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Impact of water quality and interferences of ion selective electrodes on electrolyte dosage

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Abstract

Fluid and electrolyte imbalances are frequently encountered in hospital settings and can significantly affect patient health, influencing vital functions such as nerve conduction, muscle contraction, and acid-base balance. Accurate determination of serum ion concentrations is essential for effective clinical management, and various analytical methods, including ion-selective electrodes (ISE), are widely employed for this purpose. This study focuses on the use of ISE technology for measuring sodium (Na⁺), potassium (K⁺), and chloride (Cl⁻) levels in biological samples, with particular attention to potential interferences and the impact of water quality on assay accuracy. Our laboratory employs the indirect ISE method using the Abbott Architect ci 8200 analyzers, ensuring high specificity and precision. A comprehensive quality management system (QMS) in accordance with ISO 15189 standards is implemented to monitor all stages of electrolyte analysis, from pre-analytical to post-analytical processes. This system includes rigorous internal and external quality control measures, regular calibration, and the use of high-purity water, processed through a multi-stage water treatment system to minimize contaminants. The results from our quality control processes demonstrate that the laboratory consistently maintains the accuracy and reliability of electrolyte measurements. By addressing interferences related to sample matrix effects, assay conditions, and water quality, we aim to provide clinicians with the most accurate data for informed decision-making in patient care.

Keywords: Water Quality; Ion Selective Electrodes; Electrolyte Dosage; Ion interference; Medical laboratory

1. Introduction

Fluid and electrolyte imbalances are commonly encountered in hospital settings, particularly in specialized units such as nephrology and intensive care. These imbalances are crucial to monitor, as they can have significant impacts on patient health, influencing vital functions such as nerve conduction, muscle contraction, and acid-base balance. To accurately determine the concentrations of electrolytes in serum, a variety of analytical methods are employed, including flame atomic emission spectrometry (FAES), ion-selective electrodes (ISE), enzymatic techniques, and absorption spectrometry [1].

In our laboratory, we rely on the ion-selective electrode (ISE) method due to its high specificity, precision, and ability to measure multiple electrolytes simultaneously. However, the accurate and reliable interpretation of serum ion concentrations goes beyond simply choosing the appropriate method; it requires stringent quality control measures to minimize errors and interferences. Factors such as assay method interferences, matrix effects, and the quality of reagents and solvent including the water used in the laboratory can all impact the accuracy of results.

To ensure the reliability of our results and to meet the highest standards of medical practice, we have implemented a comprehensive quality management system (QMS) in accordance with the ISO 15189 standard for laboratory accreditation. This standard ensures that our laboratory operates with rigorous quality assurance practices, covering

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all aspects from sample collection and processing to analysis and reporting. By adhering to these internationally recognized standards, we aim to provide clinicians with the most accurate data possible, which in turn supports timely and informed decision-making in patient care.

2. Material and Methods

This study focuses on the methodology for determining sodium Na⁺, potassium K⁺ and chloride Cl⁻ levels using ionselective electrodes (ISE), as well as the interferences associated with this technique and the quality of water used in our laboratory.

2.1. Electrolyte Determination Method: Ion-Selective Electrodes (ISE)

Ion-selective electrode (ISE) analysis is an electrochemical method widely used for the determination of ion concentrations in aqueous solutions and biological fluids. It operates by measuring the electrochemical activity of specific ions in a solution. The method relies on one of the following electrochemical principles: potentiometry, amperometry, or conductivity measurements [1].

Electrochemistry involves the study of the conversion between chemical energy and electrical energy, which is achieved through redox reactions. These reactions either generate an electric current or use an electric current to drive a chemical reaction. In the ISE setup, an electrochemical cell consists of two electrodes connected by an ion bridge. Each electrode is immersed in a solution that contains its respective ions, forming a redox couple. At each half-cell, a potential difference (E) is generated between the electrode and the solution. This potential difference is measured by a millivoltmeter when comparing the potential of one half-cell to a reference half-cell [2].

Principles of Operation: Among the various electrochemical techniques, potentiometry is the most commonly used for ISE measurements. In potentiometry, the potential difference between two electrodes immersed in a sample solution is measured. The setup includes:

External Reference Electrode (ERE): This is a stable electrochemical half-cell with a constant potential (E_{ERE}). Potassium (K⁺) and chloride (Cl⁻) ions from the ERE diffuse through a porous pellet into the solution, maintaining electrical contact between the two electrodes. The junction potential (E_j) is established at the interface of the porous pellet.

