MAJOR ARTICLE

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

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Background. In suspected acute bacterial meningitis (ABM), cerebral computerized tomography (CT) is recommended before lumbar puncture (LP) if mental impairment. Despite guideline emphasis on early treatment, performing CT prior to LP implies a risk of delayed treatment and unfavorable outcome. Therefore, Swedish guidelines were revised in 2009, deleting impaired mental status as a contraindication for LP without prior CT scan. The aim of the present study was to evaluate the guideline revision.

Methods. The Swedish quality registry for community-acquired ABM was analyzed retrospectively. Door-to-antibiotic time and outcome were compared among patients treated 2005–2009 (n = 394) and 2010–2012 (n = 318). The effect of different LP–CT sequences was analyzed during 2008–2012.

Results. Adequate treatment was started 1.2 hours earlier, and significantly more patients were treated <2 hours from admission 2010–2012 than 2005–2009. Compared with CT before LP, immediate LP resulted in 1.6 hours earlier treatment, significant increase in door-to-antibiotic times of <1 and <2 hours, and a favorable outcome. In 2010–2012, mortality was lower (6.9% vs 11.7%) and the risk of sequelae at follow-up decreased (38% vs 49%) in comparison with 2005–2009. Treatment delay resulted in a significantly increased risk for fatal outcome, with a relative increase in mortality of 12.6% per hour of delay.

Conclusions. The deletion of impaired mental status as contraindication for prompt LP and LP without prior CT scan are associated with significantly earlier treatment and a favorable outcome. A revision of current international guidelines should be considered.

Keywords. bacterial meningitis; lumbar puncture; guidelines; time to treatment; outcome.

Acute bacterial meningitis (ABM) is a rare but potentially life-threatening disease. Despite modern antibiotic treatment, use of corticosteroids, and advanced intensive care, ABM is still associated with a mortality of about 10%–30% and a high risk of neurological deficits [1–8]. ABM leads to cerebral edema and increased intracranial pressure (ICP) that may result in brain herniation, which is a major cause of morbidity and mortality [5, 9–13]. Lumbar puncture (LP) is the mainstay in the diagnosis of ABM; however, a long-standing controversy exists regarding the potential risk of LP-induced brain herniation [10, 11, 14–17]. Current international guidelines use the "red flags" of papilledema, focal neurological signs, moderate to severe impairment of mental status, immunocompromised state, and new onset seizures to identify patients with an increased risk of a cerebral mass lesion and elevated ICP and, thus, with contraindications to immediate LP. In these patients, cerebral computed tomography (CT) before LP is recommended [18–20]. Similar guidelines were introduced in Sweden in 2004. However, as in other international reports, CT was performed too often and adherence to the recommendations to start antibiotics

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before CT in suspected ABM was limited [3, 7, 21–23]. Several studies underline the importance of early treatment [2, 4, 7, 24]. Furthermore, recent studies indicate that CT scan before LP often delays the treatment process [7, 21, 22, 25] and that the diagnostic treatment sequence of CT–LP–antibiotics is common and constitutes a risk factor for unfavorable outcome [7]. These facts, in combination with the lack of firm evidence for some of the contraindications for prompt LP [16, 17], resulted in a revision of the Swedish guidelines in 2009 in which moderate to severe impairment of mental status and new onset seizures as contraindications to initial LP were deleted.

The main purpose of the present study was to evaluate the effects of this 2009 revision on time to adequate antibiotic treatment and outcome. In addition, the performance of CT before LP was evaluated.

MATERIALS AND METHODS

Data Collection and Review Procedure

Data from the Swedish quality registry for acute community-acquired bacterial meningitis (SQRM) in adults were analyzed retrospectively. In this registry, demographic, clinical, etiological, and management data are registered consecutively during hospital stay and at follow-up visits 2–6 months after discharge. Until December 2007, a paper form was used and sent to the central registration office. Starting in January 2008, the registry has been Internet based and complemented with more detailed information about clinical and management issues. The local specialists in infectious diseases at each of the 22 Swedish infectious disease clinics set the ABM diagnoses using conventional diagnostic criteria throughout the period 2005–2012. ABM was defined as community acquired if the patient had not been hospitalized or operated on within 30 days before admission. The diagnoses were based on clinical criteria with or without cerebrospinal fluid (CSF) analyses. Positive culture and/or polymerase chain reaction and/or microscopy and/or antigen detection in CSF were noticed in 425 (59.7%) patients, and positive blood cultures were obtained in 470 (66.0%) of the total material from 712 patients. The cultures were negative and the etiological diagnosis unknown in 85 patients (11.9%). In 42 of these 85 patients, CSF findings (leukocyte count or glucose, protein, or lactate levels) supported the ABM diagnosis. The diagnosis was based on clinical findings alone in the remaining 43 patients.

