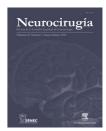


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## Clinical research

# Value of cerebrospinal fluid lactate for the diagnosis of bacterial meningitis in postoperative neurosurgical patients

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#### ABSTRACT

Objective: To evaluate the diagnostic value of CSF lactate ( $L_{CSF}$ ) for the diagnosis of bacterial meningitis (BM) following neurosurgery, and compare it with other CSF markers.

Methods: Prospective study of consecutive neurosurgical postoperative patients admitted to the Intensive Care Unit (ICU) at Maciel Hospital. Patients with clinical suspicion of BM were categorised, according to preset criteria, into 3 groups: (1) proven BM; (2) probable BM, and (3) excluded BM. CSF markers were plotted in a receiver operating curve (ROC) to evaluate their diagnostic accuracy.

Results: The study included 158 patients. We obtained 46 CSF samples from patients with clinical suspicion of BM by lumbar puncture (LP): 10 corresponded to proven BM, 4 to probable BM and 32 to excluded BM. Mean lactate in CSF ( $L_{CSF}$ ) was:  $10.72 \pm 4.68$  mM for proven BM, 6.07  $\pm 0.66$  mM for probable BM and  $3.06 \pm 1.11$  mM for excluded BM (P < .001 for proven BM and probable BM vs excluded BM; P = NS for proven BM vs probable BM).  $L_{CSF}$  displayed a better diagnostic accuracy for BM in the 2 scenarios studied: (1) positive bacterial CSF culture or Gram stain as positive control (gold standard) (sensitivity: 87%, specificity: 94%, cut-off value: 5.9 mM), and (2) combination of proven BM and probable BM as positive control (sensitivity: 92%, specificity: 100%, cut-off value: 5.2 mM).

Conclusions: According to our results, determination of  $L_{CSF}$  is a quick, sensitive and specific test to identify the need for antimicrobial therapy in neurosurgical postoperative patients with clinical suspicion of BM.

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# Valor del lactato en líquido cefalorraquídeo para el diagnóstico de meningitis bacteriana en el postoperatorio de neurocirugía

RESUMEN

Palabras clave: Meningitis bacteriana Objetivo: Evaluar el valor diagnóstico del lactato en líquido cefalorraquídeo (LCR) para el diagnóstico de meningitis bacteriana (MB) después de una neurocirugía, y compararlo con otros marcadores bioquímicos del LCR.

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Infección posquirúrgica Neurocirugía Lactato en LCR Diagnóstico Métodos: Estudio prospectivo de pacientes sometidos a neurocirugía admitidos consecutivamente en la Unidad de Cuidados Intensivos (UCI) del Hospital Maciel. Los pacientes con sospecha clínica de MB, fueron categorizados por criterios predeterminados en tres grupos: (1) MB probada, y (2) MB probable, y (3) MB excluida. Los marcadores de LCR fueron analizados de acuerdo a la curva ROC (receiver operating curve) para evaluar su exactitud diagnóstica.

Resultados: Se estudiaron 158 pacientes. 46 presentaron sospecha clínica de MB, de los cuales se obtuvieron muestras de LCR mediante realización de punción lumbar: 10 fueron MB probada, 4 fueron MB probable y 32 MB excluida. La media de lactato en LCR fue:  $10,72\pm4,68\,\mathrm{mM}$  para MB probada,  $6,07\pm0,66\,\mathrm{mM}$  para MB probable y  $3,06\pm1,11\,\mathrm{mM}$  para MB excluida (p<0,0001 para MB probada y MB probable vs MB excluida; p=NS para MB probada vs MB probable). El lactato en LCR demostró la mayor exactitud diagnóstica para MB en los 2 escenarios estudiados: (1) cultivo bacteriano o tinción de Gram positivo en LCR como control positivo (sensibilidad: 87%, especificidad: 94%, valor de corte: 5,9 mM); y (2) combinación de MB probada y MB probable como control positivo (sensibilidad: 92%, especificidad: 100%, valor de corte: 5,2 mM).

Conclusión: De acuerdo a nuestros resultados, la medición de lactato en LCR es un método diagnóstico rápido, sensible y específico para identificar la necesidad de iniciar antibioterapia en pacientes con sospecha clinica de MB postquirúrgica.

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# Introduction

Bacterial meningitis (BM) is an uncommon (0.5–4%) but serious nosocomial infection that complicates patients following intradural procedures, with a mortality of 20–40%. It increases ICU and hospital length of stay, makes further surgery necessary and increases the overall cost of hospital care. Its diagnosis is difficult due to: non-specific clinical signs, other co-infections, alterations of markers of CSF by surgical brain manipulations and bleeding. Also, these patients are prone to be under broad spectrum antibiotic therapy due to other extra neurological infections. <sup>1–5</sup>

Prompt diagnosis and combined medical and eventually surgical management, therefore, remain the cornerstone for the prevention of adverse outcome.<sup>6</sup>

In the last few years,  $L_{CSF}$  levels have received increasing attention as a valid ancillary test for diagnosis of postoperative BM due to the ease, precision and rapidity with which it is measured in the clinical laboratory. However, there are still some controversies about its value such as the cut off level, the influence of neutrophils and erithrocytes on  $L_{CSF}$ , and with what gold standard should we compare  $L_{CSF}$  with.<sup>7–9</sup>

The present study was performed to evaluate the diagnostic usefulness of  $L_{\text{CSF}}$  for detection of postoperative BM, and compare it with other markers of CSF (cellularity, protein, glucose and CSF/blood glucose ratio).

## Patients and methods

We conducted a prospective study of consecutive patients admitted to Maciel Hospital ICU who had intradural neuro-surgical procedures from December 2008 to February 2010. All patients received prophylactic Cefazoline peri-operatively, as a single dose on induction.

Clinical parameters examined were: age, sex, simplified acute physiology score (SAPS II), diagnosis, type of surgical procedure, type of intracranial device inserted, antibiotic regimen initiated before BM appears, ICU length of stay and outcome. Patients were followed until discharge from the ICU.<sup>10</sup>

Patients with clinically suspected BM were identified. Suspected BM was defined as: fever and neurological deterioration (alteration on mental status, seizures or stiff neck), or neurological deterioration without another proven cause. A LP was performed in these patients, after a Computed Tomography (CT) cranial scan was performed to exclude significant brain midline shift or mass effect.

CSF obtained from LP was collected into sterile polystyrene tubes and immediately submitted for analysis. CSF culture and Gram stain were performed. Leukocytes, neutrophils and erythrocytes were assessed by cell counting with a calibrated Fuchs-Rosenthal chamber after staining with toluidine blue. Total CSF protein was determined using the benzethonium chloride precipitation technique standardized to the biuret method. Assessment of CSF glucose and lactate was determined using glucose/lactate oxidase enzymatic method (ABL 700 Series, Radiometer). <sup>11</sup>

Patients with clinically suspected BM were categorized according to the following preset criteria, into three groups: (1) proven BM: positive bacterial CSF culture or Gram stain; (2) presumed BM: negative CSF culture or Gram stain and CSF leucocyte count >  $1000/\mu$ l (>50% neutrophils), in patients treated with antibiotics at the time of LP; and (3) non-BM or excluded BM: negative CSF culture and Gram stain with leucocyte count <  $1000/\mu$ l.

Continuous data were compared by the Student's t-test. Fisher's exact test was used to evaluate categorical data (p value < 0.05 was considered to be significant). The CSF markers were analyzed to determine specificity, sensitivity, positive (PPV) and negative predictive value (NPV). Receiver Operating Characteristic (ROC) curve was used to evaluate the

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