Selective Ionic Electrode (Internal Reference Electrode, ERI): This electrode is immersed in a reference solution, separated from the sample by a selective membrane that allows specific ions (e.g., sodium, potassium, chloride) to pass through. The membrane generates a potential that is proportional to the ion concentration in the sample. These two electrodes are connected by a salt bridge to ensure electrical continuity.

ISE methods can be divided into two types: direct and indirect. Direct ISE methods involve the direct measurement of the undiluted sample, whereas indirect methods require sample dilution before analysis [3]. In our laboratory, the indirect ISE method is used with the Abbott Architect ci 8200 analyzers.

2.2. Interferences Related to the Assay Method

Ion-selective electrodes are widely used in clinical laboratories for their ability to deliver rapid, reliable, and costeffective measurements of key analytes, even from small sample volumes and diverse sample types. However, ensuring the accuracy of results requires a thorough understanding of potential interferences that can affect the measurement process.

Interference occurs when external substances or conditions distort the results of a measurement method. In clinical testing, interferences can arise due to several factors, including the type of sample (plasma, serum, blood), the sample's composition (e.g., presence of metabolites, drugs, or herbal products), the collection method (venous, arterial, or capillary blood), and how the sample is processed and stored. Identifying and mitigating these interferences is critical for preventing misdiagnoses and ensuring accurate test results [4].

2.2.1. Common Interferences in ISE Measurements

Sampling Site: Samples obtained from catheters or cannulas may be contaminated by intravenous fluids, introducing potential interference. To reduce this risk, it is recommended to flush the catheter or cannula thoroughly before sample collection. Studies have provided guidelines on the appropriate volumes for flushing to ensure accurate results [5].

Surfactants Acting on the Membrane: Surfactants present in calibration solutions, rinsing buffers, or quality control solutions can alter the behavior of the ISE membrane, leading to erroneous readings. Prolonged exposure to such solutions, especially if the electrodes are inadequately washed or come into contact with solutions containing surfactants, can cause significant interference. For example, benzalkonium-based surfactants, commonly used in medical devices to prevent thrombosis and infections, can lead to falsely elevated potassium levels when using ISEs [6-7]. Furthermore, contamination from antiseptic hand sanitizers in capillary samples has been reported to introduce unexpected interference.

Sample Matrix: The matrix of the sample can have a profound effect on the electrode's response. For example, protein deposition on the ISE membrane can alter its physical properties, potentially causing delayed sensor response or, in extreme cases, complete sensor failure if the membrane becomes fully covered [8]. Protein accumulation can also influence the liquid junction potential [9]. Additionally, the presence of erythrocytes in the sample can modify the residual liquid junction potential, leading to positive interference in sodium (Na⁺) measurements, with reported increases of up to 1.8 mmol/L when using an unrestricted liquid-liquid junction [10]. Blood clots adhering to the electrode membranes can also impede the flow of calibration solutions, further affecting electrode performance.

Pseudohyponatremia: This condition, often linked to hyperlipidemia and hyperproteinemia, can lead to pseudohyponatremia in indirect ISE methods. Excess lipids or proteins can displace some of the sample's aqueous volume, reducing the amount available for ion measurement and distorting the results. This phenomenon can lead to falsely low sodium concentrations (pseudohyponatremia) when protein concentrations are abnormally high [11]. Similar pseudo-effects can occur for chloride (Cl⁻), with changes in protein levels potentially causing variations in sodium, potassium, and chloride readings. For example, variations of 8 to -7 mmol/L for Na⁺, -0.5 to 0.4 mmol/L for K⁺, and 4 to -9 mmol/L for Cl⁻ have been documented [12]. To mitigate these issues, direct ISE methods, ultracentrifugation, or lipid compensation agents can be used to improve measurement accuracy [13].

2.3. Water Quality in the Laboratory

Water is a critical reagent in clinical laboratories, used for a wide variety of applications, including sample dilution, reagent preparation, and equipment cleaning. The quality of water directly impacts the accuracy of all assays, particularly those involving electrolytes. For reliable results, high-purity water is required.

In our laboratory, the water used for analysis is sourced from city drinking water, which contains various dissolved minerals and contaminants. To minimize the impact of these impurities, the water undergoes comprehensive treatment and demineralization through a water purification system.Water contamination with inorganic ions, such as sodium, calcium, magnesium, bicarbonate, chloride, sulfate, and zinc, can interfere with electrolyte measurements. These ions can cause significant errors, particularly in the determination of potassium (which has a very narrow normal range). Therefore, effective water treatment is essential to avoid inaccuracies in electrolyte results [14].