From the registry, gender, age, etiology, mental status on admission, corticosteroid treatment, type of antibiotics, treatment start before or after LP, time from admission to treatment, mortality, neurological sequelae, and hearing deficits at follow-up were recorded. Mental status on admission was assessed by the first managing physician at the emergency department and recorded using the reaction level scale (RLS) [26], the Glasgow coma scale (GCS), or both. The time from admission to treatment start was registered as definite intervals: 0–0.5, 0.5–1, 1–2, 2–3, 3–4, 4–6, 6–8, 8–12, or >12 hours. The time point for admission was defined as the time for triage at the first admitting hospital. Adequate antibiotic treatment was defined as intravenous beta-lactam antibiotics (penicillin G, third-generation cephalosporin, or meropenem), for which the isolated bacteria were sensitive according to susceptibility testing at local laboratories and administered in doses recommended for ABM. In patients with unknown etiology, third-generation cephalosporin ± ampicillin or meropenem was assessed as adequate. Mortality was recorded during hospital stay, and neurological or hearing deficits were registered at follow-up 2–6 months after discharge. Neurological sequelae were specified as headache, cognitive dysfunction/dementia, vertigo or fatigue causing limitations of daily activity, epileptic seizures, ataxia, or persistent neurological deficits. Hearing disability was defined by the patient as new onset of impairment, and audiometry was performed when appropriate.

From 2008, the registry also contained information about the diagnostic sequence of cerebral CT scan in relation to LP and start of antibiotic treatment.

Analytical Plan and Statistics

To evaluate possible effects of the guideline revision in use starting in January 2010, registry data from 2005 to 2009 were compared with data from 2010 to 2012. The primary analysis was time from admission to start of adequate antibiotic treatment; secondary analyses were mortality during hospital stay and persisting neurological and hearing deficits at follow-up. The effects on the endpoints were adjusted for differences in demographic characteristics, etiology, mental status, corticosteroid treatment, and use of antibiotics. Additionally, the effects of diagnostic treatment sequences on time to treatment and outcome were analyzed.

The 2-tailed Fisher exact test was used to evaluate categorical outcomes across groups of demographic, etiological, clinical, and management data. The Mann–Whitney test was conducted to compare numeric outcomes. Multivariate analyses with logistic or linear regression were performed to investigate the covariation of parameters.

Estimation of the mean time to treatment was calculated using the midpoints of the registered intervals. If this time to treatment was longer than 12 hours, time to treatment was set to 14 hours.

Ethics

The ethics committee at Karolinska University Hospital approved the study (Dnr 04–1085/1). The patients were informed that the clinical data registered in SQRM could be applied anonymously for research purposes.

RESULTS

There were 394 patients registered during 2005–2009 and 318 during 2010–2012 (Table 1). When the 2 periods were compared,

Table 1. Characteristics of the Patients Admitted During the Study Periods

Characteristic	2005–2012 n = 712 (%)	2005–2009 n = 394 (%)	2010–2012 n = 318 (%)	*P* Value 2005–2009 vs 2010–2012
Female	371 (52.1)	198 (50.3)	173 (54.4)	NS
Male	341 (47.9)	196 (49.7)	145 (45.6)	
Median age [range]	61 [17–95]	61 [17–92]	60 [17–95]	NS
Etiology:				
Streptococcus pneumoniae	361 (50.7)	202 (51.3)	159 (50.0)	NS
Neisseria meningitides	86 (12.1)	43 (10.9)	43 (13.5)	NS
Haemophilus influenza	47 (6.6)	31 (7.9)	16 (5.0)	NS
Listeria monocytogenes	28 (3.9)	15 (3.8)	13 (4.1)	NS
Streptococcus spp.	41 (5.8)	18 (4.6)	23 (7.2)	NS
Other bacteria	64 (9.0)	35 (8.9)	29 (9.1)	NS
Unknown[a]	85 (11.9)	50 (12.7)	35 (11.0)	NS
Mental status on admission:	n = 571	n = 284	n = 287	
RLS >2/GCS <12	215 (37.7)	113 (39.8)	102 (35.5)	NS
RLS ≤2/GCS ≥12	356 (62.3)	171 (60.2)	185 (64.5)	NS
Antibiotic treatment:				
Cefotaxime + Ampicillin	296 (41.6)	172 (43.7)	124 (39.0)	NS
Cefotaxime	126 (17.7)	71 (18.0)	55 (17.3)	NS
Meropenem	214 (30.1)	102 (25.9)	112 (35.2)	<.01
Other antibiotics	76 (10.7)	49 (12.4)	27 (8.5)	NS
Corticosteroid treatment:	n = 651	n = 350	n = 301	NS
Yes	488 (75.0)	271 (77.4)	217 (72.1)	NS

