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REVIEW ARTICLE

Pre-analytical criteria in blood culture sample collection

Criterios preanalíticos en la toma de muestras de hemocultivo

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Abstract The pre-analytical process in blood culture sample collection is essential to ensure the accuracy in detecting pathogenic microorganisms in blood, which is crucial in diagnosing bacteremia and fungemia. This article reviews the main pre-analytical criteria associated with sample collection, considering aspects such as proper puncture site selection, strict aseptic techniques, blood volume collected, timing with febrile episodes, and the optimal number of samples. Sample contamination remains a significant challenge, impacting both the validity of results and the patient's clinical management. Evidence suggests that effectively disinfecting the site with 70% alcohol and chlorhexidine, sterile materials, and staff training are essential to minimize errors. Furthermore, collecting at least two blood cultures to increase diagnostic sensitivity is emphasized. This article emphasizes that strict adherence to pre-analytical criteria optimizes clinical laboratory resources and enhances patient care while improving the results' quality.

Keywords blood cultures, pre-analytical phase, good clinical laboratory practices.

Resumen El proceso preanalítico en la toma de muestras para hemocultivos es fundamental para garantizar la precisión en la detección de microorganismos patógenos en sangre, siendo crucial en el diagnóstico de bacteriemias y fungemias. Este artículo revisa los principales criterios preanalíticos asociados a la obtención de muestras, considerando aspectos como la selección adecuada del sitio de punción, técnicas de asepsia estrictas, volumen de sangre recolectado, sincronización con episodios febriles y el número óptimo de tandas. La contaminación de las muestras sigue siendo un desafío significativo, impactando tanto en la validez de los resultados como en la gestión clínica del paciente. La evidencia sugiere que prácticas como la desinfección efectiva del sitio con alcohol al 70 % y clorhexidina, el uso de materiales estériles, y la capacitación del personal sanitario, son esenciales para minimizar errores. Además, se destaca la importancia de la recolección de al menos dos tandas de hemocultivos para aumentar la sensibilidad diagnóstica. Este artículo enfatiza que la adherencia rigurosa a los criterios preanalíticos, además de mejorar la calidad de los resultados, optimiza los recursos del laboratorio clínico y la atención del paciente.

Palabras clave hemocultivos, fase preanalítica, buenas prácticas de laboratorio clínico.

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PUBLIS EDITORIAL

Introduction

Blood cultures are a diagnostic tool in the clinical laboratory to identify the presence of microorganisms in the blood. They are part of the standard recommendations for managing sepsis, a condition with a mortality rate ranging from 25.5 to 32% in patients in intensive care units and 35% in hospitalized patients. Studies suggest that, in Latin America, the prevalence of sepsis and the associated mortality could be higher than in developed countries (Cohen et al., 2015; Dellinger et al., 2012; Vincent et al., 2014).

One in five deaths worldwide is related to sepsis, disproportionately affecting children in impoverished areas. A study revealed that in 2017, 48.9 million cases of sepsis were recorded globally, with 11 million deaths accounting for 20% of all deaths worldwide (WHO, 2020); 85% of sepsis cases occurred in low- and middle-income countries. Sepsis occurs when organs stop functioning properly due to an uncontrolled immune response to an infection. Although sepsis does not always result in death, it can leave severe sequelae in survivors (WHO, 2020).

Blood cultures, as part of the recommended measures for managing sepsis, have been associated with reduced mortality when performed appropriately (Levy et al., 2012). The clinical laboratory encompasses the pre-analytical, analytical, and post-analytical phases. Some recommendations highlight key aspects such as incubation time, the number and type of bottles, blood volume, reporting contaminants, and the limitations of current systems for blood cultures (Weinstein & Doern, 2011).

Optimizing this process should focus on three main objectives: improving the isolation and identification of true pathogens, reducing the presence of contaminants, and enhancing the detection of infections associated with central catheters. Inefficient antisepsis processes have increased the likelihood of isolating contaminants in blood cultures, leading to diagnostic uncertainty, prolonged hospital stays, and increased healthcare costs (Maldonado et al., 2018).

This article reviews the main pre-analytical criteria associated with sample collection, considering aspects such as appropriate site selection for puncture, strict aseptic techniques, blood volume collected, synchronization with febrile episodes, and the optimal number of sets.

