Earlier Treatment and Improved Outcome in Adult Bacterial Meningitis Following Guideline Revision Promoting Prompt Lumbar Puncture

To the Editor—We congratulate Glimaker et al for their study on the timing of lumbar puncture (LP), delay in antibiotic treatment, and outcome in a large nationwide retrospective database of patients with bacterial meningitis, in which they show that early treatment improves outcome [1]. The authors state that in patients with suspected bacterial meningitis, an altered level of consciousness or new-onset seizures should not be a reason to perform a cranial computed tomographic scan before doing the LP, as it delays the time to antibiotic treatment.

Bacterial meningitis is often suspected, but only a minority of patients are eventually diagnosed with the disease [2, 3]. The differential diagnosis may include viral meningitis, tuberculous meningitis, stroke with concomitant infection, subdural empyema, and cerebral abscess [4]. The information considering patients in whom bacterial meningitis was suspected, but who were eventually diagnosed with a different condition, is not present in the study by the authors, while these patients also have the risk of complications due to the LP. A meta-analysis of cerebral abscess patients showed that clinical deterioration attributed to an LP occurred in 7% of patients with brain abscess in whom LP was performed [5]. Therefore, studies assessing the diagnostic sequence used in bacterial meningitis and outcome should include patients with suspected bacterial meningitis, as this is the at-risk population for LP-related complications.

Another issue with the study is that the authors compared 2 time periods to assess the effect of introduction of the guideline. Between these time periods, other interventions may have been introduced that could have influenced prognosis. The authors previously reported on intracranial pressure monitoring that improved outcome between time periods, which includes the same patient group [6]. Dexamethasone was introduced as standard adjunctive therapy between 2004 and 2006. Timing is important for this drug given together with the first dose of antibiotics, dexamethasone is beneficial, but administered after clinical deterioration, corticosteroids are ineffective. As timing of steroid therapy is not provided, this may also be a confounding factor [7].

The diagnostic criteria the authors have used to define bacterial meningitis are “clinical criteria with or without cerebrospinal fluid analysis.” As the authors rightfully claim, cerebrospinal fluid is a mainstay in the diagnosis of bacterial meningitis, so patients with no LP should have been excluded from this study. Furthermore, the clinical criteria for bacterial meningitis are not specified by the authors. The clinical presentation of bacterial meningitis can be atypical [8], and therefore it is unclear what patient population was included in this study.

Finally, it is unclear at what point the physicians were asked to fill out the questionnaire on timing of treatment. If this is not done shortly after admission, a recall bias may occur, in which physicians may be tempted to respond that they complied with the new guideline and that timing of antibiotics was short.

We encourage every attempt to shorten time to antibiotic treatment in patients with bacterial meningitis, as there is no question this improves outcome. However, the current study leaves too many questions unanswered to provide meaningful data on the best diagnostic strategy in patient suspected to have bacterial meningitis.

Note

Potential conflict of interest. Both authors: No reported conflicts.

Both authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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Clinical Infectious Diseases® 2015;61(4):663–4
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DOI: 10.1093/cid/civ361

Reply to Brouwer and van de Beek

TO THE EDITOR—We appreciate Brouwer and van de Beek’s thoughtful comments to our registry study of acute bacterial meningitis (ABM) [1]. The large sample size enabled multivariate analyses and adjustment for relevant confounders showing earlier treatment and favorable clinical outcome after guideline revision deleting impaired mental status as a contraindication for immediate lumbar puncture (LP) in cases without signs of a cerebral mass lesion or impending herniation. The rationale for this revision has been reviewed in detail [2]. Brouwer and van de Beek raise some concern about the recommendation to revise current international guidelines [3, 4].

We demonstrated that LP in unconscious patients with ABM was not associated with any risks, consistent with other reports [5–7]. However, we agree that in cases with suspected ABM, several differential diagnoses, not included in the present study, should be considered, weighing possible risks with immediate LP against potential risks associated with delayed LP due to prior computed tomography (CT) [2, 8–11]. International guidelines are based on the Hashbun et al study in which specified clinical features predicted abnormal CT findings, not necessarily contraindicating LP [9]. On the contrary, Gopal et al showed that the clinician’s overall impression is the strongest positive predictor of CT-identified lesions contraindicating LP [8]. Too many CTs are performed, and adherence to the international guidelines is poor [12]. Brain abscess, the most important differential diagnosis, is often associated with focal neurological signs and a longer duration of cerebral symptoms [13]. The risk of LP-induced herniation in patients with brain abscess is difficult to assess because information about clinical findings temporally related to LP have seldom been clarified. Brouwer et al estimated this risk at 7% [13], whereas figures around 1%–2% have been reported by others [4, 14]. Furthermore, these figures are probably even lower in patients without focal neurological signs, and this risk should be balanced against the indisputable risk of delaying ABM treatment, with an increase in mortality of 1%–4% per hour of delay [1, 15].

There are pros and cons regarding the inclusion of patients in whom the diagnosis was made without cerebrospinal fluid (CSF) analysis. This patient group included some of the most severely ill with impending herniation, and to increase the external validity of the study, we included these patients in the outcome analysis. Our results did not change after excluding these patients.

The physicians were asked to fill out the questionnaire during their patient’s hospital stay. Because new guidelines were implemented in 2004 as well as in 2009, it is unlikely that physicians were tempted to state that they complied more with the guidelines during 2010–2012 than during 2005–2009. The recommendations to start corticosteroids together with antibiotics and to consider intracranial pressure monitoring were introduced in 2004. Similar use of these adjuunctive therapies was observed between the 2 periods.

We fully agree to encourage every attempt to shorten time to treatment in patients with ABM. CSF analyses are often the key to rapid treatment in clinical practice, and LP before CT is associated with significantly earlier treatment and a favorable outcome [1, 16]. Available data and evidence warrant a revision of the current international guidelines, toward promoting early LP.

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Potential conflicts of interest. All authors: No potential conflicts of interest.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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