Where data are missing, the number (n) of patients with available data is given. For statistics, the 2-tailed Fisher exact test was used except for age, which was analyzed using the Mann–Whitney test.

Abbreviations: GCS, Glasgow coma scale; NS, not statistically significant; RLS, reaction level scale.

[a] Culture-negative diagnoses; in 42 of these 85 patients, cerebrospinal fluid findings (cell count or glucose, lactate, or protein levels) supported the diagnosis. In the remaining 43 patients, the diagnosis was based on clinical findings alone.

no significant differences were observed for gender, age, etiologies, mental status on admission, or corticosteroid treatment. Meropenem was used significantly more often during 2010–2012, whereas cefotaxime, alone or in combination with ampicillin, was used more often during 2005–2009.

Time to Treatment

Adequate antibiotic treatment was initiated within 1 hour from admission in 192 (31.5%) of the 609 patients and within 2 hours in 312 (51.2%) of the 609 patients with available data. Information about time to treatment during the 2 study periods was reported with similar frequency, 86% in 2005–2009 and 84% in 2010–2012. In 2010–2012, significantly more patients were treated within 2 hours and significantly fewer received treatment more than 3 hours and more than 12 hours, respectively, after admission compared with those in 2005–2009 (Figure 1). On average, treatment was started 1.18 hours earlier (95% confidence interval [CI], .46–1.90 hours; $P < .01$) in 2010–2012 than in 2005–2009.

Treatment delay was significantly less frequent in patients aged <60 years, in patients with meningitis caused by *Neisseria meningitides*, and in patients with impaired mental status (Table 2). When adjusted for these factors along with gender, corticosteroid treatment, and choice of antibiotic treatment in the multivariate analyses, the odds ratios (ORs) for receiving adequate antibiotic treatment in less than 1 hour and in less than 2 hours after admission in 2010–2012 were 1.82 (95% CI, 1.15–2.89; $P < .05$) and 2.07 (95% CI, 1.34–3.20; $P < .01$), respectively.

Outcome

The overall mortality was 68/712 (9.6%). The mortality rate was 46/394 (11.7%) in 2005–2009 and 22/318 (6.9%; $P < .05$) in 2010–2012 (Figure 2).

Age and mental status at admission significantly affected outcome (Table 2). Although not reaching statistical significance, mortality with pneumococcal meningitis was higher compared with meningococcal meningitis. After adjusting for these confounding factors as well as antibiotic treatment, corticosteroid treatment, and gender, the reduction in mortality in 2010–2012 vs that in 2005–2009 no longer reached statistical significance, with an adjusted OR of 0.63 (95% CI, .32–1.25; $P = .19$). However, treatment delay was significantly associated with an increased risk for fatal outcome, with a relative increase in

