index allows the non-invasive monitoring of the oxygenation without requiring a gasometric study.

Step 3. Evaluate the pH status: determine if the blood pH indicates acidosis (<7.35), alkalosis (>7.45) or if it is within the normal range (7.35 – 7.45). The suffix “emia” is used when the pH is outside the normal range and “osis” when there is an acid-base alteration in which the pH is within the normal range.

Step 4. Characterize the primary disorder, which is the component that can explain the pH value: through the analysis of the metabolic (HCO_3^-) or respiratory (pCO_2) component, in order to determine the origin or the predominance of the acid-base disorder (Table 2).

Step 4.1. If the disorder is metabolic, the three theories (Henderson-Hasselbalch, base excess and Peter-Stewart) should be applied in order to establish the differential diagnosis, assess the magnitude of the alteration and characterize the metabolic disorder (see Figure 1.1).

Step 5. Determine the compensatory response or the mixed disorder: subsequent to the identification of the primary disorder (metabolic or respiratory), it should be verified if the other component makes the compensation of the pH or if actually adds some other

acid-base disorder. If both the measurement of the pH and the pCO_2 are abnormal it is considered a mixed acid-base disorder (Table 2 and Table 4).

Step 6. Identify the evolution of the disorder: through the increase or decrease of the pH/HCO_3^-/pCO_2 variables it is possible to determine the time of evolution of the acid-base disorder as acute, subacute and chronic (Table 3)

Step 7. Evaluate the perfusion: the ratio between the CO_2 delta (arterial CO_2 – venous CO_2) and the arteriovenous oxygen content difference, $C(a\text{-}v)O_2$ (arterial oxygen content, CaO_2, and venous oxygen content, CvO_2). The $C(a\text{-}v)O_2$ depends on the SaO_2, the SvO_2 and the hemoglobin, 1 g of hemoglobin transports 1.34 mL of O_2.[3,7,16,18,29,30,32–38].

Table 1: Normal serum parameters

Parameter	Normal Value
pH	7.35 – 7.45
pCO_2 (mmHg)	35 – 45
HCO_3^- (mmol/L)	20 – 24
pO_2 (mmHg)	80 – 100
SaO_2 (%)	95 – 100
BE	-2 to +2
Lactate (mmol/L)	< 2
Na^+ (mEq/L)	135 – 145
K^+ (mEq/L)	3.5 – 5.5
Cl^- (mEq/L)	95 – 105

pH: hydrogen-ion potential; pCO_2: partial pressure of carbon dioxide; HCO_3^-: bicarbonate ion; pO_2: partial pressure of oxygen; SaO_2: arterial oxygen saturation; BE: base excess; Na^+: sodium ion, K^+: potassium ion, Cl: chloride ion

Table 2: Primary disorders and expected compensations

Primary disorder	pH	pCO2	HCO_3^-	Compensatory change	
Respiratory acidosis	< 7.35	> 45	-	HCO_3^-	↑
Metabolic acidosis	< 7.35	-	< 20	pCO_2	↓
Respiratory alkalosis	> 7.45	< 35	-	HCO_3^-	↓
Metabolic alkalosis	> 7.45		> 24	pCO_2	↑

pH: hydrogen-ion potential; pCO_2: partial pressure of carbon dioxide; HCO_3^-: bicarbonate ion

Table 3: Evolution of acid-base disorders

Disorder	Status	pH	pCO_2	HCO_3^-
Respiratory acidosis	Acute	↓	↑	-
	Subacute	↓	↑	↑
	Chronic	-	↑	↑
Metabolic acidosis	Acute	↓	-	↓
	Subacute	↓	↓	↓
	Chronic	-	↓	↓
Respiratory alkalosis	Acute	↑	↓	-
	Subacute	↑	↓	↓
	Chronic	-	↓	↓
Metabolic alkalosis	Acute	↑	-	↑
	Subacute	↑	↑	↑
	Chronic	-	↑	↑

