HSR (LONDON),
HOUGHTON STREET REVIEW JOURNAL
ISSN: 2058-5519|Impact factor-15.9
http://houghtonstreetreview.com/index.php/hsr

MOLECULAR-PHYSIOLOGICAL ARCHITECTURE OF HOMEOSTATIC BUFFER SYSTEMS IN THE HUMAN ORGANISM AND STRATEGIES FOR THEIR CLINICAL-PHARMACEUTICAL OPTIMIZATION

Jumayeva Robiyabonu Alisher qizi

2nd-year student, Faculty of Pediatrics, Kimyo International University in Tashkent, Tashkent, Uzbekistan

Abdiyeva Feruza Iskandarovna

Acting Associate Professor, Department of Medical and Biological Sciences, Kimyo International University in Tashkent, Tashkent, Uzbekistan

Doi: https://doi.org/10.5281/zenodo.21817754

Abstract: This article analyzes the molecular and physiological characteristics of homeostatic buffer systems, which play a crucial role in maintaining acid–base balance in the human body, as well as their clinical and pharmaceutical significance, based on contemporary scientific literature. The roles of the bicarbonate, phosphate, and protein (hemoglobin) buffer systems in maintaining homeostasis are discussed from the perspectives of the Henderson–Hasselbalch equation and modern acid–base theories. In addition, the mechanisms underlying the development of metabolic acidosis and metabolic alkalosis, the compensatory responses of the lungs and kidneys, and contemporary pharmacological approaches to the correction of acid–base imbalance are reviewed. The findings of the literature analysis indicate that a comprehensive understanding of homeostatic buffer systems has significant scientific and practical value for improving the diagnosis and treatment of critically ill patients.

Keywords: homeostasis, buffer systems, acid–base balance, bicarbonate buffer, phosphate buffer, hemoglobin, Henderson–Hasselbalch equation, metabolic acidosis, metabolic alkalosis, clinical pharmacology.

INTRODUCTION

Homeostasis, which ensures the stability of the internal environment of the human body, plays a fundamental role in maintaining the continuity and coordination of all physiological processes. One of the key components of homeostasis is acid–base balance, which is essential for preserving enzymatic activity, metabolic processes, ion exchange, and the functional integrity of biomolecules at the cellular level. Under normal physiological conditions, the arterial blood pH is maintained within a narrow range of 7.35–7.45. Significant deviations from this range may impair cellular metabolism, reduce enzyme activity, and lead to the development of life-threatening pathological conditions [1].

The maintenance of acid–base balance is achieved through the coordinated actions of the bicarbonate, phosphate, and protein (particularly hemoglobin) buffer systems, together with the respiratory and renal regulatory mechanisms. These systems maintain hydrogen ion concentration within physiological limits, thereby preventing the development of metabolic and respiratory acid–base disorders [1,2].

HSR (LONDON),
HOUGHTON STREET REVIEW JOURNAL
ISSN: 2058-5519|Impact factor-15.9
http://houghtonstreetreview.com/index.php/hsr

In clinical practice, disturbances of acid–base balance are frequently encountered in patients with sepsis, diabetic ketoacidosis, acute and chronic kidney disease, severe hypoxia, and shock. Under these conditions, accurate assessment of the compensatory capacity of buffer systems and the rational selection of pharmacological correction strategies are crucial for improving the effectiveness of intensive care management [3,4].

In recent years, alongside the classical Henderson–Hasselbalch approach, Stewart's strong ion theory has gained increasing acceptance in clinical practice for the evaluation of acid–base disorders. These complementary approaches provide a deeper understanding of the molecular mechanisms underlying metabolic disturbances, facilitate more accurate interpretation of laboratory findings, and contribute to the development of individualized therapeutic strategies [2,3].

The aim of this review article is to analyze, based on contemporary scientific literature, the molecular and physiological characteristics of homeostatic buffer systems, their role in maintaining acid–base balance, and their significance in modern clinical and pharmaceutical practice.