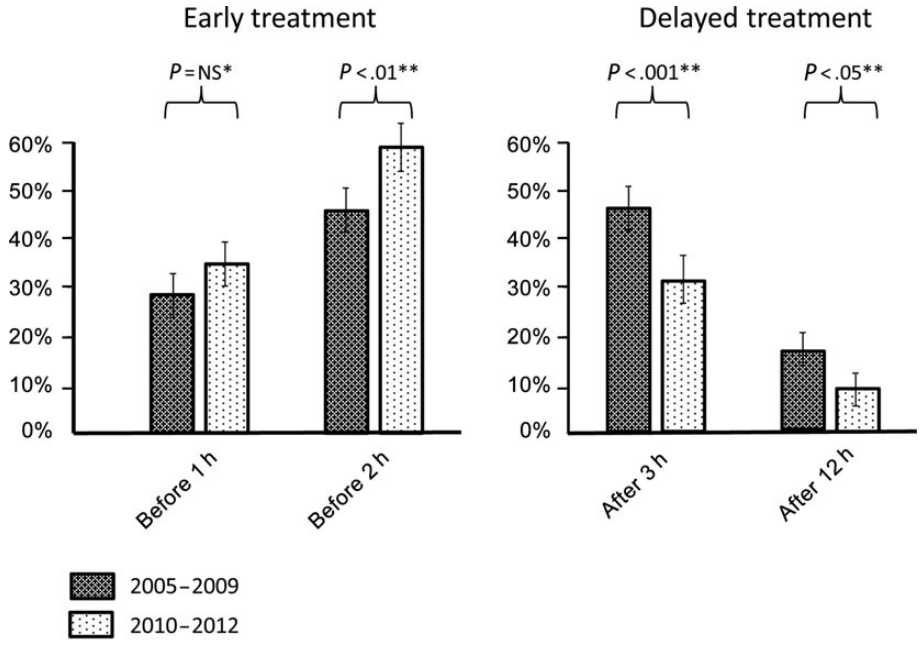

Figure 1. Time from admission to start of antibiotic treatment in patients admitted during 2005–2009 and 2010–2012. Information was available for 609 patients (342 from the first period and 267 from the second period). Early treatment was defined as time to treatment of <2 hours and late treatment as time to treatment of >3 hours. Two-tailed Fisher exact test was used for *P* values. Lines represent the 95% confidence interval. * Indicates adjusted for confounders; this difference was statistically significant ($P < .05$). ** Indicates adjusted for confounders; these differences remained or increased. Abbreviation: NS, not statistically significant.

mortality of 8.8% (95% CI, 3.4%–14.4%; $P < .01$) per hour treatment delay and of 12.6% (95% CI, 3.1%–23.1%; $P < .01$) after adjusting for all confounding factors (Figure 3).

Information about hearing disability or neurological deficits at follow-up 2–6 months after discharge was reported in 535 patients and in similar frequencies during the 2 study periods

Table 2. Main Demographic, Etiological, and Clinical Variables in Relation to Treatment Start, Mortality and Sequelae

Variable	n (%)	Treatment <1 h From Admission: n/n Available Data (%)	Treatment <2 h From Admission: n/n Available Data (%)	Mortality: n/n Available Data (%)	Sequelae[a] in Survivors: n/n Available Data (%)
Gender:	n = 712	n = 609	n = 609	n = 712	n = 535
Male	341 (47.9)	95/294 (32.3)	159/294 (54.1)	35/341 (10.3)	99/258 (38.4)
Female	371 (52.1)	97/315 (30.8)	152/315 (48.3)	33/371 (8.9)	136/277 (49.1)
P Value		NS	NS	NS	<0.05
Age:	n = 712	n = 609	n = 609	n = 712	n = 535
>60 y	363 (51.0)	76/307 (24.9)	135/307 (44.0)	45/363 (12.4)	130/254 (51.2)
≤60 y	349 (49.0)	116/299 (38.8)	176/299 (58.9)	23/349 (6.6)	103/281 (36.7)
P Value		<.001	<.001	<.05	<.001
Etiology:	n = 712				
Streptococcus pneumoniae	361 (50·7)	103/310 (33.2)	168/310 (54.2)	40 /361 (11.1)	144/275 (52.4)
Neisseria meningitides	86 (12.1)	34/74 (45.9)	55/74 (74.3)	4/86 (4.7)	13/64 (20.3)
P Value		<.05	<.01	NS	<.001
Mental status on admission:	n = 571	n = 502	n = 502	n = 571	n = 421
RLS >2/GCS <12	215 (37.6)	91/182 (50.0)	128/182 (70.3)	31/215 (14.4)	81/151 (53.6)
RLS ≤2/GCS ≥12	356 (62.3)	66/320 (20.1)	132/320 (41.3)	20/356 (5.6)	105/270 (38.9)
P Value		<.001	<.001	<.001	<.01

Fisher exact test was used for *P* values.

Abbreviations: GCS, Glasgow coma scale; NS, not statistically significant; RLS, reaction level scale.

[a] Neurological and/or hearing deficits at follow-up 2–6 months after discharge.