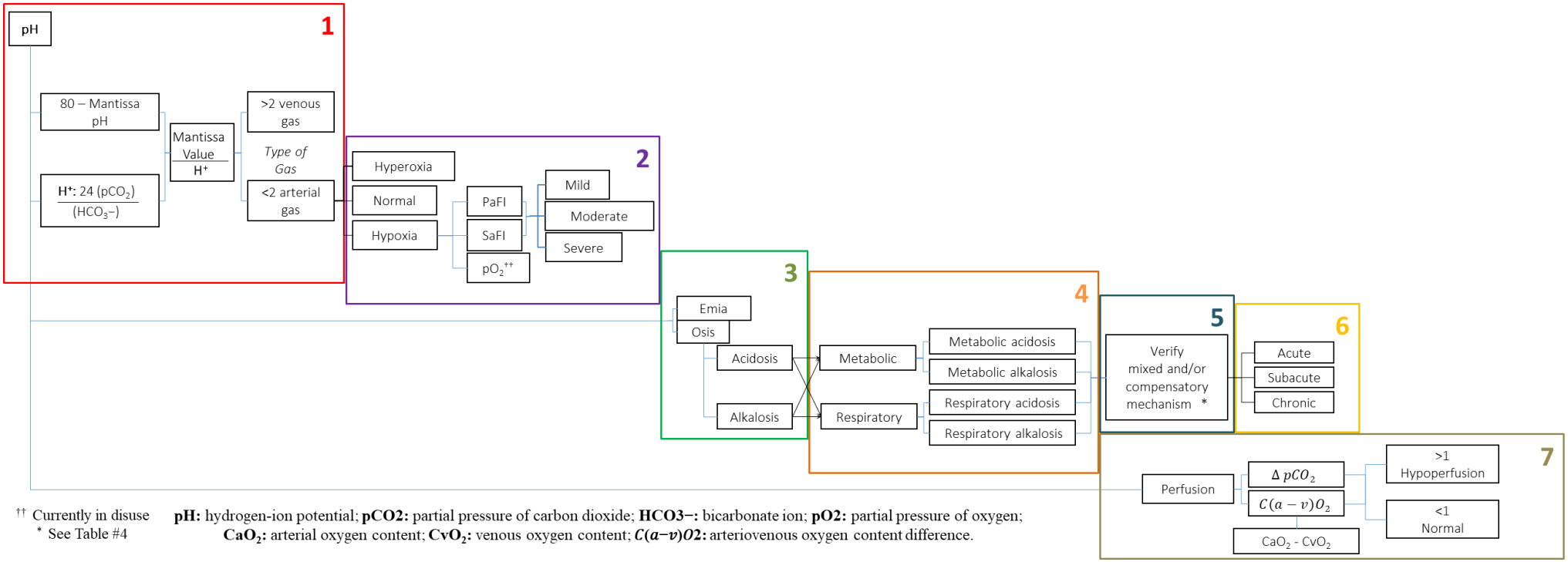
pCO_2: partial pressure of carbon dioxide; HCO_3^- : bicarbonate ion

Table 4: Primary disorders and compensatory responses

Primary Disorder	Expected result
Metabolic acidosis	Expected $pCO_2 = (1.5 \times HCO_3^- + 8) \pm 2$
Metabolic alkalosis	Expected $pCO_2 = (0.7 \times HCO_3^- + 23) \pm 2$
Acute respiratory acidosis	Expected $HCO_3^- = 24 + 0.1 \times (pCO_2 - 40)$
Chronic respiratory acidosis	Expected $HCO_3^- = 24 + 0.4 \times (pCO_2 - 40)$
Acute respiratory alkalosis	Expected $HCO_3^- = 24 - 0.2 \times (40 - pCO_2)$
Chronic respiratory alkalosis	Expected $HCO_3^- = 24 - 0.5 \times (40 - pCO_2)$