According to the Clinical and Laboratory Standards Institute (CLSI) guidelines, Clinical Laboratory Reagent Water (CLRW) is recommended for biochemical testing. CLRW is defined by its high ionic purity (resistivity > 10 M Ω ·cm), low organic carbon content (TOC < 500 ppb), low bacterial load (< 10 CFU/mL), and effective particle removal (particles > 0.22 µm). Some applications, such as autoclave use and equipment cleaning, may require special reagent water (SRW) or instrument feed water (IFW) [14].

2.4. Water Treatment System

To ensure that the water used in our laboratory meets the stringent quality standards required for electrolyte assays, we have implemented a multi-stage water treatment system. This system is monitored daily by the biomedical department to check for key parameters such as resistivity and pH. The water treatment process includes filtration, softening, reverse osmosis, ion exchange, microfiltration, and UV photo-oxidation. This ensures that the water is free of ionic contaminants and other impurities that could affect test results.

2.5. Quality Control of Electrolyte Measurements

To maintain high standards in electrolyte testing, our laboratory employs a comprehensive quality control (QC) system. Three main types of QC are utilized:

2.5.1. Internal Quality Control (IQC)

Routine internal checks are carried out to monitor the performance of laboratory equipment and ensure the accuracy of measurements.

2.5.2. Outsourced Internal Quality Control (OIQC)

Control samples are shared and compared with other laboratories to assess consistency and performance accuracy.

2.5.3. External Quality Control (EQC)

External assessments are conducted through inter-laboratory comparisons of control samples, providing an additional layer of verification.

Control charts, such as Levey-Jennings plots, are used to track performance over time and identify any discrepancies or potential issues with the assay methods.

3. Results

3.1. Quality management system

Our laboratory employs a comprehensive quality management system encompassing all stages of electrolyte determination.

3.1.1. Pre-Analytical Stage

The pre-analytical stage involves defining the requirements for electrolyte testing, including the type of tube, sampling conditions (e.g., avoiding the use of a tourniquet for potassium levels), sample packaging, timing, and required volume. The sample must be transported under optimal conditions and as quickly as possible to ensure accuracy. Once received in the laboratory, samples are processed promptly by technicians who undergo continuous training to maintain high standards of laboratory operation. Centrifuges are calibrated for temperature and speed, and our laboratory is under a metrology contract with accredited organizations to ensure the accuracy of centrifuge performance.

3.1.2. Analytical Stage

During the analytical stage, our laboratory adheres to a quality policy that includes method verification according to scope A of the NF ISO 15189 standard. We implement internal quality controls at the beginning and end of each batch, as well as external quality controls and assessments to ensure ongoing accuracy and reliability.

3.1.3. Post-Analytical Stage

In the post-analytical stage, results are subjected to technical and biological validation. They are interpreted in the context of clinical information and the patient's medical history. If discrepancies arise in hydro-electrolytic assessments, we communicate with clinicians to discuss potential re-sampling or the need for additional testing to resolve the issue.

3.2. Water treatment system in our laboratory

The laboratory's water treatment plant is monitored daily by the hospital's biomedical department, which checks resistivity, pH, and various other parameters in accordance with the manufacturer's recommendations and international standards. Notably, our laboratory is the first public medical laboratory in Morocco to establish a contract with a service provider for regular water quality control. This provider collects and analyzes samples in an accredited laboratory to ensure the ultra-pure water meets the stringent requirements for electrolyte assays and other parameters. The water treatment process begins with a pretreatment phase involving filtration through various types of filters. Following this, the water is softened using a salt and resin system, then stored in a tank before proceeding to the main purification system. This comprehensive system integrates five treatment technologies: adsorption, reverse osmosis, ion exchange, microfiltration, and photo-oxidation. Initially, pre-treated water flows through an inlet solenoid valve into a pre-treatment reservoir. This reservoir is designed to protect the reverse osmosis membranes from colloids, suspended particles, and excess free chlorine. The water then passes through the disinfection port and is filtered by one or two reverse osmosis units connected in series. After reverse osmosis, the permeate undergoes conductivity measurement before entering the UV chamber. Here, the water is exposed to intense UV light, which provides continuous bacterial control through photo-oxidation and helps to break down organic molecules. The partially purified water then flows through an ion exchange cartridge that removes ionic impurities. Subsequently, the water's resistivity

and temperature are measured using dedicated probes. Finally, the water is filtered through a 0.2 μ m filter to ensure high bacterial protection. After these purification steps, the water is ready for distribution to the laboratory analyzers [15].