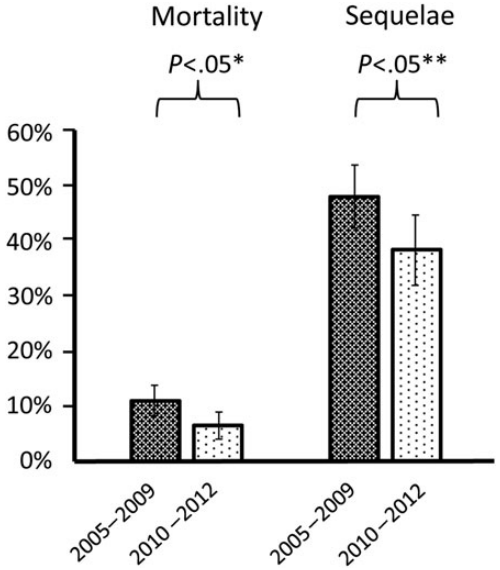

Figure 2. On the left is the mortality rate for 394 patients admitted in 2005–2009 and 318 patients admitted in 2010–2012. On the right is the rate of neurological deficits and/or hearing disability at follow-up (2–6 months after discharge) in the 296 patients admitted in 2005–2009 and the 239 patients admitted in 2010–2012 from whom this information was reported. Two-tailed Fisher exact test was used for *P* values. Lines represent the 95% confidence interval. * Indicates adjusted for confounders; this difference was not statistically significant (*P* = .19). ** Indicates adjusted for confounders; this difference remained.

(85% in 2005–2009 and 81% in 2010–2012). Sequelae were observed in 144/296 (48.6%) patients in 2005–2009 and in 91/239 (38.1%) in 2010–2012 ($P < .05$; Figure 2). The risk of sequelae was significantly associated with gender, age, etiology, and mental status on admission (Table 2). After adjusting for these and other confounders, there was still a significant reduction in sequelae during 2010–2012 vs 2005–2009, with an OR of 0.54 (95% CI, .35–.84; $P < .01$).

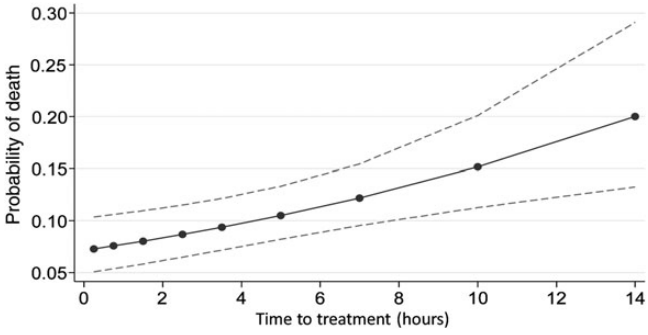

Figure 3. Probability of death related to time from admission to start of antibiotic treatment with 95% confidence intervals.

Sequence of Lumbar Puncture and Treatment

LP was performed in 651/712 (91.4%) patients and preceded antibiotic treatment start in 205 (38.7%) of 530 patients, where this sequence was recorded. Similar door-to-antibiotic times were seen whether antibiotics were started before LP or LP preceded treatment. LP was performed before treatment significantly more often in 2010–2012 (125/290 = 43.1% patients) compared with 2005–2009 (80/240 = 33.3% patients; $P < .05$).

Sequence of Lumbar Puncture and Computerized Tomography of the Brain

Information on LP with or without prior CT was available in 414 of the 495 patients in 2008–2012. Cerebral CT scan was performed in 345 (83.3%) of the 414 patients; in 236 (57.0%) patients, CT was performed before LP (Table 3). This sequence was associated with an average treatment delay of 1.6 hours (95% CI, .7–2.5 hours; $P < .01$) and significantly increased mortality and sequelae among survivors compared with those 178 patients in whom LP was executed without prior CT (109 with CT later and 69 without CT). Similar mental status at presentation and age were noted in the 2 groups, whereas pneumococcal etiology was more common and meningococcal etiology was rarer in patients who underwent LP after CT. After adjusting for these and other potential confounders, the increased risk for fatal outcome remained, though it was not statistically significant, whereas the risk for sequelae remained significant and the difference in time to treatment increased. Antibiotics were not administered before neuroimaging in 125 (39.2%) of 319 patients with available data regarding the CT treatment sequence.