pCO_2: partial pressure of carbon dioxide; HCO_3^- : bicarbonate ion

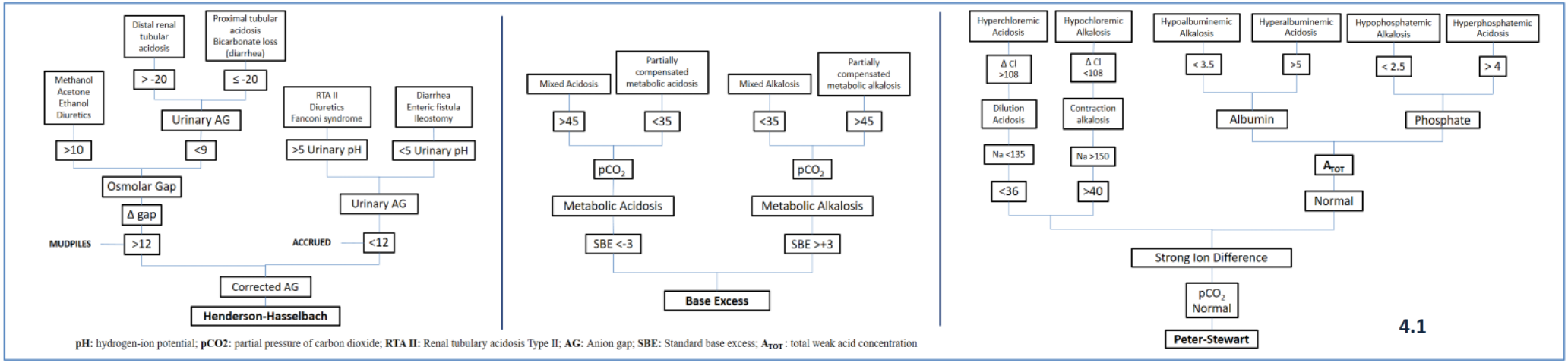
Figure 1: Diagnostic algorithm proposal for acid-base disorders



†† Currently in disuse
* See Table #4

pH: hydrogen-ion potential; **pCO2:** partial pressure of carbon dioxide; **HCO3−:** bicarbonate ion; **pO2:** partial pressure of oxygen; **CaO_2:** arterial oxygen content; **CvO_2:** venous oxygen content; **$C(a-v)O2$:** arteriovenous oxygen content difference.

Figure 1.1: The three theories to assess acid-base imbalance



pH: hydrogen-ion potential; **pCO2:** partial pressure of carbon dioxide; **RTA II:** Renal tubulary acidosis Type II; **AG:** Anion gap; **SBE:** Standard base excess; A_{TOT} : total weak acid concentration

Illustrative Case

Below, the diagnostic algorithm for the diagnosis of the acid-base disorders proposed in Figure 1 is applied to the following clinical case:

Clinical Case: A 52-year-old female is admitted to the ICU, with a history of high blood pressure, type II diabetes mellitus, heart failure with left ventricular ejection fraction of 35%, the patient underwent a surgical intervention consisting of an open cholecystectomy, and in the first postoperative day she presented signs of hemodynamic instability associated with anemia requiring a new intervention due to bleeding of the gallbladder bed. Two days later, she presented fever, tachycardia, tachypnea, disorientation, and a decrease in diastolic blood pressure with requirement of oxygen with FiO_2: 0.5. The presumptive diagnosis was a septic shock with tissue hypoperfusion, associated with subphrenic abscess. The following are the laboratory parameters:

Arterial Gases	HCO_3^-: 18 mEq/L
pH: 7.17	SvO_2= 72%
pCO_2: 25 mmHg	BE: - 16
pO_2: 84 mmHg	
HCO_3^-: 11 mEq/L	**Chemical Panel**
SaO_2: 78%	Na^+: 135 mEq/L
BE: - 14	K^+: 3.5 mEq/L
	Cl^-: 100 mEq/L
Venous Gases	P: 2.5 mg/dl
pH: 7.1	Lactate: 8 mmol/L
pCO_2: 26 mmHg	Hemoglobin: 10.4 g/dl
pO_2: 70 mmHg	Albumin: 2 gr/dl

Based on the analytical sequence, **(Step 1)** we begin with the verification of the type of gas obtained, applying the formula as follows:

$$\textbf{Type of gas} = \frac{\textbf{80 – Mantissa pH}}{\textbf{24 (pCO2)/HCO3–}};$$

Then, replacing values:

$$\text{Type of gas} = \frac{(80 - 17)}{(24)\ (25\ \text{mmHg})\ /11\ \text{mEq/L}} = 1.15$$

A value of 1.15 is obtained, which indicates **arterial gas**. Therefore, we proceed with the analysis.

