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REVIEW ARTICLE

Usefulness of blood and cerebrospinal fluid laboratory testing to predict bacterial meningitis in the emergency department☆

A. Julián-Jiménez[a,*], **M.I. Morales-Casado**[b]

[a] *Servicio de Urgencias, Complejo Hospitalario de Toledo, Toledo, Spain*
[b] *Servicio de Neurología, Complejo Hospitalario de Toledo, Toledo, Spain*

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Abstract
Introduction: The classic clinical presentation of bacterial meningitis (BM) is observed in less than half of the cases in adults, and symptoms are less specific in children, the elderly or immunocompromised, and other chronic patients. The usual signs and symptoms do not provide optimal sensitivity and specificity for distinguishing possible BM from viral meningitis (VM), which may lead to a delay in the appropriate antimicrobial therapy. Society therefore stands to benefit from the development of effective, objective, and rapid tools able to predict and identify patients with BM. These tools include laboratory tests for blood and cerebrospinal fluid (CSF). The aim of this review is to summarise recently published scientific evidence in order to clarify existing controversies and compare the usefulness and diagnostic ability of the different parameters used to predict BM.
Development: Systematic search of the main bibliographic databases and platforms to identify articles published between January 2000 and January 2016. We selected 59 articles that meet the objectives of this review.
Conclusions: CSF lactate, proportion of polymorphonuclear leucocytes, and CSF glucose, as well as serum procalcitonin (PCT), are the independent factors most predictive of bacterial aetiology. The model that combines serum PCT and CSF lactate achieves the highest predictive power for BM, with a sensitivity and specificity exceeding 99%. We should consider BM when CSF lactate >33 md/dL and/or PCT > 0.25 ng/mL.

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* Corresponding author.
E-mail address: agustinj@sescam.jccm.es (A. Julián-Jiménez).

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Utilidad de las determinaciones analíticas en sangre y líquido cefalorraquídeo para predecir meningitis bacterianas en el servicio de urgencias

Resumen
Introducción: La presentación clínica clásica de la meningitis bacteriana (MB) se da en menos de la mitad de los casos en adultos y es menos específica en niños, ancianos, inmunodeprimidos y otros pacientes crónicos. Los signos y síntomas habituales no proporcionan una sensibilidad ni especificidad óptimas para distinguir una posible MB de una meningitis viral (MV), lo que puede originar un retraso en el inicio del tratamiento antimicrobiano adecuado. Por ello, existe un gran interés en disponer de herramientas objetivas útiles e inmediatas para sospechar y distinguir los casos de MB de los de MV. Entre ellas se encuentran las determinaciones urgentes en suero y en líquido cefalorraquídeo (LCR). El objetivo de esta revisión es poner de manifiesto las evidencias científicas publicadas recientemente, aclarar las controversias existentes y comparar la utilidad y la capacidad diagnóstica de los diferentes parámetros analizados para predecir MB.
Desarrollo: Se realizó una búsqueda sistemática en las principales plataformas bibliográficas y de bases de datos desde enero de 2000 hasta enero de 2016, seleccionándose finalmente 59 artículos que cumplían con los objetivos de la revisión.
Conclusiones: El lactato, la proporción de polimorfonucleares y la glucorraquia en el LCR, así como las concentraciones séricas de procalcitonina (PCT), son los factores independientes con mayor capacidad predictiva de etiología bacteriana. El modelo que combina la PCT sérica con el lactato en LCR consigue el mayor poder predictivo de MB, con una sensibilidad y especificidad superiores al 99%. Se debe considerar una MB cuando el lactato en LCR sea > 33 mg/dl y/o la PCT sérica sea > 0,25 ng/ml.