RESEARCH OBJECTIVE

The aim of this study was to analyze the molecular and physiological characteristics of homeostatic buffer systems in the human body based on contemporary scientific literature, to evaluate their role in maintaining acid–base balance and their clinical and pharmaceutical significance, and to scientifically assess the compensatory capacity of buffer systems in severe metabolic disorders, as well as the effectiveness of pharmacological correction of acid–base imbalance, using retrospective clinical data obtained from 42 patients treated in the intensive care unit (ICU).

Research Objectives

- To analyze the molecular and physiological characteristics of the major homeostatic buffer systems in the human body
- To evaluate the roles of the bicarbonate, phosphate, and protein (hemoglobin) buffer systems in maintaining acid–base balance
- To describe the compensatory mechanisms of the lungs and kidneys based on contemporary scientific literature
- To analyze the retrospective clinical data of 42 patients treated in the intensive care unit
- To evaluate the clinical effectiveness of pharmacological correction methods used in patients with metabolic acidosis

To formulate evidence-based scientific conclusions regarding the clinical application of homeostatic buffer systems based on the obtained findings.

MATERIALS AND METHODS

This study was conducted using a retrospective observational design. In the theoretical part of the study, national and international scientific literature on homeostatic buffer systems, acid–base balance, and their clinical and pharmaceutical correction was systematically reviewed. The practical part was based on a retrospective analysis of medical records from patients treated in the intensive

HSR (LONDON),
HOUGHTON STREET REVIEW JOURNAL
ISSN: 2058-5519|Impact factor-15.9
http://houghtonstreetreview.com/index.php/hsr

care unit (ICU), using a clinical database developed during the scientific supervisor's 25 years of clinical practice.

The study material consisted of the medical records of 42 patients who were treated for cardiogenic shock and severe hypoxia. In all patients, acid–base balance parameters, arterial blood gas analysis, and laboratory changes observed during treatment were evaluated. The retrospective analysis included arterial blood pH, partial pressure of carbon dioxide (pCO_2), bicarbonate concentration (HCO_3^-), the severity of metabolic disturbances, and the infusion therapy administered.

According to the treatment strategy, the patients were divided into two groups. The first group included 22 patients who received conventional sodium bicarbonate ($NaHCO_3$) infusion therapy for the correction of metabolic acidosis. The second group consisted of 20 patients treated with tris(hydroxymethyl)aminomethane (THAM) and balanced polyionic buffer solutions. In both groups, the dynamics of acid–base balance parameters were assessed before and during treatment, and the obtained results were comparatively analyzed.

No patient-identifying information was used during the study. Medical records were retrospectively reviewed exclusively for scientific purposes, and the confidentiality of all patient data was strictly maintained. The collected data were analyzed to evaluate the relationship between clinical and laboratory parameters and to determine the effectiveness of pharmacological correction of acid–base imbalance.

LITERATURE REVIEW

The maintenance of acid–base balance is one of the fundamental physiological mechanisms that ensures the continuity of all biochemical processes in the human body. According to contemporary scientific literature, the maintenance of physiological blood pH is achieved through the coordinated interaction of buffer systems, the respiratory system, and the renal compensatory mechanisms [5].

Boron and Boulpaep emphasize that buffer systems serve as the first line of defense against acid–base disturbances by limiting rapid fluctuations in hydrogen ion concentration immediately following an acid or alkali load. They report that the bicarbonate buffer system represents the principal extracellular buffering mechanism, and its effectiveness depends not only on the concentration of bicarbonate ions but also on the lungs' ability to eliminate carbon dioxide and the kidneys' capacity to reabsorb bicarbonate [5].

According to the modern acid–base theory proposed by Stewart, blood pH is determined not only by bicarbonate concentration but also by the strong ion difference (SID), the partial pressure of carbon dioxide (pCO_2), and the concentration of weak acids. This approach has been widely recognized as an important complement to the traditional Henderson–Hasselbalch model, particularly in the assessment of severe metabolic acid–base disorders [6].

In his studies, Kellum highlighted the importance of a comprehensive interpretation of laboratory parameters in the evaluation of metabolic acidosis and alkalosis in critically ill patients. According to the author, simultaneous assessment of arterial blood gases, electrolyte concentrations,

HSR (LONDON),
HOUGHTON STREET REVIEW JOURNAL
ISSN: 2058-5519|Impact factor-15.9
http://houghtonstreetreview.com/index.php/hsr

and buffer capacity allows for a more accurate determination of disease severity and facilitates the selection of the most appropriate therapeutic strategy [7].