Then, **(Step 2)** the oxygenation degree of the patient is identified with the Pa/Fi index as follows:

$$\textbf{Oxygenation degree} = \frac{\textbf{pO2}}{\textbf{FiO2}};$$

Then, replacing values,

$$\text{Oxygenation degree} = \frac{84\ \text{mmHg}}{0.5} = 168\ \text{mmHg}$$

This result indicates **moderate hypoxemia**, range (<200 – >100).

In relation to the acid-base disorder, **(Step 3)** in this case, the pH is below 7.35 indicating an **acidosis.**

(Step 4) The HCO_3^- is decreased indicating the primary disorder as a **metabolic acidosis** (see table 2).

(Step 5) Using the formula to assess for compensation would yield a calculated pCO_2 as follows (see table 4):

Expected pCO_2 = (1.5 x HCO_3^- + 8) ± 2;

Then,

Expected pCO_2 = (1.5 x 11 mEq/L + 8) ± 2 = 24.5 mmHg ± 2;

Therefore, since the calculated pCO_2 (24.5 mmHg) is lower than the measured (25 mmHg), the patient has a **mixed disorder: metabolic acidosis and respiratory alkalosis**.

Then, **(Step 6)** the pH, HCO_3^- and pCO_2 are decreased indicating a **subacute metabolic acidosis** (see table 3).

Since it is a metabolic disorder, it is continued **(Step 4.1)** with the application of the three theories:

(A) Henderson-Hasselbalch: the difference between serum anions and cations is calculated as follows:

$$\textbf{AG = (serum } Na^{+} \textbf{ + serum } K^{+}\textbf{) - (serum } Cl^{-} \textbf{ + serum } HCO_3^{-}\textbf{)}$$

Then, replacing values,

$$AG = (135\ mEq/L + 3.5\ mEq/L) – (100\ mEq/L + 11\ mEq/L) = 27.5$$

Next, the result must be corrected because this case is a critical patient, through the following formula:

$$\textbf{Corrected AG = Calculated AG + 2.5 (Normal albumin – Measured albumin)}$$

Then,

$$\text{Corrected AG} = 27.5 + 2.5\ (4.5\ g/dl – 2\ g/dl) = 33.75$$

This result indicates **metabolic acidosis with increased AG.** In order to verify that there is no other underlying acid-base disorder, the AG delta is calculated as follows:

$$\textbf{Δ Gap = Corrected AG – Calculated AG}$$

Replacing values,

$$\Delta \text{ Gap} = 33.75 - 27.5 = 6.25$$

Because this value is >6 the **metabolic acidosis with increased AG is confirmed**. Due to the presence of increased lactate (8 mmol/L) (See table 1) and following the mnemonic

"**MUDPILES**", it is considered a **hyperlactatemic metabolic acidosis secondary to septic shock** (see Figure 1.1).

(B) Regarding the calculation of the base excess, the corrected BE equation must be used as follows:

$$BE = (HCO_3^- - 24.4) + (8.3 \times \text{albumin} \times 0.15) + (0.29 \times \text{phosphate} \times 0.32) \times (\text{pH} - 7.4),$$

Then, replacing values:

$$BE = (11 - 24.4 \text{ mEq/L}) + (8.3 \times 2 \text{ gr/dl} \times 0.15) + (0.29 \times 2.5 \text{ mg/dl} \times 0.32) \times (7.17 - 7.4) = -10.9$$

Since the BE is -10.9, the metabolic acidosis is confirmed. In addition, the pCO_2 <35 mmHg is indicating a partially compensated metabolic acidosis (see Figure 1.1).