Introduction

Meningitis is an inflammatory disease of the leptomeninges causing characteristic changes in the cerebrospinal fluid (CSF). Although it may be caused by autoimmune alterations or physical processes (after chemotherapy or radiotherapy), the most frequent aetiology is infectious, especially viral infection, which accounts for up to 80% of cases.[1] In fact, it is the most frequent infection of the central nervous system.[1] Bacterial meningitis (BM) is associated with several typical CSF findings: marked pleocytosis (normally >300 leucocytes/mm^3) with a predominance of polymorphonuclear neutrophils (PMN), together with high protein levels (>45 mg/dL) and low glucose levels (<60% of simultaneously measured blood glucose).[1] BM is not among the most frequently treated infections in hospital emergency departments (EDs) for any age group[2]; however, it is the type of infection which most frequently meets criteria for sepsis, severe sepsis, or septic shock.[3] Furthermore, the associated complication and mortality rates, even in the ED or within 24 hours of admission, are very high relative to the low incidence of BM, although it is not ranked among the 10 most common causes of death in the ED.[4] As a result, diagnostic and treatment decisions made within the first minutes have a direct impact on survival of patients with acute BM[5] and on the persistence of sequelae, particularly cognitive sequelae, after the acute phase.[6] Remaining alert to potential bacterial aetiology of acute meningitis (AM) is therefore essential even during triage or the first assessment of the patient.[7] Nonetheless, the situation still poses a challenge since microbial cultures and tests must be used to determine bacterial or viral aetiology.[8]

The classic clinical symptoms[9] (headache, nausea or vomiting, fever, altered mental state, stiff neck, and/or signs of meningeal irritation) appear in less than half of all adult patients and are much less specific in children,[10] elderly individuals,[11] immunocompromised patients, diabetic patients, and other patients with chronic diseases.[1,12] Therefore, the sensitivity and specificity of these signs and symptoms are not optimal for distinguishing between possible BM and viral meningitis (VM).[1,13] This may lead to delays in the administration of an appropriate antibiotic treatment.[5,14,15]

These 2 infectious diseases present a stark difference in terms of prognosis: in the case of VM, symptoms are generally self-limiting, whereas bacterial infection represents a medical emergency, as described above.[1] EDs therefore need accurate, fast-acting tools enabling discrimination between BM and VM. These tools include blood testing in the ED, leucocyte count, lactate test, and biomarkers of infection and inflammation (BII). In addition to procalcitonin (PCT)[16–20] measurement, which is known for its high diagnostic power for bacterial infection, CSF analysis is considered the key diagnostic test.[1,8] However, early CSF analysis results are occasionally similar for BM and VM, especially during the first hours of progression.[1,11] Furthermore, microbiological tests often perform poorly in EDs.[8] For this reason, recently published studies assign lactate

levels a higher predictive diagnostic power for BM than cell count (pleocytosis), percentage of PMN, or CSF glucose level.[21,22]

The aims of this article are to review the recently published scientific evidence, to resolve the current controversies, and to compare the usefulness and diagnostic power of the different blood and CSF parameters analysed in EDs to predict BM.

Development

For this article, we conducted a literature search of the 3 most relevant databases (PubMed, Scopus, and Cochrane Library) using the following keywords:

(1) ''acute meningitis'', (2) ''biomarkers'', (3) ''C reactive protein (CPR)'', (4) ''procalcitonin'', (5) ''lactate'', and also (6) (1 and 2), (7) (1 and 3), (8) (1 and 4), and (9) (1 and 5). We obtained 4557 results, and initially selected 132 articles (letters to the editor, original articles, brief original articles, reviews, and meta-analyses) published in Spanish or English in the 15 years prior to January 2016. We finally included 59 articles meeting our selection criteria.

We first analysed the blood measurements and then the CSF measurements usually used in EDs for diagnosing AM (by the ED physician or on-call neurologist).

