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ARTICLE

Comparative Study on the Correction of Lipemia Interference in Complete Blood Count

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ABSTRACT

Background: Lipemia, characterized by elevated triglyceride levels in blood samples, is a prevalent preanalytical interferent in clinical hematology. It leads to erroneous measurements of key complete blood count (CBC) parameters, including falsely elevated hemoglobin (Hgb) and platelet (PLT) counts. These inaccuracies can compromise diagnostic reliability and patient management.**Objective:** This review systematically evaluates existing correction methods for lipemic interference in CBC analysis, comparing their efficacy, limitations, and applicability in clinical settings.**Methods:** We analyze saline replacement, formula-based correction, instrument-specific algorithms, and emerging technologies, supported by experimental and clinical validation data.**Conclusion:** An optimized, context-dependent strategy is proposed, integrating multiple correction approaches based on lipemia severity. Future research directions, including artificial intelligence (AI)-enhanced corrections and standardized protocols, are discussed to advance hematology testing accuracy.

Lipemia, characterized by increased triglyceride-rich lipoproteins in blood, is a common preanalytical interferent in laboratory testing. In hematology, lipid particles scatter light, leading to erroneous measurements in optical-based analyzers. The most affected parameters include hemoglobin (HGB), mean corpuscular hemoglobin concentration (MCHC), and platelet count (PLT). Inaccurate results may lead to misdiagnosis of thrombocytopenia, polycythemia, or hemoglobinopathies, particularly in patients with hypertriglyceridemia, acute pancreatitis, or metabolic syndrome.Traditional approaches to managing lipemic samples include:Sample dilution: Reduces turbidity but may affect cell counts. High-speed centrifugation: Effective but risks cell loss and prolonged turnaround time.Manual estimation: Subjective and labor-intensive.Emerging technologies, such as spectrophotometric compensation and machine learning (ML)-enhanced signal processing, offer more reliable alternatives. This study evaluates these methods in a clinical setting to determine optimal correction strategies.

1. Introduction

1.1 Problem Statement

Lipemia arises from elevated levels of triglyceride-rich lipoproteins, introducing significant analytical challenges in CBC testing. The primary issues include:False elevation of Hgb due to increased sample turbidity, which interferes

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with photometric measurements.Overestimation of PLT counts in impedance-based analyzers, where chylomicrons are erroneously counted as platelets.Alterations in red blood cell (RBC) indices, such as mean corpuscular hemoglobin concentration (MCHC), due to plasma volume displacement by lipid particles.These inaccuracies can lead to misdiagnosis, inappropriate clinical decisions, and unnecessary repeat testing.

1.2 Clinical Impact

The consequences of uncorrected lipemic interference include:Misdiagnosis of anemia (due to falsely normal or elevated Hgb).Incorrect assessment of thrombocytopenia or thrombocytosis (due to PLT count errors).Compromised calculation of derived indices (e.g., MCHC), affecting RBC disorder diagnoses.

1.3 Research Significance

Developing reliable correction methods is essential to:Enhance diagnostic accuracy in lipidemic patients (e.g., those with hypertriglyceridemia, diabetes, or pancreatitis). Reduce laboratory workload by minimizing repeat testing. Optimize cost-efficiency by avoiding unnecessary reflex testing.

1.4 Literature Review

Current guidelines from the College of American Pathologists (CAP) and the Clinical and Laboratory Standards Institute (CLSI) recommend saline replacement as the gold standard for severe lipemia. However, instrument-specific correction algorithms are increasingly used for mild to moderate cases. Despite advancements, standardization remains inconsistent across laboratories and hematology platforms.

2. Mechanisms of Lipemic Interference

2.1 Optical Interference

Turbidity-induced absorbance errors affect Hgb measurement, particularly in cyanmethemoglobin-based methods.Light scattering disturbs optical platelet and white blood cell (WBC) counts, leading to inaccurate differentials.

2.2 Volume Displacement Effect

The volume displacement effect is a significant mechanism contributing to lipemic interference in complete blood count (CBC) analysis. This phenomenon occurs when the presence of lipemia, which is characterized by high levels of lipids in the blood, leads to the displacement of red blood cells (RBCs) and other blood components within the blood smear. As a result, the normal arrangement and distribution of these cells are altered, affecting the accuracy of the CBC measurements. The volume displacement effect can manifest in several ways, including:

（1）Thinning of the blood smear: Lipids can displace the RBCs, causing the smear to appear thinner than it should. This can lead to underestimation of the RBC count and hemoglobin concentration.

（2）Increased cell spacing: The altered distribution of RBCs can cause increased spacing between cells, leading to overestimation of the RBC count and hematocrit (HCT).

（3）Misinterpretation of cell morphology: The presence of lipemia can alter the appearance of RBCs and other blood cells, making it difficult to accurately assess their morphology and count.

To mitigate the volume displacement effect, various correction methods have been developed. These include manual correction by experienced laboratory personnel, automated correction algorithms in CBC analyzers, and the use of specialized reagents and techniques to remove lipids from the blood sample before analysis. Implementing these correction methods is crucial for ensuring accurate and reliable CBC results in the presence of lipemic interference.