Lumbar Puncture in Patients With Impaired Mental Status

LP was performed in 167/208 patients with moderately to severely impaired mental status (RLS ≥3 or GCS ≤11), with a mortality of 9.6% (16/167). Of these, 130 patients were admitted in 2008–2012 with information about the CT–LP sequence. Fifty-five patients underwent LP without prior CT; among these patients, 3 died and 11 suffered from neurological sequelae. In the 75 patients in whom CT preceded LP, 6 died and 33 had neurological sequelae. In 55 patients with RLS ≥4 or GCS ≤8, information about the CT–LP sequence was obtained. Of 30 patients who underwent LP without prior CT, 2 died and neurological sequelae occurred in 4 compared with 1 death and 11 with sequelae in the remaining 25 patients in whom CT preceded LP.

DISCUSSION

In 2004, the Swedish guidelines for ABM were revised, mainly according to the Infectious Diseases Society of America guidelines [19]. Recommendations to administer corticosteroids

Table 3. Main Outcomes and Main Confounders Related to Different Sequences of Lumbar Puncture and Computerized Tomography of the Brain

Outcome and Confounders	LP Without Prior CT	LP After CT	*P* Value
Number of patients (%): n = 414	178 (43.0)	236 (57.0)	
Outcomes:			
Treatment <1 h: n/n available data (%): n = 343	60/154 (39.0)	47/189 (24.9)	<.01
Treatment <2 h: n/n available data (%): n = 343	95/154 (61.7)	91/189 (48.1)	<.05
Mortality:	6/178 (3.4)	27/236 (11.4)	<.01
Sequelae[a] in survivors: n/n available data (%): n = 334	32/151 (21.2)	65/183 (35.5)	<.01
Favorable outcome[b]: n/n available data (%): n = 367	119/157 (75.8)	92/210 (43.8)	<.001
Confounders			
Age >60 y	86/178 (48.3)	102/236 (43.2)	NS
RLS ≥3/GCS ≤11 on admission: n/n available data (%)	55/160 (34.4)	75/221 (33.9)	NS
Pneumococcal etiology:	68/178 (38.2)	129/236 (54.7)	<.01
Meningococcal etiology:	38/178 (21.3)	21/236 (8.9)	<.01

Main outcomes were time from admission to adequate antibiotic treatment, mortality, and sequelae and main confounders were age, mental status on admission, and etiology. Two-tailed Fisher exact test was used for *P* values.

Abbreviations: CT, computerized tomography; GCS, Glasgow coma scale; LP, lumbar puncture; NS, not statistically significant; RLS, reaction level scale.

[a] Neurological and/or hearing deficits at follow-up 2–6 months after discharge (proportions of survivors with available data).

[b] Recovery to normal activity without neurological or hearing deficits at follow-up 2–6 months after discharge (proportions of all patients with available data).

together with the first dose of antibiotics and a restrictive approach to early LP with CT before LP in patients presenting with "red flags" were adopted. The necessity to start antibiotics before CT in suspected ABM was emphasized. At follow-up, median duration to antibiotic treatment was found to exceed 2 hours, which was longer than that reported in 1994–2004 [16]. Even if this duration was in agreement with that reported by others [2, 4, 7, 21, 22, 24, 25, 27], the risk with delayed treatment had to be balanced against potential risks associated with LP. The documentation for LP-induced herniation in unconscious adults with elevated ICP alone was found to be limited, with available data showing that LP could be performed without serious consequences [3]. Also taking into account that increased ICP cannot be ruled out by a CT investigation, it was concluded that CT before LP added little to the management of ABM in adults without focal neurological signs or signs of imminent herniation.

In 2009, Swedish recommendations for ABM management in adults were revised. Deletion of moderately to severely impaired consciousness and new onset seizures as contraindications to immediate LP constituted the major change. The reasons for this change have been discussed in detail elsewhere [16, 17]. In addition to being issued on the Swedish Society for Infectious Diseases home page (www.infektion.net), the new recommendations were presented in a national medical journal in 2008 [28, 29] and at the annual Swedish Medical Conference in 2009.

The present results demonstrate that after the change in the guidelines, adults with ABM were treated, on average, more than 1 hour earlier. This finding held after confounding factors were considered. Optimally, in ABM, use of antibiotics and corticosteroids should be initiated within 0.5–1 hour from admission [18–20]. During 2010–2012, treatment starts were achieved within 1 hour in 35% of the cases and within 2 hours in 60%. Although far from the recommended time frames, these figures are higher than those for 2005–2009 as well as most findings from other countries that had treatment starts a median of 2–4 hours after arrival [2, 4, 7, 21, 22, 24, 25, 27]. In line with previous findings, old age and nonmeningococcal etiology were associated with delayed treatment, and severely impaired mental status was associated with earlier treatment [2, 7, 12, 13].