Blood analysis

Leucocyte count

As in most bacterial infections, leucocytosis (>11 000-12 000 leucocytes/mm^3) is frequently detected in acute BM.[23,24] Classic studies associate higher levels of peripheral leucocytes with marked neutrophila with infections due to *Streptococcus pneumoniae*.[25] The mean peripheral leucocyte count in children with BM is approximately 17 000 leucocytes/mm^3 (values vary by study), as opposed to a mean of 9100 leucocytes/mm^3 measured in VM, with a statistical significance of $P < .001$.[26] A recent Spanish study in adults[27] found mean values of 17 500 leucocytes/mm^3 for BM and 11 096 leucocytes/mm^3 for VM, which translates into an area under the ROC curve (AUC) of 0.756 ($P = .003$). Nevertheless, we also found studies reporting leucocyte counts below the leucocytosis range, even in BM.[28] In both cases, this was the blood test with the lowest AUC for distinguishing between BM and VM, as confirmed by a recent article.[29] One study even reports that blood leucocyte count in elderly patients (>75 years) does not reveal statistically significant differences for distinguishing between BM and VM.[11] Therefore, blood leucocyte count is confirmed to have the lowest predictive power for BM, below that of C-reactive protein (CRP) and PCT.[20] However, it should be noted that leucocyte count (>12 000 leucocytes/mm^3 or <4000 leucocytes/mm^3) is one of the 4 diagnostic criteria for systemic inflammatory response syndrome and therefore, for sepsis, with the associated prognostic implications.[23,24]

Biomarkers

Biomarkers are defined as measurable molecules in a biological sample which may be used as an indicator of the status (normal or pathological) of a biological process, allowing monitoring of the process based on concentration of the biomarker.[16] Increased, decreased, or stable biomarker values reflect the progression of the disease and the response to treatment.[16,30]

To date, many studies have published data on different BII involved in diagnosing AM and establishing aetiology and prognosis.[16,20,30] We describe below the most relevant biomarkers used in everyday clinical practice, divided as measured in the blood (in this section) or in the CSF (in a subsequent section).

C-reactive protein

CRP is an acute-phase protein synthesised in the liver in response to interleukin-6 (IL-6) and IL-8, and increases both in infectious (viral and bacterial) and inflammatory (chronic and acute) processes.[16,17,30]

Synthesis starts in the first 4 to 6 hours following process onset, although peak synthesis is recorded at approximately 36 to 48 hours. CRP levels may remain elevated for days despite correct treatment and improvement of the patient's condition.[16,17,30] However, detection is easy, reproducible, and inexpensive. Normal values (0-8 mg/L) depend on age, sex, and race.[16,31]

Several studies report increased values in the context of bacterial infections,[32] including BM; however, its poor kinetics and the increase observed in the context of other inflammatory and viral processes limit its usefulness as an independent BII, especially in elderly patients (diagnostic usefulness decreases with age) and in patients with oncohaematological or autoimmune disease or cirrhosis, among others.[11,16] In any case, most of the studies place CRP above leucocyte count for predicting BM vs VM.[11,16,27] Before the use of PCT measurement was generalised, CRP was the most widely studied BIIs in cases of BM.[33]

In patients with negative CSF cultures, CRP achieves a sensitivity of 86% and a specificity of 84%, with a cut-off point (CP) of 37 mg/L for distinguishing between BM and VM.[11] Another recent study reports an AUC of 0.916 with a 95% confidence interval (95% CI) of 0.838 to 0.994 ($P < .001$); despite this diagnostic power being lower than that of PCT, it is higher than that of leucocyte count.[27]

CRP remains a stable and reliable biomarker, performing similarly to PCT in paediatric populations, especially in cases with isolated *S. pneumoniae* or *Neisseria meningitidis*.[34] However, other studies report a poorer ability to distinguish between VM and BM and demonstrate that concentrations overlap with those observed in non-infectious aetiologies, reducing the specificity of this parameter for distinguishing between types of AM.[35] In adults older than 75, increased CRP values in cases of BM are not statistically significant for distinguishing between VM and BM, with an AUC of only 0.514 and a specificity of 43%.[11]