Pre-analytical phase

The pre-analytical phase is considered the critical stage in the blood culture process. During this phase, failures are most likely to occur due to errors made by the responsible staff, which compromises the reliability of the results. Previously, this process was entirely manual, but in developed cities, automation and robotization have started to be implemented to improve the accuracy and efficiency of this stage (Aray-García et al., 2023).

Despite technological advances, errors during this phase persist globally, affecting the quality of blood culture results. A reduction in the incidence of these errors has been observed thanks to technological innovations (Aray-García et al., 2023). Maldonado et al. (2018), in a study at Hospital Ángeles Pedregal in Mexico, found that of 1,598 blood cultures, only 213 were positive, representing a success rate of 13%. The most frequent microorganisms found were Escherichia coli (43%), of which 35 (16%) were resistant to extended-spectrum beta-lactamases (ESBL), Burkholderia cepacia (6%), and Enterococcus faecalis (5%) in the Gram-negative group, and Staphylococcus epidermidis (9%) and Staphylococcus aureus (6%) in the Gram-positive group (Enberg et al., 2020).

The research at Hospital Ángeles Pedregal in Mexico City concluded that the rate of positive blood cultures was slightly higher than that reported in previous studies. They observed a higher frequency of positivity for E. coli, supporting the idea that microbial populations vary by hospital (Enberg et al., 2020). In this context, Maldonado et al. (2018) emphasized the need for all institutions to have written protocols that include detailed procedures for sample collection and the techniques and products used in antisepsis.

Maldonado et al. (2018) evaluated various institutional protocols and noted that 66.7% of the protocols specified the number of bottles and blood volume per blood culture set, and 60.0% included sample rejection criteria. However, these studies revealed that not all protocols contain the information necessary to ensure a correct pre-analytical phase (Maldonado et al., 2018).

On the other hand, the SEIMC (Spanish Society of Infectious Diseases and Clinical Microbiology), in its Clinical Microbiology Procedures, highlighted that the detection of bacteremia and fungemia is a priority in the Clinical Microbiology Service of health institutions due to their diagnostic and prognostic relevance. These processes are associated with high mortality (10 to 30%), depending on the type of patient, the origin of the infection, and initial management (Aray-García et al., 2023).

Sepsis requires a blood culture as a first-line test for diagnosis; however, literature indicates that the sensitivity for detecting bacteremia in blood cultures is low, with a growth rate of less than 10% (Maldonado et al., 2018).

The laboratory study process begins with the clinician's request for analysis, who must provide detailed and accurate information to ensure the quality of the results. The request should include essential data such as a unique identification code (request number), type of request (routine or urgent), and patient identification details (name, surname, medical record number, etc.) (Plebani, 2015). It is essential to include relevant clinical and demographic information, such as date of birth, gender, and diagnosis, to facilitate proper interpretation of results (Rojo et al., 2010).

Administrative data must also be included, such as the requesting physician, the report destination, and the administrative person responsible for the request (Vélez-Cevallos et al., 2023). Transcribing this data into the laboratory information system (LIS) can lead to errors if not done carefully, highlighting the importance of clear protocols and agreements between clinicians and the laboratory (Rodríguez, 2021).

The Clinical Laboratory Best Practices Guide by the Ministry of Public Health (MSP) of Ecuador, in its Form No. 15: Request for Examinations, establishes that the basic required information includes patient data (name, surname, ID number, age, gender, contact address or phone), requesting physician's information (name, phone, address, and professional code), and details of the requested examinations (such as previous studies, medication use, drug monitoring, type of biological sample, and date/time of sample collection) (Rojo et al., 2010). In institutions with digital systems, professionals can make direct requests through the laboratory information system (LIS) or web platforms to facilitate the management process and avoid transcription errors (Maldonado et al., 2018).

Once the analysis request and patient appointment are made, the next step is sample collection, which can be performed by nursing staff if the patient is already admitted (Aray-García et al., 2023). According to the guidelines of the "Dr. Abel Gilbert" Specialty Hospital in Guayaquil, based on the Ministry of Public Health (MSP) guidelines, it is recommended to take two blood cultures within 24 hours, with intervals of at least 20 to 30 minutes between them, and from different puncture sites.

