

ORIGINAL

## Evaluation of CSF Physicochemical Analysis in The Diagnosis of CNS Infections in Post-Surgical Patients

### Valoración del Físicoquímico del LCR en el Diagnóstico de Infecciones del SNC en Pacientes Postquirúrgicos

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#### ABSTRACT

**Introduction:** central nervous system (CNS) infections in post-surgical patients represent a serious complication with high morbidity and mortality. The physicochemical analysis of cerebrospinal fluid (CSF) is a key diagnostic tool that allows for the evaluation of parameters such as glucose, proteins, and lactate to detect infections. With the development of molecular techniques, such as PCR, the accuracy in pathogen detection has improved. However, there are still questions regarding the reliability of traditional methods compared to these advanced techniques, especially in patients who have received prior antibiotic treatment.

**Objectives:** the primary objective of this study is to evaluate the reliability of the physicochemical analysis of CSF as a diagnostic tool for CNS infections in post-surgical patients and to compare it with alternative methods such as PCR, bacterial cultures, and biological markers. The study aims to determine the sensitivity and specificity of each method to improve diagnostic accuracy in this clinical context.

**Method:** this study is a systematic literature review that includes studies evaluating the physicochemical analysis of CSF, PCR, and bacterial cultures in post-surgical patients with suspected CNS infection. Scientific databases were used, applying specific inclusion and exclusion criteria to ensure the relevance and quality of the selected studies.

**Results:** the results suggest that although the physicochemical analysis of CSF is useful as an initial tool, it has limitations in terms of sensitivity and specificity in patients who have received antibiotic treatment, with sensitivity ranging between 60 % and 70 %. In contrast, multiplex PCR offers superior sensitivity and specificity, reaching 92 % and 98 %, respectively. The combination of methods, including the use of biomarkers such as procalcitonin, improves diagnostic accuracy by 30 % compared to traditional physicochemical analysis.

**Conclusion:** the physicochemical analysis of CSF remains useful as an initial test, but its effectiveness is limited in post-surgical patients who have received antibiotic treatment. Combining this analysis with molecular techniques and biomarkers significantly enhances the accuracy and speed of diagnosis, thereby supporting a comprehensive diagnostic approach that optimizes the clinical management of CNS infections in the post-surgical context.

**Keywords:** Central Nervous System Infections; Post-Surgical Diagnosis; PCR and Cultures; Meningitis; CSF Analysis.

#### RESUMEN

**Introducción:** las infecciones del sistema nervioso central (SNC) en pacientes postquirúrgicos representan una complicación grave con alta morbilidad y mortalidad. El análisis físicoquímico del líquido cefalorraquídeo (LCR) es una herramienta diagnóstica clave que permite evaluar parámetros como la glucosa, proteínas y

lactato para la detección de infecciones. Con el desarrollo de técnicas moleculares, como la PCR, se ha mejorado la precisión en la detección de patógenos. No obstante, existen dudas sobre la fiabilidad de los métodos tradicionales en comparación con estas técnicas avanzadas, especialmente en pacientes que han recibido tratamiento antibiótico previo.

**Objetivo:** el objetivo principal de este estudio es evaluar la fiabilidad del análisis fisicoquímico del LCR como herramienta diagnóstica en infecciones del SNC en pacientes postquirúrgicos y compararlo con métodos alternativos como la PCR, cultivos bacterianos y marcadores biológicos. Se busca determinar la sensibilidad y especificidad de cada método para mejorar la precisión diagnóstica en este contexto clínico.

**Método:** este estudio es una revisión sistemática de literatura que incluye estudios que evalúan el análisis fisicoquímico del LCR, la PCR y los cultivos bacterianos en pacientes postquirúrgicos con sospecha de infección del SNC. Se utilizaron bases de datos científicas, aplicando criterios de inclusión y exclusión específicos para asegurar la relevancia y calidad de los estudios seleccionados.

**Resultados:** los resultados sugieren que el análisis fisicoquímico del LCR, aunque útil como herramienta inicial, presenta limitaciones en términos de sensibilidad y especificidad en pacientes que han recibido tratamiento antibiótico, mostrando una sensibilidad entre el 60 % y el 70 %. En contraste, la PCR multiplex ofrece una sensibilidad y especificidad superiores, alcanzando el 92 % y 98 %, respectivamente. La combinación de métodos, incluyendo el uso de biomarcadores como la procalcitonina, mejora la precisión diagnóstica en un 30 % en comparación con el análisis fisicoquímico tradicional.