Therefore, we should use and interpret CRP values with caution in elderly patients with such severe processes as suspected BM. Over 50% of patients with fever in EDs undergo CRP tests (but not PCT tests)[19,36] to distinguish between viral and bacterial infections, and more than 40% of all infectious processes in EDs affect elderly patients.[3] We must therefore be aware of the diagnostic limitations of CRP measurements for confirming or ruling out bacterial aetiology of AM in this population.[37,38]

Procalcitonin

Procalcitonin, a polypeptide precursor of calcitonin, is a protein containing 116 amino acids, and is mainly synthesised in the thyroid gland and the lungs (Kultschitzky or neuroendocrine cells). PCT remains almost undetectable in healthy subjects in normal conditions; values below 0.05 ng/mL are considered normal.[16,17,39] Many tissues have been observed to produce PCT during bacterial infections and sepsis in response to the stimulus of tumour necrosis factor α, IL-6, and IL-8, after recognition of bacterial components (such as lipopolysaccharides in gram-negative cells or lipoteichoic acid in gram-positive cells).[16,17] Increases in PCT concentration, which depend directly on bacterial load and/or presence of endotoxins, are measurable within just 3 to 4 hours of BM onset; peak values are observed at approximately 12 hours and half-life is 20 to 36 hours.[16,40] Decreasing PCT values, on the other hand, may confirm positive response to an appropriate antimicrobial treatment and a good progression at 12 to 24 hours. This particular kinetic behaviour is very useful for emergency decisions when there is initial suspicion of BM. This, together with the excellent diagnostic power of this biomarker (higher than that of leucocytes and PCR) and the fact that its predictive ability is maintained in elderly patients,[11,38] oncohaematological and neutropenic patients,[42] and those with kidney failure,[41] cirrhosis, or autoimmune diseases,[43] have made it the ideal serum BII for aetiological diagnosis, prognostic assessment, and management of patients with BM.[11,16,18,20,27,29] Previous studies describe and validate this role of PCT in other severe infectious processes (sepsis,[16,23,44] bacteraemia,[16,45] severe pneumonia,[46,47] etc.).

Early studies, conducted more than 10 years ago, already suggested that the diagnostic power of PCT was significantly higher than that of leucocyte count or PCR concentration, although the small sample sizes used and the study methodologies limit the reliability of these results.[48,49] However, there is controversy regarding the optimal CP, which varies greatly from study to study (mainly due to differences in sample size and the technique used for measuring PCT), ranging from 0.23 ng/mL to 5 ng/mL (to obtain sensitivity and specificity values above 90% in all studies).[11,16,18,20,27,29,39] According to one of the most relevant studies, conducted by Viallon et al.[18] and including 254 patients with AM (35 with BM and 181 with VM), a CP $\geq$ 0.28 ng/mL for PCT provided the greatest diagnostic power, achieving a sensitivity of 95%, a specificity of 100%, a positive predictive value (PPV) of 100%, and a negative predictive value (NPV) of 97%, with an AUC of 0.99 (95% CI, 0.99-1). These results are very similar to those obtained by 2 more recent studies, which reported higher CPs (PCT $\geq$ 0.8 and 0.74 ng/mL, respectively) obtaining similar sensitivity and specificity. In a very recent meta-analysis including 9 studies and 725 patients, Vikse et al.[20] confirmed these excellent results, obtaining a sensitivity of 90% (95% CI, 84%-94%), a specificity of 98% (95% CI, 97%-99%,), and an odds ratio (OR) of 287 (95% CI, 55-1409). In the light of these results, ED physicians should regard initial PCT levels >0.25 to 0.5 ng/mL as potentially diagnostic of BM.[16,20] The necessary microbiology tests should be performed[8] and appropriate antibiotic treatment should be started immediately.[5]

By age group, PCT diagnostic power is higher than that of CRP in children,[11,34,50] adults, and elderly patients,[11,20] and is not affected by the limitations of CRP.