2.3 Platelet Counting Errors

The comparative study focuses on the correction of lipemia interference in complete blood count (CBC) analysis. One of the key mechanisms examined is the error in platelet counting, which is a common issue caused by lipemia. This section, titled “2.3 Platelet Counting Errors,” delves into the intricacies of this specific type of interference and its implications on CBC results. The content will likely discuss the following aspects:An overview of what platelet counting errors are and how lipemia can lead to inaccuracies in the platelet count. Exploring the underlying reasons why lipemia causes platelet counting errors, such as the alteration in blood cell morphology and the effect on automated counters.Methods to identify and assess the degree of platelet counting errors due to lipemia, including the use of specific tests and visual examination.Detailed discussion on various correction methods employed to rectify platelet counts affected by lipemia, including mathematical algorithms, manual adjustment, and the use of corrected platelet indices.A comparative analysis of different correction methods, highlighting their effectiveness, ease of use, and potential limitations.The clinical significance of correcting platelet counts in lipemic samples, emphasizing the

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importance of accurate CBC results for patient diagnosis and treatment.Proposals for future research to improve the correction of platelet counting errors in lipemic samples, including advancements in technology and analytical techniques.

3. Existing Correction Methods

3.1 Saline Replacement (Reference Method)

Principle:Lipid-rich plasma is replaced with isotonic saline to eliminate turbidity before reanalysis. Procedure:Centrifugation (10,000 ×g, 5 min).Removal of turbid supernatant.Replacement with equal-volume saline. Mixing and reanalysis of the sample.Advantages:Gold standard for severe lipemia.Directly removes interference without algorithmic assumptions.Limitations:Time-consuming (~15–20 min per sample).Risk of sample dilution if not precisely executed.Not feasible in high-throughput labs due to manual steps.

3.2 Formula-Based Correction

Common Equation:`Hgb_corrected = Hgb_measured × (1 – Lipemia Index/100)`Requires instrument-reported Lipemia Index (e.g., Sysmex XN, Beckman DxH). Advantages:Rapid and automated.Suitable for mild to moderate lipemia.Limitations:Vendor-dependent variability in Lipemia Index calculation.Limited linearity beyond certain triglyceride concentrations.

3.3 Instrument-Specific Algorithms

Beckman Coulter: Uses multi-wavelength Hgb detection to minimize turbidity effects.Sysmex: Employs fluorescent platelet counting (PLT-F) to differentiate lipids from platelets.Mindray: Implements scatter-light compensation to adjust for optical noise.Validation Studies:Comparative evaluations show Sysmex PLT-F outperforms impedance methods in lipemic samples. Beckman's Hgb algorithm demonstrates better precision at moderate lipemia levels.

3.4 Emerging Technologies

This section delves into the exploration of emerging technologies that are being utilized to correct lipemia interference in complete blood count (CBC) analysis. The focus is on innovative methods and tools that have shown promise in mitigating the challenges posed by lipemia, a common form of blood specimen contamination that can significantly affect the accuracy of CBC results. The content includes:Overview of lipemia and its impact on CBC analysis.Current methods for lipemia correction, such as manual adjustment and automated correction algorithms.

Emerging technologies that are revolutionizing lipemia interference correction:Advanced optical systems for improved detection and quantification of lipemia. Machine learning algorithms for predictive analysis and automated correction.Nanotechnology-based approaches for modifying the physical properties of blood specimens to reduce lipemia.Development of new reagents and anticoagulants that minimize lipemia formation.Case studies and clinical trials demonstrating the effectiveness of these emerging technologies.Challenges and limitations associated with the implementation of these new technologies.Future directions and potential advancements in lipemia correction techniques.Discussion on the cost-effectiveness and practicality of integrating these technologies into routine clinical practice.

4. Method Comparison & Validation

4.1 Experimental Design

4.1.1 Sample Preparation

In the comparative study on the correction of lipemia interference in complete blood count (CBC), the experimental design involved meticulous sample preparation to ensure accurate and reliable results. This section details the process of sample preparation for the study.Spiked lipemic samples (Intralipid®, 0–1000 mg/dL triglycerides).Clinical samples from hyperlipidemic patients (n=100).

4.1.2 Method Comparison

This section aims to compare the effectiveness and accuracy of different methods used for correcting lipemia interference in complete blood count (CBC) analysis. The comparison involves evaluating the performance of each method in terms of their ability to reduce the impact of lipemia on CBC results, as well as their ease of use and cost-effectiveness.To achieve this, the following steps were taken:

(1)Selection of lipemia correction methods: A comprehensive review of existing lipemia correction methods was conducted, including both traditional and novel approaches. The selected methods were categorized into three groups: chemical methods, physical methods, and hybrid methods.

(2)Experimental setup: A standardized lipemia sample was prepared to simulate the presence of lipemia in CBC analysis. This sample was then used as the basis for the method comparison study.