**Conclusión:** el análisis fisicoquímico del LCR sigue siendo útil como prueba inicial, pero su eficacia es limitada en pacientes postquirúrgicos con tratamiento antibiótico. La combinación con técnicas moleculares y biomarcadores mejora significativamente la precisión y rapidez del diagnóstico, proponiéndose así un enfoque diagnóstico integral que optimice el manejo clínico de las infecciones del SNC en el contexto postoperatorio.

**Palabras clave:** Infecciones del Sistema Nervioso Central; Diagnóstico Postquirúrgico; PCR y Cultivos; Meningitis; Análisis del LCR.

## INTRODUCTION

Central nervous system (CNS) infections in post-surgical patients represent a significant clinical challenge due to their high morbidity, diagnostic complexity, and the need for timely therapeutic interventions. In this context, cerebrospinal fluid (CSF) analysis remains one of the most widely used diagnostic tools. This analysis, which includes the evaluation of physicochemical parameters such as glucose, proteins, lactate, and pleocytosis, provides relevant initial information for detecting infections such as meningitis or brain abscesses. However, its diagnostic efficacy can be compromised by multiple factors, especially in patients who have received prior antibiotic treatment, significantly reducing traditional CSF analysis's sensitivity and specificity.

Given this scenario, this systematic review is intended as a solid methodological tool to synthesize the available scientific evidence regarding the diagnostic value of physicochemical analysis of CSF in post-surgical patients with suspected CNS infection. Through a rigorous analysis of the literature published between 2000 and 2024, we aim not only to evaluate the usefulness of traditional methods but also to compare them with molecular techniques such as PCR and the detection of biomarkers such as procalcitonin, which have shown promising results in terms of diagnostic accuracy.

The methodological design includes selecting relevant studies in English, Spanish, and Portuguese using recognized biomedical databases such as PubMed, SciELO, Google Scholar, Oxford Academic, and Elsevier. Research that meets strict inclusion criteria focusing on post-surgical patients and reporting diagnostic metrics, such as sensitivity, specificity, or predictive values, will be included. In turn, articles of low quality, without full access, or that do not fit the objective of this review will be excluded.

This work seeks to provide a critical and up-to-date view of the real value of CSF physicochemical analysis in the post-surgical clinical setting, pointing out its limitations, advantages, and possible diagnostic complements. Integrating different methods will allow us to establish informed recommendations for better clinical decision-making, optimizing the management of CNS infections in a context where diagnostic accuracy and speed are essential to improve patient outcomes.

Is physicochemical analysis of cerebrospinal fluid reliable as a first-line tool for diagnosing central nervous system infections in post-surgical patients compared to other methods, such as multiplex PCR and bacterial cultures, considering the possible limitations of standard CSF testing after antibiotic administration?

## Objective

This study evaluates the reliability of cerebrospinal fluid physicochemical analysis as a diagnostic tool for central nervous system infections in post-surgical patients compared to alternative methods such as PCR, other

molecular methods, and cultures.

## **METHOD**

### **Study design**

This systematic review will focus on assessing physical-chemical analyses of CSF in diagnosing central nervous system infections in post-surgical patients. This study design allows for a synthesis and critical analysis of the available literature to provide an accurate and evidence-based answer to the research question.

This type of study (systematic review) was chosen because it integrates the findings of multiple previous evaluations related to the topic. Through this approach, observational studies, clinical trials, and retrospective analyses that evaluate the physicochemical characteristics of CSF (such as glucose, proteins, and lactate, among others) and their role in the identification and diagnosis of CNS infections, particularly in the context of post-surgical patients, will be collected.

### **Study population**

The study population will consist of scientific articles published in the “primary search source” mentioned above on assessing CSF physicochemical properties in diagnosing CNS infections in post-surgical patients.

In addition to the bibliographic search strategy already mentioned, rigorous inclusion and exclusion criteria will be used to ensure the relevance and quality of the studies included.

### **Inclusion criteria**

- Articles published in English, Spanish, or Portuguese found in the primary search source related to CSF assessment in post-surgical patients
- Studies that include post-surgical patients with suspected CNS infection
- Articles that report the use of CSF physicochemical analysis for diagnosis in a post-surgical context
- Studies comparing the results of physicochemical analysis with molecular methods and cultures
- Studies with clinical results, including measures of sensitivity, specificity, or predictive values
- Articles published between 2000 and 2024

### **Exclusion Criteria**

- Studies evaluating CSF exclusively outside the context of CNS infection
- Articles without full access to the text or incomplete relevant information
- Studies limited to a tiny population
- Publications in databases or journals of questionable quality
- Articles evaluating non-human populations

### **Sample selection and size**

The sample will comprise studies selected systematically from the databases above. The selection will follow the established inclusion and exclusion criteria, reviewing titles, abstracts, and full texts. No minimum sample size will be established, as the size will depend on the number of relevant studies.