(C) Peter-Stewart, the decreased pCO_2 indicates a respiratory alkalosis. Then, the SID is calculated as follows:

$$\textbf{SID = serum } Na^+ \textbf{ + serum } K^+ \textbf{ - serum } Cl^-$$

Then, replacing values,

$$SID = (135\ mEq/L + 3.5\ mEq/L - 100\ mEq/L) = 38.5\ mEq/L$$

The result obtained is within the normal range (36 – 40 mEq/L), and for this reason the A_{TOT} must be assess: the decreased albumin indicates a hypoalbuminemic alkalosis and hyperlactatemic organic acidosis (See Figure 1.1).

Finally, **(Step 7)** the perfusion is assessed as follows: **First,** the $C(a\text{-}v)O_2$ is evaluated as the different between CaO_2 and CvO_2. The $C(a\text{-}v)O_2$ depends on the SaO_2, the SvO_2 and the hemoglobin, 1 g of hemoglobin transports 1.34 mL of O_2. The CaO_2 and CvO_2 are calculated as follows:

$$\textbf{CaO}_2 \textbf{ = (Hb x 1.34 x SaO}_2\textbf{);}$$

$$CaO_2 = (10.4\ g/dl \times 1.34 \times 0.78) = 10.87\ vol\%$$

And,

$$\textbf{CvO}_2 \textbf{ = (Hb x 1.34 x SvO}_2\textbf{);}$$

CvO_2 = (10.4 g/dl x 1.34 x 0.72) = 10.03 vol%

Then, the $C(a\text{-}v)O_2$ is assessed:

$$\mathbf{C(a\text{-}v)O_2 = CaO_2 - CvO_2;}$$

$C(a\text{-}v)O_2$ = 10.87 vol% – 10.03 vol% = 0.83 vol%

Second, the Δ pCO_2 is calculated as the difference between venous pCO_2 and arterial pCO_2:

$$\mathbf{\Delta\ pCO_2 = Venous\ pCO_2 - Arterial\ pCO_2;}$$

Δ pCO_2 = 26 mmHg – 25 mmHg = 1 mmHg

Third, using these parameters: $C(a\text{-}v)O_2$ and Δ pCO_2 the perfusion is assessed through the following formula:

$$\mathbf{Perfusion = \frac{\Delta\ pCO2}{C(a-v)O2}}$$

Then, replacing values,

$$Perfusion = \frac{1\ mmHg}{0.83\ vol\%} = 1.19$$

The result obtained indicates **hypoperfusion** because the value is above 1 (See figure 1)

Conclusion

The use of a logical and systematic approach is necessary to properly interpret the parameters of the blood gasometry and timely identify the acid-base disorder. In clinical practice, the Henderson-Hasselbalch theory is a simplified and easy to measure model, the base excess provides an estimate of the magnitude of the acid-base disorder, and the theory of Peter-Stewart allows a more correct interpretation of the metabolic alterations mainly in the complex disorders of the critical patient. The incorporation of the three theories in a diagnostic algorithm facilitates a greater understanding of the pathophysiological mechanisms and allows us to identify a more precise therapeutic objective to correct the underlying disorder in the different clinical contexts of the patient.

Conflicts of Interest

The authors declared no conflicts.