In addition to being of great help in aetiological diagnosis, some studies report the use of PCT to monitor the progression of infection, since it exponentially decreases after the first 24 to 48 hours in patients receiving an appropriate antibiotic treatment.[51,52] Furthermore, PCT concentrations higher than 1 ng/mL are suggestive of bacteraemia,[16,27] with the associated implications for prognosis.

Blood lactate

Blood lactate is considered the best marker of tissue hypoperfusion and hypoxia, and is included in all assessment recommendations for patients with sepsis, severe sepsis, and septic shock in EDs.[23,24] However, it has no capacity to distinguish between bacterial and viral aetiology or other causes of non-infectious systemic inflammatory response syndrome. Therefore, determination of blood lactate concentration is recommended in AM as a prognostic factor of severity, mortality, and treatment response.[16,17,30] Patients with any infectious process showing blood lactate levels >2 to 2.5 mmol/L should be more intensively monitored since they present higher mortality rates during admission and at 30 days of presentation,[16,53] even in situations of haemodynamic stability with or without bacteraemia.[54,55] This excellent prognostic power for severity and mortality was also confirmed in elderly patients.[56]

CSF analysis

CSF analysis has classically been considered the gold standard in AM diagnosis. The variables analysed include leucocyte count (pleocytosis) and percentage of PMN in the count, CSF glucose level and the proportion relative to simultaneously measured blood glucose, protein level, and lactate concentration.[1,8,57,58]

Leucocyte count

Normal CSF leucocyte count is <5 to 10 leucocytes/mm^3, comprising mainly mononuclear cells; in newborns, levels may reach 30 leucocytes/mm^3. Pleocytosis (100-10 000 leucocytes/mm^3) occurs in the vast majority of cases

of BM with predominance of PMN, especially after the first 24 hours from bacterial infection.[1,59] Its diagnostic power for identifying bacterial aetiology has been widely studied for a number of years. Several CPs have been established; one study reports a CP of 118 leucocytes/mm^3, with a sensitivity of 80% and a specificity of 85% to identify BM,[11] although the majority of authors consider it necessary to increase this CP to a minimum of 300 leucocytes/mm^3 to consistently obtain sensitivity and specificity values above 80%.[1,28,58,59] In any case, and regardless of the CP used, the total number of CSF leucocytes presents lower diagnostic power and AUCs compared with the remaining CSF parameters analysed.[11,18,29,59] Furthermore, it should be noted that this occurs at all ages[11] (especially in newborns, elderly and immunocompromised patients, in whom its discriminant ability for BM decreases).[59,60] Previous antibiotic treatment is known to interfere with CSF leucocyte count, causing them to vary greatly.[59] Low CSF leucocyte count is associated with a poorer prognosis in patients with BM.[61] There are no specific differences to be taken into account with regards to elderly patients.[11] A recent study in children ($\leq$14 years) establishes an optimal CP of 321 leucocytes/mm^3, with a sensitivity of 80.6% and a specificity of 81.4% for distinguishing between BM and VM.[62]

Percentage of PMN

PMN account for >50% of total leucocyte count in acute BM cases.[1,58,59] A recent study reports that figures >60% would achieve sensitivity and specificity values of 69% and 77%, respectively, with a PPV of 89%.[63] Decreased CSF glucose and lactate are statistically significant predictors of BM vs VM, as is a PMN percentage >50%, with an OR of 20.19 (95% CI, 8.31-49.09; $P = .002$).[29]

Protein levels

Another classically studied CSF parameter is protein level. Levels should not exceed 45 to 50 mg/dL in healthy individuals.[1,58] They are slightly elevated in cases of VM (mean of 56 mg/dL) and clearly higher in BM (mean of approximately 135 mg/dL).[63] According to Viallon et al.,[18] protein levels above 188 mg/dL are associated with sensitivity and specificity of 87% and 93%, respectively, a PPV of 67%, and an AUC of 0.93 for distinguishing between BM and VM. However, the great majority of recent studies in children, adults, and elderly patients report a lower predictive ability and discrete AUC in comparison with the percentage of PMN, glucose CSF level, or lactate concentration.[11,27,29,50,59,61,63]