### **Data collection plan**

MESH terms (mentioned in the literature search strategy) will be used for data collection to ensure accuracy and relevance in the search for studies on the physicochemical analysis of CSF and its role in diagnosing CNS infections in post-surgical patients. Keywords will be used to tailor the search to the survey context. Searches will be conducted in databases such as PubMed, SciELO, Google Scholar, Oxford Academic, and Elsevier, allowing for the inclusion of studies published between 2000 and 2024 that address traditional CSF analysis methods and modern techniques such as PCR. Articles that meet the aforementioned inclusion and exclusion criteria will be selected.

The search process will include studies in Spanish, English, and Portuguese, broadening the range of sources reviewed. This strategy aims to gather sufficient data to answer the research question and allow for a comprehensive evaluation of the reliability of physical-chemical CSF analysis, especially in comparison with molecular techniques. It will also provide a solid overview of the existing literature.

### **Scope of study**

The scope of the study is developed in the virtual modality of the Inter-American Open University, where time and effort will be devoted to exhaustively analyzing the selected articles and implementing the strategy and planning outlined above.

### **Data collection instruments**

The selected articles must meet the previously established inclusion and exclusion criteria. The search for

articles will be carried out in the database above. This selection process will be based on a review of titles, abstracts, and full texts to ensure the relevance of each study. The Jadad scale will be applied to assess the methodological quality of the selected studies. This instrument is widely recognized for its ability to determine the quality of clinical trials, evaluating aspects such as randomization, double-blinding, and the description of withdrawals and dropouts. The Jadad scale assigns a score from 0 to 5, with higher scores indicating better methodological quality. Studies with low scores will be considered at high risk of bias, which will influence their inclusion in the final analysis.

### Data analysis plan

This will focus on rigorously organizing and synthesizing the data obtained from the selected studies. The key variables to be analyzed will be the sensitivity, specificity, and other predictive values of the different diagnostic methods evaluated, specifically the physicochemical analysis of CSF, PCR, and bacterial cultures in diagnosing central nervous system infections in post-surgical patients.

Data collection will allow for the presentation of the main information from each study, including:

- Author, year of publication, type of study, and sample size.
- Characteristics of the study population (post-surgical patients).
- Diagnostic methods evaluated and their results (sensitivity, specificity, predictive values).
- Methodological quality assessment using the Jadad scale

### Study biases and limitations

It is essential to consider factors that may introduce bias and limit the validity of the results. First, there is a risk of selection bias due to variability in the available studies. Some relevant studies may not be included if they are not accessible in the selected databases or published in languages that are not part of the inclusion criteria. Likewise, studies with negative or inconclusive results may not be published, leading to publication bias that affects the overall view of the topic.

In terms of study design, many of the articles reviewed may be observational or retrospective studies, which are at greater risk of bias compared to controlled clinical trials. This may influence the quality and reliability of the data extracted.

Another significant limitation is the heterogeneity between studies in terms of the characteristics of the population studied and the diagnostic methods used. This variability may make it difficult to compare results directly and, in some cases, limit the possibility of conducting a robust meta-analysis. Likewise, differences in administering previous treatments, such as antibiotics, may affect diagnostic results, creating confusion that cannot always be adequately controlled in the studies analyzed.

Finally, the included studies may be influenced by diagnostic technologies such as PCR, which are not available in all health centers. This could limit the generalization of the results to different clinical contexts.

These limitations will be taken into account when interpreting the findings. They will be reflected in the discussion of the results to provide a critical and balanced view of the topic.

### Resources needed

First, a computer and internet access will be necessary to access the following

- Access to scientific databases: Access to biomedical databases such as PubMed, SciELO, Google Scholar, Oxford Academic, and Elsevier will be essential. This will ensure the possibility of consulting and downloading articles relevant to the review.
- Access to libraries or academic institutions: Since some articles may not be available free of charge, it may be necessary to access academic institutions or libraries with subscriptions to scientific journals to obtain the studies needed for the review.
- Tools for evaluating the quality of studies: Tools such as the Jadad scale will be used to evaluate the methodological quality of the selected studies.
- Time and human resources: The proper execution of the study will require sufficient time to conduct the search, selection, quality assessment of the studies, and writing of the final report.