Figure 1 Specialized Water Treatment System at Mohammed VI University Hospital, Oujda Central Laboratory [15]

3.3. Quality control results of the ionogram of our laboratory

Quality is defined as the ability of a set of intrinsic characteristics to meet specified requirements [16]. Quality control (QC) is essential for evaluating, correcting, and validating the processes leading to the reporting of patient test results. Every medical analysis laboratory must implement a quality assurance system to build trust with patients and prescribing physicians. This system must be continuous and include a comprehensive record of all quality controls performed.

3.3.1. Internal Quality Control (IQC)

IQC involves a set of procedures implemented within the laboratory to ensure the quality of test results as they are generated [17]. This includes routine checks and calibrations to monitor the performance of testing procedures and equipment.

3.3.2. Outsourced Internal Quality Control (OIQC)

OIQC involves multiple laboratories evaluating the same batch of control samples. These results are compared periodically, usually monthly, to assess accuracy and consistency. It is important to note that outsourced internal quality control is not classified as external quality control (EQC).

3.3.3. External Quality Control (EQC)

EQC, or External Quality Assessment (EQA), involves assessing laboratory performance through inter-laboratory comparisons of unknown control samples by a third-party organization on a specified schedule [18]. This process helps evaluate the laboratory's accuracy and reliability in comparison with other laboratories.

The results of IQC are often represented using "control charts." The Levey-Jennings chart is a common tool used for this purpose. It plots each IQC result against time and decision limits calculated from the standard deviation of the result population. Levey-Jennings diagrams can illustrate internal quality controls for various tests, such as blood and urine sodium levels and blood potassium levels.



Figure 2 Internal quality control results of blood sodium represented on the Levey-jenning graphs for the month of September



Figure 3 Internal quality control results of urine sodium represented on the Levey-jenning graphs for the month of September 2021



Figure 4 Internal quality control results of blood potasium represented on the Levey-jenning graphs for the month of September 2021

4. Discussion

Hydro electrolytic imbalances are commonly encountered in daily laboratory operations, especially when measuring electrolyte levels, which are crucial for maintaining water balance, nerve conduction, and muscle function. Our laboratory employs the indirect ion-selective electrode (ISE) method for analyzing electrolyte levels. This technique relies on the measurement of the electrical potential generated between an ion-selective membrane and a reference electrode, as described by the Nernst equation [19]. Specific electrodes for sodium, potassium, and chloride are designed to allow the passage of only the targeted ions, ensuring precise measurement of ionic concentrations. This potential is compared to pre-established calibrators and converted into ion concentrations.

One of the key concerns related to the accuracy of electrolyte measurements is the management of analytical interferences. These interferences can be classified into two categories: those related to the assay method and those related to the quality of the water used. Regarding the assay method, various sources can disrupt results, such as the composition of the sample and the collection site. For example, the presence of proteins or other molecules in the sample can lead to deposition on the ISE membrane, altering its physical properties and potentially causing a delayed sensor response or, in severe cases, complete sensor failure if the membrane becomes fully coated [8]. A particularly documented phenomenon in clinical laboratories is pseudo-hyponatremia, which can occur in hyperlipidemia or hyperproteinemia. In such cases, the amount of water in the sample is reduced due to displacement by lipids or proteins, leading to an artificially low sodium concentration. However, this interference generally does not affect direct ISE methods, where the sample is not diluted, unlike the indirect ISE method, which involves sample dilution [11, 20].

The quality of water used in analytical procedures is also a critical factor influencing the accuracy of electrolyte measurements. Water used for reagent preparation, sample dilution, and equipment cleaning can introduce contaminants that may interfere with the analysis, including inorganic ions such as sodium, calcium, magnesium, bicarbonate, chloride, sulfate, and zinc. Even low concentrations of these ions can affect results, particularly for potassium measurement, which is highly sensitive to ionic concentration variations [15]. To minimize these interferences, our laboratory uses an advanced water treatment system, the MEDICA system from Veolia. This system incorporates multiple purification technologies, such as reverse osmosis, ion exchange, and microfiltration, to ensure that the water meets strict purity standards. It is continuously monitored for parameters such as resistivity, pH, and bacterial presence to ensure it does not contain contaminants that could skew electrolyte measurement results. High

resistivity water (greater than 10 M Ω ·cm) is essential to minimize the introduction of ions that could compromise the accuracy of electrolyte assays.

A robust quality management system (QMS) is essential in any laboratory conducting diagnostic tests. Our laboratory's QMS covers all stages of the electrolyte analysis process, from pre-analytical to post-analytical phases. Ensuring the quality of results at each stage is crucial. During sample collection, it is essential to follow strict conditions, such as avoiding the use of a tourniquet when collecting a sample for potassium measurement, to prevent concentration errors caused by hemoconcentration. Samples are also transported rapidly, and centrifugation conditions are carefully monitored to ensure sample homogeneity.