Glucose level

Decreased CSF glucose concentration is caused by bacterial metabolism, and is a typical finding in cases of BM.[1] It is also dependent on simultaneously measured blood glucose level, and has been shown to represent 60% to 80% of that value under normal circumstances.[1,59] Therefore, we assume that CSF should contain >40 to 50 mg/dL of glucose. Thus, in presence of normal blood glucose levels, it has been suggested that a CP < 40 mg/dL of glucose would provide a sensitivity of 97% and a specificity of only 49% for distinguishing between BM and VM[18] (with no significant variations between age groups[50,60]). However, CSF glucose level is not the most appropriate parameter for differentiating types of AM; rather, we should consider the CSF/blood glucose ratio, since blood glucose levels can be modified by concomitant illnesses, time of day, and other factors related with alcohol consumption and stress.[1,64] A recent study establishes that a CP of 0.36 for the CSF/blood glucose ratio yields excellent results, with sensitivity and specificity both at 92.9%.[64] Another novel study establishes that a CSF glucose level below 60% of blood glucose level is observed in 95% of patients with BM, with an OR of 20.82 (95% CI, 8.86-48.96; $P = .001$). This parameter, CSF lactate concentration, PMN percentage, and blood PCT level are the 4 individual factors found to be predictive of BM.[29]

Lactate

Lactate is an end product of cellular anaerobic metabolism; therefore, increased CSF lactate levels are to be expected in bacterial processes.[65] A CSF lactate concentration of 0 to 35 mg/dL is considered normal; one important characteristic is that this does not depend on the blood lactate level.[66] Blood lactate concentration should be taken into account, as is the case with CSF glucose levels.[59] However, as in the case of pleocytosis, it should be noted that CSF lactate levels considerably decrease when antibiotic treatment has been administered previously.[22,66,67]

For several decades, increased lactate concentration has been associated with BM,[1,58] although there is controversy regarding its true diagnostic yield.[59] In recent years, lactate has again been reported to be the diagnostic marker with the highest sensitivity for BM in CSF analyses,[68] with an almost incomparable yield, achieving an AUC of 1 and sensitivity and specificity both at 100%, with an established CP > 35 mg/dL.[26]

Lactate level measurement to distinguish bacterial from viral aetiology is equally useful in children and in adults, with the controversy also focusing on the most suitable CP. A CP of >33 mg/dL is currently recommended, since it obtains a sensitivity of 95% and a specificity of 93.6%,[69] although other studies consider a wider interval, ranging between 23 and 48 mg/dL; these provide better AUC results, reflecting predictive power for bacterial aetiology of AM.[21,70] Studies in elderly patients are more limited, for which reason no specific CP for that age group has been established to date.[21]

Although the most frequently selected CP is 35 mg/dL, some studies in adults have also obtained better results with a CP of 33 mg/dL: AUC of 0.942 (95% CI, 0.886-0.999; $P < .001$), 89.8% sensitivity, and 86.9% specificity.[29]

Two recent meta-analyses[21,22] have confirmed the excellent predictive power of lactate concentration and its higher diagnostic yield in comparison with other CSF measurements. A meta-analysis by Huy et al.[21] of 25 articles (1703 patients) reported excellent predictive power for lactate, with an AUC of 0.984 for CSF lactate concentration;

this is significantly higher than that of other measurements (CSF glucose level, CSF/blood glucose ratio, protein level, and total pleocytosis). This suggests that lactate concentration may be used as a simple marker for diagnosis of BM (although the article also reports that it would be advisable to measure the remaining parameters for maximum reliability). The second meta-analysis (Sakushma et al.[22]), including 33 studies and 1885 patients, establishes an optimal CP for CSF lactate concentration of 35 ± 1 mg/dL, which obtains excellent results: a sensitivity of 0.93 (95% CI, 0.89-0.96), a specificity of 0.96 (95% CI, 0.93-0.98), a positive likelihood ratio of 22.9 (95% CI, 12.6-41.9), a negative likelihood ratio of 0.07 (95% CI, 0.05-0.12), and an OR of 313 (95% CI, 141-698). As stated previously, the meta-analysis showed reduced diagnostic power of lactate in patients who had previously received antimicrobial drugs, with sensitivity decreasing to 0.49 (95% CI, 0.23-0.75).[22]