### Schedule of activities

1. Search and selection of articles: 1 week
2. Evaluation and review of articles: 3 weeks
3. Data extraction and analysis: 2 weeks
4. Writing of the final report: 2 weeks

## RESULTS AND DISCUSSION

The literature review suggests that physicochemical analysis of CSF, although useful, has limitations when

used as the sole diagnostic method for CNS infections in post-surgical patients. This method evaluates parameters such as glucose, protein, lactate, and pleocytosis, which may suggest the presence of disease. However, its sensitivity and specificity decrease considerably, especially in patients who have received antibiotics, which affects its reliability in critical diagnoses. In these contexts, studies have reported that the sensitivity of CSF physicochemical analysis ranges from 60 % to 70 %, with a specificity of 55 % to 65 % in post-surgical patients with prior antibiotic treatment, which increases the risk of false negatives and delays in diagnosis and treatment.<sup>(1)</sup>

Research highlights that, although initial and accessible, CSF analysis shows a 30 % probability of false negatives in patients who have already received antibiotics due to alterations in glucose and protein levels, compromising its effectiveness.<sup>(2)</sup> Other studies have found that physical-chemical analysis of CSF in patients with rheumatological conditions is insufficient to diagnose CNS infections accurately. These findings indicate that in complex settings such as the post-surgical setting, CSF analysis alone does not provide the accuracy necessary for timely and effective intervention.<sup>(3)</sup>

Furthermore, although the physical-chemical analysis of CSF provides relevant preliminary information, its ability to differentiate between bacterial and viral infections is limited, leading to difficulties in interpretation in emergencies. In fact, in post-surgical patients, the physical-chemical analysis of CSF is accurate only 65 % of the time in differentiating between types of infections, which is insufficient in clinical settings where rapid decision-making is required.<sup>(4)</sup>

On the other hand, advances in molecular techniques such as multiplex PCR have shown significant improvement in sensitivity and specificity. According to studies, multiplex PCR allows for rapid and accurate detection of pathogens such as *Neisseria meningitidis* and *Streptococcus pneumoniae*, achieving sensitivities of 92 % and specificities of 98 % in patients undergoing antibiotic treatment. These figures far exceed those of the physical-chemical analysis of CSF.<sup>(5)</sup> This approach reduces the time to diagnosis by 40 % compared to traditional methods, allowing for earlier and more effective interventions.<sup>(5,6)</sup>

Although considered the gold standard for confirming bacterial infections, bacterial cultures have limitations in terms of sensitivity and time. In patients who have not received antibiotics, cultures have a sensitivity of around 70 %. However, in patients who have previously received antibiotics, this figure drops to less than 50 %, limiting their usefulness in situations where accuracy and speed of diagnosis are crucial.<sup>(6)</sup>

The use of biomarkers such as procalcitonin and C-reactive protein has also been investigated in the context of CNS infections. Studies conclude that procalcitonin has a sensitivity of 89 % and a specificity of 83 % for differentiating between bacterial and viral meningitis, representing a valuable tool in settings where advanced molecular techniques are unavailable.<sup>(7)</sup> Similarly, procalcitonin, when used with the physical-chemical analysis of CSF, has improved diagnostic accuracy by 25 %, facilitating the identification of bacterial infections in post-surgical patients.<sup>(8,9)</sup>

Recent studies have indicated that procalcitonin in the CSF of post-surgical patients helps detect intracranial infections with a sensitivity of 85 %. These results reinforce that, although traditional CSF analyses are functional, biomarkers such as procalcitonin can effectively complement diagnosis when molecular resources are limited.<sup>(9)</sup>

Finally, other studies found that combining procalcitonin with physicochemical analysis of CSF increases diagnostic accuracy by 30 % for detecting bacterial infections in emergency departments, which is especially relevant in emergency settings where time is critical for clinical intervention.<sup>(10)</sup>

In summary, the results of this review suggest that physicochemical analysis of CSF remains useful as an initial tool in diagnosing CNS infections in post-surgical patients. Still, its effectiveness is limited in patients treated with antibiotics. Implementing advanced techniques such as multiplex PCR, cultures, and the use of biomarkers, particularly procalcitonin, complement CSF analysis and significantly improve diagnostic accuracy and speed, optimizing clinical outcomes in these patients.

## CONCLUSIONS

In conclusion, this review highlights the importance of a combined diagnostic approach that integrates the physical-chemical analysis of CSF with advanced techniques such as multiplex PCR, biomarkers such as procalcitonin, and cultures. This protocol optimizes diagnostic accuracy and shortens response times, improving patient prognosis and optimizing resource use in healthcare systems. Implementing this approach represents an effective strategy for addressing diagnostic challenges in CNS infections in post-surgical patients, providing a solid foundation for high-quality clinical care.

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#### CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

#### AUTHOR CONTRIBUTION

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