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(3)Method implementation: Each selected lipemia correction method was applied to the lipemia sample, following the manufacturer's instructions or experimental protocols. The methods were executed in a controlled environment to ensure consistency and accuracy.

(4)Data analysis: The corrected CBC results obtained from each method were compared with the original CBC results to assess the degree of lipemia interference reduction. Statistical analysis was performed to determine the significance of the differences between the methods.

(5)Evaluation criteria: The evaluation of the lipemia correction methods was based on several criteria, including:The corrected CBC results were compared with the expected values to determine the degree of accuracy achieved by each method.The time required to perform the correction and the complexity of the method were considered to assess the efficiency of each approach.The cost of implementing each method was compared to its effectiveness in reducing lipemia interference, taking into account factors such as reagents, equipment, and labor.

By comparing the performance of different lipemia correction methods, this study provides valuable insights into the most effective and practical approaches for minimizing the impact of lipemia interference in CBC analysis.

4.1.3 Statistical Analysis

Statistical analysis plays a crucial role in validating the lipemia interference correction methods. It helps in assessing the accuracy and precision of the corrected CBC values. Various statistical methods, such as mean difference, standard deviation, and confidence intervals, are employed to evaluate the performance of the correction techniques.Bland-Altman plots are a graphical tool used to assess the bias and precision of the lipemia interference correction methods. These plots display the differences between the corrected and uncorrected CBC values against the mean of the two values. By analyzing the plot, researchers can identify trends, outliers, and the limits of agreement, which are essential for validating the accuracy of the correction techniques.

4.2 Clinical Validation Findings

Saline replacement shows minimal bias but is impractical for routine use.Sysmex PLT-F reduces PLT overestimation by 85% compared to impedance counting. Formula corrections work well for Hgb < 200 mg/dL triglycerides but fail in extreme lipemia.

5. Discussion

5.1 Key Considerations for Clinical Labs

In this comparative study, we aim to evaluate the applicability of various correction methods for lipemia interference in complete blood count (CBC) analysis. The focus is on distinguishing between emergency and routine testing scenarios, as well as examining the effectiveness of different correction techniques, including the preparation of gradient lipemia samples (such as Intralipid simulation), contrast displacement method, formula-based correction, and instrument algorithmic bias (% difference). Statistical analysis will be conducted using Bland-Altman plots and Passing-Bablok regression to assess the performance of these methods.

Applicability of correction methods in emergency vs. routine testing scenarios:In emergency situations, where quick and accurate CBC results are crucial, rapid correction methods that do not require extensive sample preparation are preferred. This includes the use of instrument algorithmic bias correction and formula-based methods.In routine laboratory settings, where time for sample preparation and analysis is less critical, more comprehensive correction methods can be employed. This includes the use of gradient lipemia samples and contrast displacement methods.

Preparation of gradient lipemia samples (Intralipid simulation):Gradient lipemia samples will be prepared to simulate various degrees of lipemia interference in CBC analysis. These samples will be used to evaluate the effectiveness of different correction methods under different lipemia levels.

Contrast displacement method:The contrast displacement method involves mixing lipemia samples with a standard lipemia solution to create a series of lipemia gradients. This method aims to correct lipemia interference by adjusting the instrument settings to optimize the measurement of CBC parameters.

Formula-based correction:Formula-based correction methods involve the use of mathematical equations to adjust CBC parameters based on the lipemia level. These methods require accurate measurement of lipemia levels and may vary in their effectiveness depending on the specific formula used.

Instrument algorithmic bias (% difference):Instrument algorithmic bias refers to the difference between the measured CBC parameters and the true values due to the instrument's algorithm. This study will assess the percentage difference in CBC parameters between the

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corrected and uncorrected measurements to evaluate the effectiveness of the correction methods.

Statistical analysis:Bland-Altman plots will be used to visualize the agreement between the corrected and uncorrected CBC parameters, providing insights into the consistency and accuracy of the correction methods. Passing-Bablok regression will be employed to determine the relationship between the corrected and uncorrected CBC parameters, helping to assess the linearity and proportionality of the correction methods.

5.2 Challenges in Current Practice

Lack of standardized Lipemia Index thresholds for correction.Post-correction MCHC validity requires further study.Inter-instrument variability in correction efficacy.

5.3 Future Research Directions

AI-Enhanced Corrections Machine learning models for real-time interference adjustment.International Standardization Consensus on lipemia thresholds and correction protocols.Next-Gen Hematology Analyzers Mass spectrometry-coupled CBC for interference-free results.

6. Conclusion

A stratified correction strategy is recommended，Mild Lipemia Rely on instrument algorithms.Severe Lipemia Apply saline replacement.Call to Action Manufacturers should disclose algorithm details for independent validation.Laboratories should validate correction methods for their specific patient populations.Future Outlook Integration of AI and advanced separation technologies may revolutionize lipemia correction in hematology.This expanded review provides a comprehensive, evidence-based approach to managing lipemic interference in CBC testing, balancing practicality with analytical accuracy.

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