Procalcitonin

As with serum PCT levels, researchers have studied CSF PCT values to distinguish between BM and VM. A recent publication compares the diagnostic power of serum and CSF PCT concentrations, concluding that blood PCT measurement is much more useful than the CSF value.[71] Although one study found significant differences between CSF PCT concentration in BM vs VM (4.71 ± 1.59 ng/mL vs 0.13 ± 0.03 ng/mL), it only included 19 and 11 patients in each group.[72] In any case, although additional studies have assessed the usefulness of CSF PCT levels, their diagnostic power is very limited and the results obtained are inferior to those of the remaining analysed variables.[30–33] Therefore, CSF PCT determination is currently not recommended.[73–75]

Mixed models (blood and CSF analysis)

Although some authors have suggested assessing or associating several CSF measurements to increase EDs' ability to diagnose BM,[18,20,22,28] few studies have reported that combining blood and CSF analyses increases diagnostic power.[18,29] Furthermore, BIIs' diagnostic yield for bacterial infection has been compared with that of emergency CSF measurements.[18,48,59] Therefore, there is great interest in studying CSF lactate (as the optimal individual prognostic measurement for BM)[21,22] and PCT (the best serum predictor)[11,20,27] concentrations in the same model, as has previously been indicated by Viallon et al.,[18] thus further increasing the predictive ability of both variables. In this way, excellent predictive ability for BM can be achieved with the tests available in EDs, whether results are available for both CSF and blood analysis, or only from a blood sample because lumbar puncture could not be performed (which occurs in 10%-30% of patients due to contraindication or failure of the technique).[8] A recent study,[29] yet to be validated, shows that combining a PCT level ≥ 0.8 ng/mL and CSF lactate ≥ 33 mg/dL results in a model which achieves an AUC of 0.992 (95% CI, 0.979-1; $P < .001$), 99% sensitivity, 98% specificity, a PPV of 99%, a NPV of 97%, a positive likelihood ratio of 55.29, and a negative likelihood ratio of 0.01. The development and validation of these models will increase diagnostic precision, which we expect to lead to the proper antibiotic drugs being administered early,[5] the appropriate microbiological cultures being ordered, and the patient being admitted to the appropriate unit.[76–78]

Conclusions

The classical clinical presentation of meningitis, observed in less than half of cases (common signs and symptoms), does not provide optimal sensitivity or specificity for distinguishing between possible BM and VM. This presentation is much less specific in children, elderly, immunocompromised patients, and other patients with chronic disorders, which may lead to a delay in the onset of an appropriate antimicrobial treatment.

There is great interest in equipping EDs with accurate, fast-acting tools enabling discrimination between BM and VM.

CSF lactate levels, PMN percentage, and glucose levels, and serum PCT concentration are the significantly associated independent factors, and are also more likely to predict bacterial aetiology. These 4 factors, which could be analysed habitually in EDs, represent a clear diagnostic approach, and should always be assessed in order to establish suspicion of BM, thus assisting us in directing the most appropriate resources and care to patients who are in urgent need.

The combination of serum PCT concentration plus CSF lactate levels achieves the greatest predictive power for BM, with sensitivity and specificity values over 99%.

EDs should consider BM when CSF lactate levels are >33 mg/dL and/or serum PCT concentration is >0.25 ng/dL.

Conflicts of interest

The authors have no conflicts of interest to declare.

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