Samples should be collected one hour before the febrile peak or at the onset of fever. They should be taken before administering antibiotics or at least one hour before the next dose. The recommended volume is 8 to 10 mL for adults and 1 to 3 mL for children, and each sample should be properly labeled with its number and time of collection. It is essential to choose the appropriate type of bottle according to the suspected microorganism (Acosta-Gnass, 2011).

The procedure includes hand hygiene, selecting the puncture site, and disinfecting the area with 70° alcohol and povidone-iodine solution. The bottle cap must be disinfected, and the samples should be inoculated without introducing air. Finally, the samples should be sent immediately to the laboratory or, if impossible, placed in an incubation oven at 35 °C in the on-call laboratory. They should never be refrigerated (Acosta-Gnass, 2011). It is important to note that there are several differences between the recommendations described by the Ministry of Public Health (MSP) of Ecuador and the SEIMC (Table 1).

Proper sample collection is crucial, as errors in extraction or handling can significantly affect the analysis results (Rodríguez, 2021). According to SEIMC, despite no universal guidelines, blood cultures are generally recommended for patients with fever (≥38 ºC), chills, leukocytosis, leukopenia, thrombocytopenia, signs of sepsis, or suspected endocarditis. Blood cultures should also be performed when bacteremia originating from a catheter is suspected (Rodríguez et al., 2017).

Once obtained, samples must be organized and transported correctly, ensuring correct identification of the samples, the request form, and the patient (Rojo et al., 2010). Transport

Table 1. Differences between the sample collection recommendations from the Ministry of Public Health of Ecuador and SEIMC

Indicator	MSP Ecuador	SEIMC
Sample volume	In children 1 to 3 mL and 8 to 10 mL in adults	Small children require between 1 and 5 mL (1:5 dilution), adults 10-20 mL (1:10 dilution).
Packaging	Does not specify	Children: 1 bottle (aerobic), Adults: 2 bottles (aerobic, anaerobic).
Antiseptic action	Application of povidone iodine solution, concentrically around the puncture site. Allow each to act for 30 to 60 seconds.	Approximately 30 seconds for chlorhexidine and between 1.5 and 2 minutes if povidone is used.

should be as quick as possible, avoiding interferences such as agitation (which can cause hemolysis) or exposure to light (to prevent degradation of components like bilirubin) (Vélez-Cevallos et al., 2023). In the case of blood cultures, it is recommended to extract blood from veins, not from catheters or umbilical cord blood, and to take samples from different puncture sites to avoid contamination (Rojo et al., 2010).

The main challenge in interpreting blood cultures is possible contamination with the skin's microbial flora during extraction. To reduce this risk, it is essential to prepare the skin meticulously, use appropriate equipment like masks and gloves, and, if necessary, perform the extraction with additional protective measures (Callejas-Díaz et al., 2022). Microorganisms commonly associated with contamination include coagulase-negative Staphylococcus, Bacillus spp., and Propionibacterium acnes, among others, although their presence in a single sample per patient should not compromise the results (Callejas-Díaz et al., 2022).

Conclusions

The pre-analytical phase in the blood culture process is crucial to ensure the quality and reliability of results, but it is also one of the most error-prone stages. Despite technological advances such as automation and robotics, errors resulting from human handling and the need for clear and universal protocols persist. The differences between the recommendations of organizations like the Ministry of Public Health of Ecuador and SEIMC highlight the need to standardize procedures and improve staff training. Proper collection, transport, and processing of samples, as well as adequate antisepsis and optimal volumes, are key elements to minimize errors and prevent contamination. Additionally, institutions need to implement detailed written protocols that cover all aspects of this phase, from sample collection to handling in the laboratory. Adopting these best practices will improve the detection of bacteremia and fungemia, optimizing diagnoses and clinical treatments related to sepsis and other severe infections.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Author contributions

Conceptualization: Carlos E. Mera, Jean P. Sanclemente. **Research:** Carlos E. Mera, Jean P. Sanclemente, Ivón Howland. **Methodology:** Ivón Howland. **Supervision:** Ivón Howland. **Validation:** Ivón Howland. **Writing the original draft:** Carlos E. Mera, Jean P. Sanclemente, Ivón Howland. **Writing, review and editing:** Carlos E. Mera, Jean P. Sanclemente, Ivón Howland.

Data availability statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Statement on the use of AI

The authors acknowledge the use of generative AI and AI-assisted technologies to improve the readability and clarity of the article.

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