During the analytical phase, we adhere to strict protocols and quality assurance procedures, such as method verification in accordance with the NF ISO 15189 standard. This includes regular internal quality controls and comparisons with external quality tests (EQC). These verifications ensure the reliability and reproducibility of results. After analysis, during result interpretation, technical and biological validation procedures are implemented to ensure that results align with clinical expectations and the patient's condition.

Westgard rules are used to evaluate the validity of results. These rules help determine whether a result should be accepted or rejected. In the case of a rejection, corrective actions are taken, guided by Ishikawa diagrams, which help identify the root cause of any anomalies. These actions address issues related to procedure, samples, or equipment. When a problem is identified with water quality, its resistivity is checked, and discrepancies are corrected. In most cases, this approach resolves the issue. However, if problems persist, further investigation is conducted using the 5M Ishikawa diagram (Manpower, Materials, Method, Machine, and Environment) to examine other underlying factors.

5. Conclusion

Electrolyte determination is a routine procedure requested by nearly every hospital department. The reliability of these results is crucial for making timely and accurate decisions in patient care. Electrolyte balance can be influenced by both the measurement method—specifically, ion-selective electrodes—and the quality of the water used. To address these concerns, our laboratory has implemented a comprehensive quality management system, which includes a state-of-the-art water treatment system to ensure high water purity and a robust quality control program to promptly address any discrepancies. It is essential for laboratories to identify and understand the nature and extent of potential interferences to avoid inaccurate clinical decisions and inappropriate treatments.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

- [1] Wiener Klinische Wochenschrift. Supplementum. Determination of electrolytes in serum and plasma. PMID: 1502823.
- [2] Rant MS, Ross JW Jr. Potassium ion-selective electrode with high selectivity for potassium over sodium.
- [3] Hirst AD, Stevens JF. Electrodes in clinical chemistry. Ann Clin Biochem.
- [4] Dimeski G. Interference testing. Clin Biochem Rev. August 2008; 29(Suppl 1): S43–8.
- [5] Malinowska E, Meyerhoff ME. Effects of nonionic surfactants on the potentiometric response of ion-selective polymeric membrane electrodes used for blood electrolyte measurements. Anal Chem.
- [6] Cook JD, Koch TR, Knoblock EC. Catheter-related erroneous electrolyte results. Clin Chem.
- [7] Lam SH, Chan MHM, Ng PC, et al. Hand cleanliness and point-of-care electrolyte analysis. Pathology.
- [8] Dybko A. Measurement errors in chemical sensors.
- [9] Rumenjak V, Milardovic S, Kruhak I, Grabaric B. Potential measurement errors in clinical blood electrolyte potentiometric (ISE) analyzers. Clin Chim Acta.

- [10] Bjister P, Vader HL, Vink CJ. Impact of erythrocytes on the direct potentiometric determination of sodium and potassium. Ann Clin Biochem.
- [11] Ladenson JH, Apple FS, Koch DD. Pseudohyponatremia caused by hyperlipidemia: a method-dependent error. Ann Intern Med.
- [12] Dimeski G, Barnett RJ. Influence of total protein concentration on plasma sodium, potassium, and chloride measurements using an indirect ion-selective electrode system. Crit Care & Resus.
- [13] Vermeer HJ, Steen G, Naus AJ, Goevaerts B, Agricola PT, Schoenmakers CH. Adjusting patient results for Beckman Coulter LX-20 assays affected by interference from hemoglobin, bilirubin, or lipids: a practical approach. Clin Chem Lab.
- [14] National Institutes of Health (NIH). Laboratory Water: Its Importance and Application. 2013; 1-22. Available at: http://orf.od.nih.gov/PoliciesAndGuidelines/Documents/DTR%20White%20Papers/Laboratory%20Water-Its%20Importance%20and%20Application-March-2013_508.pdf. Accessed November 12, 2014.
- [15] Interest of water quality in Clinical laboratory: Experience from the central laboratory of Mohammed VI University Hospital of Oujda. September 2022. DOI: 10.1016/j.matpr.2022.09.128.
- [16] ISO International Organization for Standardization.
- [17] Guide de bonne exécution des analyses de biologie médicale (GBEA).
- [18] ISO 15189 International Organization for Standardization.
- [19] US Department of Health and Human Services. Biosafety in Microbiological and Biomedical Laboratories. 5th ed. Washington, DC: US Government Printing Office; December 2009.
- [20] Ladenson JH, Apple FS, Aguanno JJ, Koch DD. Comparison of sodium measurement techniques in multiple myeloma. Clin Chem.