Funding Statement

None

References

1. Fencl V, Rossing TH. Acid-Base Disorders in Critical Care Medicine. *Annu Rev Med*. 1989;40(1):17-27. doi:10.1146/annurev.me.40.020189.000313
2. Rocktaeschel J, Morimatsu H, Uchino S, et al. Acid-base status of critically ill patients with acute renal failure: analysis based on Stewart-Figge methodology. *Crit Care*. 2003;7(4):60-66. doi:10.1186/cc2333
3. Aristizábal-Salazar RE, Calvo-Torres LF, Valencia-Arango LA, Montoya-Cañon M, Barbosa-Gantiva O, Hincapié-Baena V. Acid–base equilibrium: The best clinical approach. *Colomb J Anesthesiol*. 2015;43(3):219-224. doi:10.1016/j.rcae.2015.05.002
4. Dzierba AL, Abraham P. A practical approach to understanding acid-base abnormalities in critical illness. *J Pharm Pract*. 2011;24(1):17-26. doi:10.1177/0897190010388153
5. Palmer BF. Approach to Fluid and Electrolyte Disorders and Acid-Base Problems. *Prim Care - Clin Off Pract*. 2008;35(2):195-213. doi:10.1016/j.pop.2008.01.004
6. Day J, Pandit JJ. Analysis of blood gases and acid-base balance. *Surgery*. 2011;29(3):107-111. doi:10.1016/j.mpsur.2010.11.023
7. Siggard-Andersen O, Fogh-Andersen N. Base excess or buffer base (strong ion difference) as measure of a non-respiratory acid-base disturbance. *Acta Anaesthesiol Scand*. 1995. doi:10.1111/j.1399-6576.1995.tb04346.x
8. Sheldon M, Ali E. Practical approach to physical-chemical acid-base management: Stewart at the bedside. *Ann Am Thorac Soc*. 2015;12(1):111-117. doi:10.1513/AnnalsATS.201409-426OI
9. Fores-Novales B, Diez-Fores P, Aguilera-Celorrio LJ. Evaluación del equilibrio ácido-base. Aportaciones del método de Stewart. *Rev Esp Anestesiol Reanim*.

2016;63(4):212-219. doi:10.1016/j.redar.2015.04.004

10. P. Oliver, O. Rodríguez, J. L. Marín, M. Muñoz, E. Guillén, G. Valcárcel, A. Galán FRC. Estudio de la oxigenación e interpretación de la gasometría arterial. 2014;(2014):17.
11. Williams AJ. ABC of oxygen: assessing and interpreting arterial blood gases and acid-base balance. *BMJ*. 1998;317(7167):1213-1216.
12. Hopkins E, Sharma S. *Physiology, Acid Base Balance*.; 2018.
13. Koeppen BM. The kidney and acid-base regulation. *Adv Physiol Educ*. 2009;33(4):275-281. doi:10.1152/advan.00054.2009
14. Prieto De Paula JM, Franco Hidalgo S, Mayor Toranzo E, Palomino Doza J, Prieto De Paula JF. Alteraciones del equilibrio ácido-base. *Dial y Traspl*. 2012;33(1):25-34. doi:10.1016/j.dialis.2011.06.004
15. Kamel KS. Diagnostic Use of Base Excess in Acid–Base Disorders. *N Engl J Med*. 2018;379(5):494-496. doi:10.1056/NEJMc1806372
16. Greenbaum J, Nirmalan M. Acid – base balance : The traditional approach. *Curr Anaesth Crit Care*. 2005;16:137-142. doi:10.1016/j.cacc.2005.03.009
17. Atherton JC. Role of the kidney in acid–base balance. *Anaesth Intensive Care Med*. 2015;16(6):275-277. doi:10.1016/J.MPAIC.2015.03.002
18. Hamilton PK, Morgan NA, Connolly GM, Maxwell AP. Understanding Acid-Base Disorders. *Ulster Med J*. 2017;86(3):161-166.
19. Paulev PE, Zubieta-Calleja GR. Essentials in the diagnosis of acid-base disorders and their high altitude application. *J Physiol Pharmacol*. 2005;56 Suppl 4:155-170.
20. Edwards SL. Pathophysiology of acid base balance: the theory practice relationship. *Intensive Crit care Nurs*. 2008;24(1):28-38; quiz 38-40. doi:10.1016/j.iccn.2007.05.003

21. Kurtz I. Renal Tubular Acidosis: H+/Base and Ammonia Transport Abnormalities and Clinical Syndromes. *Adv Chronic Kidney Dis*. 2018;25(4):334-350. doi:10.1053/j.ackd.2018.05.005