Adrogué and Madias, based on the analysis of studies on the management of metabolic acidosis, concluded that sodium bicarbonate infusion should not be routinely administered in all cases. They emphasized that the choice of therapeutic intervention should be individualized according to the underlying cause of the metabolic disturbance, arterial blood gas findings, and the patient's overall clinical condition. Therefore, individualized treatment has become one of the fundamental principles of modern intensive care medicine [8].

Overall, the reviewed literature demonstrates that homeostatic buffer systems do not function independently but rather operate as an integrated, multi-level physiological defense mechanism responsible for maintaining acid–base homeostasis. A comprehensive understanding of the molecular and physiological properties of these systems provides an important scientific basis for improving diagnostic approaches and optimizing pharmacological correction strategies in critically ill patients.

RESULTS

A retrospective analysis was performed using the medical records of 42 patients treated for cardiogenic shock and severe hypoxia in the intensive care unit (ICU). Arterial blood gas parameters, acid–base balance (ABB) indicators, and the effectiveness of the pharmacological correction methods used during treatment were evaluated in all patients.

According to the therapeutic approach, the patients were divided into two groups. The first group consisted of 22 patients who received conventional sodium bicarbonate ($NaHCO_3$) infusion therapy for the correction of metabolic acidosis. The second group included 20 patients treated with tris(hydroxymethyl)aminomethane (THAM) and balanced polyionic buffer solutions.

The retrospective analysis demonstrated that, in the group treated exclusively with sodium bicarbonate, the partial pressure of carbon dioxide (pCO_2) in arterial blood plasma remained, on average, 18% higher than the expected level during treatment. This finding was associated with delayed restoration of intracellular acid–base homeostasis in some patients and a prolonged recovery from metabolic disturbances.

In contrast, patients treated with THAM and balanced polyionic buffer solutions exhibited a more stable recovery of acid–base balance. During treatment, arterial blood pH gradually increased from 7.21 to 7.38, approaching the physiological range. No episodes of recurrent hypoxia or metabolic deterioration were observed in this group, and normalization of acid–base balance was accompanied by a favorable clinical course.

The obtained results suggest that correction of metabolic acidosis based solely on sodium bicarbonate infusion may not always provide optimal therapeutic efficacy. The use of THAM in combination with balanced polyionic buffer solutions resulted in a more physiological restoration of acid–base homeostasis. These findings indicate that pharmacological support of buffer systems plays an important role in improving treatment outcomes in patients with severe hypoxia and metabolic acid–base disorders.

HSR (LONDON),
HOUGHTON STREET REVIEW JOURNAL
ISSN: 2058-5519|Impact factor-15.9
http://houghtonstreetreview.com/index.php/hsr

DISCUSSION

The findings of the present study demonstrated that the effectiveness of pharmacological approaches for correcting acid–base imbalance differs considerably in patients with metabolic acidosis and severe hypoxia. Retrospective analysis showed that patients treated with conventional sodium bicarbonate ($NaHCO_3$) infusion exhibited an increase in arterial pCO_2, whereas those receiving tris(hydroxymethyl)aminomethane (THAM) and balanced polyionic buffer solutions demonstrated a more stable restoration of arterial blood pH toward the physiological range.

These findings are consistent with the physiological concepts described by Boron and Boulpaep, who emphasized that although the bicarbonate buffer system is the principal extracellular defense mechanism against acid–base disturbances, its effectiveness depends on adequate pulmonary elimination of carbon dioxide and normal renal bicarbonate handling. Consequently, in patients with severe hypoxia or respiratory dysfunction, correction with sodium bicarbonate alone may not always achieve the desired therapeutic outcome [5].

The results are also supported by Stewart's modern acid–base theory, which proposes that acid–base homeostasis is determined not only by bicarbonate concentration but also by the strong ion difference (SID), the partial pressure of carbon dioxide (pCO_2), and the concentration of weak acids [6]. In the present retrospective analysis, changes in pCO_2 were closely associated with treatment response, further supporting Stewart's concept that comprehensive assessment of acid–base physiology provides a more accurate evaluation of metabolic disorders than bicarbonate concentration alone.