The decrease in door-to-antibiotic time in 2010–2012 that occurred following the guideline revision was associated with a concomitant decrease in mortality. This decrease did not result in a compensatory increased risk for neurological or hearing deficits; on the contrary, the rate of sequelae also decreased significantly (Figure 2). Whereas the significance remained for sequelae after adjusting for confounding factors, this was not the case for mortality. Mortality, however, was significantly associated with delayed antibiotic treatment, which is consistent with findings by others [2, 4, 7, 25]. In the current study, there was a relative increase in mortality of about 13% for each hour of delay. Thus, the shorter door-to-antibiotic time likely contributed to the improved outcome observed in 2010–2012.

During 2008–2012, cerebral CT scan was performed in 83% of the patients. CT preceded LP in more than half of all cases and antibiotic treatment was not administered before CT in 39% of all cases. As in other studies [7, 21, 22, 25], the sequence of neuroimaging before LP resulted in a delay in adequate

antibiotic treatment of 1.6 hours and an increased risk of death or sequelae. The reason for not giving antibiotics before CT is not known. CSF analyses are important for ABM diagnosis, and LP is often required to initiate adequate treatment in clinical practice. It may be speculated that earlier Swedish guidelines made some physicians reluctant to perform LP without a prior CT scan in mentally affected patients. Although ABM is not refuted initially, the suspicion of this diagnosis may not be strong enough to initiate adequate treatment until LP is performed. The poor adherence to the recommendation to start treatment with antibiotics and corticosteroids before neuroimaging corroborates previous findings [3, 7, 21, 23, 27]. The aim of the guideline revision in 2009 was to speed up treatment by reducing the time from admission to LP and to avoid unnecessary delay associated with CT scan. The time to LP was lacking in the SQRM during the entire study period, and the sequence of LP–CT was not recorded during 2005–2007, thus, not allowing comparison between the 2 time periods. However, the combination of significantly earlier treatment and significantly more LPs before treatment start observed in 2010–2012 indirectly indicate earlier LP and more adequate diagnostic treatment management.

Mortality in patients with moderately to severely impaired mental status was relatively low compared with that of patients in other studies [3, 30]. Furthermore, mortality was similar and the risk of sequelae was lower in these severely ill patients in whom LP was executed before CT compared with those in whom CT preceded LP. These data indicate that performance of a prompt LP is safe in mentally affected patients without focal neurological deficits. This conclusion is further supported by a recent Canadian study in which favorable outcome was achieved in ABM patients with high opening pressures treated with lumbar CSF drainage [31].

To our knowledge, we are the first to evaluate the efficacy of different guidelines for initial management of ABM in adults, focusing on time to adequate treatment along with different LP–CT sequences and their effects on mortality and sequelae. The advantage with this registry study is the large number of consecutive patients, enabling evaluation of clinically significant confounders by multivariate analyses. The disadvantages are the retrospective character, lack of opportunity for stratification, and lack of explicit criteria for the clinical diagnosis of ABM and exact time point when mental status was addressed. The coverage of SQRM was higher during 2010–2012 (80%) compared with 2005–2009 (60%) according to data from the National Board of Health and Welfare in Sweden. In addition, meropenem was given more often in 2010–2012. Another limitation is the lack of comprehensive adjustment of disease severity, such as systemic compromise, low CSF leukocyte count, seizures, and comorbidity. However, age, mental status, and etiology are important factors that influence the door-to-antibiotic time, which was the primary outcome in our study [2, 7, 12, 13]. These parameters, in combination with the use of corticosteroids and the choice of antibiotic treatment, are also the most decisive for clinical outcome [1–7, 12, 13, 30]. All these confounders, that is, age, mental status, etiology, corticosteroids, and antibiotics, were included in the adjusted analyses of the present study and did not noticeably affect the results. Finally, since inclusion was based on clinical as well as laboratory findings, the generalizability in clinical practice is high.

CONCLUSIONS

Although a relatively low mortality of 6.9% was achieved, our report emphasized the difficulties and challenges of achieving adequate, timely management of adult community-acquired ABM. Further studies to evaluate different strategies for minimizing treatment delay are needed. The present study indicates that deletion of impaired mental status as a contraindication to immediate LP resulted in earlier antibiotic treatment that was associated with improved outcome and that revision of international guidelines should be considered.

Notes

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

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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