22. Kimura S, Shabsigh M, Morimatsu H. Traditional approach versus Stewart approach for acid–base disorders: Inconsistent evidence. *SAGE Open Med*. 2018;6:205031211880125. doi:10.1177/2050312118801255

23. Guidet B, Soni N, Rocca G, et al. A balanced view of balanced solutions. *Crit Care*. 2010;14(5):325. doi:10.1186/cc9230

24. Sánchez-Díaz JS, Martínez-Rodríguez EA, Méndez-Rubio LP, et al. Equilibrio ácido-base. Puesta al día. Teoría de Henderson-Hasselbalch. *Med Interna Mex*. 2016;32(6):646-660.

25. Moe OW, Fuster D. Clinical acid-base pathophysiology: disorders of plasma anion gap. *Best Pract Res Clin Endocrinol Metab*. 2003;17(4):559-574.

26. Figge J, Jabor A, Kazda A, Fencl V. Anion gap and hypoalbuminemia. *Crit Care Med*. 1998;26(11):1807-1810.

27. Fencl V, Jabor A, Kazda A, Figge J. Diagnosis of Metabolic Acid – Base Disturbances in Critically Ill Patients. *Crit Care Med*. 2000;162(18):0-5.

28. Morgan TJ. The meaning of acid-base abnormalities in the intensive care unit: part III -- effects of fluid administration. *Crit Care*. 2005;9(2):204-211. doi:10.1186/cc2946

29. Häubi S C, Moreno-Santillán A, De León-Ponce MD, et al. Teoría ácido-básico de Stewart, un nuevo paradigma en medicina crítica. *Rev Mex Anestesiol*. 2006;29(4):240-244.

30. Rastegar A. Clinical utility of Stewart's method in diagnosis and management of acid-base disorders. *Clin J Am Soc Nephrol*. 2009;4(7):1267-1274.

doi:10.2215/CJN.01820309

31. Kishen R, Honoré PM, Jacobs R, et al. Facing acid-base disorders in the third millennium - the Stewart approach revisited. *Int J Nephrol Renovasc Dis*. 2014;7:209-217. doi:10.2147/IJNRD.S62126

32. Walley KR. Use of central venous oxygen saturation to guide therapy. *Am J Respir Crit Care Med*. 2011;184(5):514-520. doi:10.1164/rccm.201010-1584CI

33. Hamm LL, Nakhoul N, Hering-Smith KS. Acid-Base Homeostasis. *Clin J Am Soc Nephrol*. 2015;10(12):2232-2242. doi:10.2215/CJN.07400715

34. Ospina-Tascón GA, Hernández G, Cecconi M. Understanding the venous–arterial CO2 to arterial–venous O2 content difference ratio. *Intensive Care Med*. 2016;42(11):1801-1804. doi:10.1007/s00134-016-4233-7

35. Zakharov S, Navrátil T, Pelclova D. Analysis of serum anion gap and osmolal gap in diagnosis and prognosis of acute methanol poisoning: clinical study in 86 patients. *Monatshefte für Chemie - Chem Mon*. 2015;146(5):787-794. doi:10.1007/s00706-014-1374-7

36. Kotrashetti V, Sonawane V, Bainade K, Lal Nath A. Renal Tubular Acidosis-An Unusual Presentation. *IOSR J Dent Med Sci Ver I*. 2015;14(12):2279-2861. doi:10.9790/0853-141216566

37. Choy KWW, Wijeratne N, Lu ZX, Doery JCC. Harmonisation of Osmolal Gap - Can We Use a Common Formula? *Clin Biochem Rev*. 2016;37(3):113-119.

38. Sánchez SMS, Fuciños LC, Cabeza EF, Mateos AG de L. Alteraciones del metabolismo ácido base: alcalosis. *Med - Programa Form Médica Contin Acreditado*. 2015;11(79):4759-4767. doi:10.1016/j.med.2015.05.013