Similarly, Kellum emphasized that interpretation of metabolic acidosis in critically ill patients should include a comprehensive evaluation of arterial blood gases, electrolyte balance, and buffer capacity rather than relying solely on blood pH values [7]. In agreement with this recommendation, our analysis demonstrated that simultaneous assessment of pH, pCO_2, and overall clinical status provided a more reliable reflection of therapeutic effectiveness than evaluation of individual laboratory parameters alone.

Adrogué and Madias reported that sodium bicarbonate administration should not be considered the optimal treatment for all cases of metabolic acidosis because excessive carbon dioxide production may aggravate intracellular acidosis despite apparent correction of extracellular pH [8]. The findings of the present study support this observation. Patients treated with sodium bicarbonate alone demonstrated elevated pCO_2 levels, whereas those receiving THAM and balanced buffer solutions achieved a more physiological restoration of acid–base homeostasis without evidence of recurrent hypoxic or metabolic deterioration.

Overall, the results of this retrospective study are in agreement with the current physiological and clinical evidence reported in the scientific literature. They indicate that successful correction of severe metabolic acidosis requires an individualized therapeutic approach based on comprehensive laboratory assessment rather than isolated correction of bicarbonate deficiency. Furthermore, the use of balanced buffer solutions appears to provide a more physiological restoration of acid–base balance in critically ill patients. Nevertheless, the present study has several limitations, including its retrospective design and the relatively small sample size (42 patients). Therefore, larger prospective

HSR (LONDON),
HOUGHTON STREET REVIEW JOURNAL
ISSN: 2058-5519|Impact factor-15.9
http://houghtonstreetreview.com/index.php/hsr

clinical studies are warranted to validate these findings and further clarify the optimal pharmacological strategies for the management of acid–base disorders.

CONCLUSION

Homeostatic buffer systems constitute one of the principal physiological mechanisms responsible for maintaining acid–base balance in the human body. The coordinated interaction of the bicarbonate, phosphate, and protein buffer systems, together with the compensatory functions of the lungs and kidneys, plays a crucial role in preserving intracellular metabolism and maintaining the functional stability of vital organs.

The retrospective analysis demonstrated that the effectiveness of pharmacological approaches for correcting acid–base imbalance differs in patients with severe hypoxia and metabolic acidosis. While conventional sodium bicarbonate ($NaHCO_3$)-based therapy was associated with increased carbon dioxide production in some cases, patients treated with tris(hydroxymethyl)aminomethane (THAM) and balanced polyionic buffer solutions showed a more stable restoration of arterial blood pH toward the physiological range.

The combined evaluation of the literature review and the retrospective clinical data from 42 patients indicates that successful management of metabolic acidosis should not rely on a single laboratory parameter or a single buffer system. Comprehensive assessment of arterial blood gas analysis, electrolyte status, buffer capacity, and the patient's overall clinical condition provides a more reliable basis for selecting the optimal therapeutic strategy.

In conclusion, a thorough understanding of the molecular and physiological characteristics of homeostatic buffer systems, together with the implementation of contemporary clinical and pharmaceutical approaches, is essential for the effective correction of metabolic disorders, improvement of clinical outcomes in critically ill patients, and enhancement of the overall effectiveness of intensive care management.

References

1. Boron WF, Boulpaep EL. Medical Physiology. Elsevier; 2016.
2. Stewart PA. Modern Quantitative Acid–Base Chemistry. Can J Physiol Pharmacol. 1983.
3. Kellum JA. Determinants of blood pH. Critical Care. 2005.
4. Adrogué HJ, Madias NE. Management of Life-Threatening Acid–Base Disorders. N Engl J Med. 2010.
5. Boron WF, Boulpaep EL. Medical Physiology. 3rd ed. Philadelphia: Elsevier; 2016.
6. Stewart PA. Modern quantitative acid-base chemistry. Canadian Journal of Physiology and Pharmacology.
7. Kellum JA. Determinants of blood pH in health and disease. Critical Care. 2000;4(1):6–14.
8. Adrogué HJ, Madias NE. Management of life-threatening acid-base disorders. The New England Journal of Medicine.