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Folafoluwa O. Odetola
Susan L. Bratton

Characteristics and immediate outcome of childhood meningitis treated in the pediatric intensive care unit

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F. O. Odetola (✉) · S. L. Bratton
Department of Pediatrics and Communicable Diseases,
Division of Pediatric Critical Care Medicine,
University of Michigan Medical School and the University of Michigan Health System,
Ann Arbor, MI 48109, USA
e-mail: fodetola@med.umich.edu
Tel.: +1-734-6158418
Fax: +1-734-6155153

Present address:
F. O. Odetola
300 North Ingalls Street,
Ann Arbor, MI 48109, USA

Abstract *Objective:* To describe patient characteristics, use of technology and mortality in children with meningitis admitted to the pediatric intensive care unit (PICU). *Design:* Retrospective cohort study. *Setting:* Fifteen US PICUs. *Patients:* All admissions with a diagnosis of meningitis between 1995 and 2000 in the Pediatric Intensive Care Unit Evaluations (PICUEs) database. *Measurements and results:* Of 559 patients with meningitis, 58% were male. The median age was 19 months and the median length of PICU stay was 2 days. The crude PICU mortality rate was 7%. Three hundred thirty-four (60%) patients had bacterial meningitis. Non-survivors had significantly higher Pediatric Risk of Mortality (PRISM) III scores and also constituted a larger proportion of the patients with bacterial meningitis, coma and shock upon PICU admission. The use of invasive devices was higher among non-survivors, patients with bacterial meningitis or those who were in coma or shock upon PICU admission. There was significant variation in the use of intracranial pressure (ICP) monitors by coma status and by institution. In multivariate analysis, patients had 1.26 higher odds of mortality for each unit increase in PRISM III score (odds ratio 1.26, 95% confidence interval: 1.19–1.34), while adjusting for other variables. *Conclusion:* In a large cohort of children admitted to the PICU with meningitis, severity of illness, particularly the presence of shock or coma, was significantly associated with both the higher use of invasive medical devices and higher mortality. There was significant variation in the use of ICP monitors among the various PICUs without statistical association with survival.

Keywords Meningitis · Medical device · Mortality · Mechanical ventilation · Intracranial pressure · Pediatric intensive care unit

Introduction

Childhood meningitis, particularly bacterial meningitis, has been associated with high case-fatality rates and the risk of persistent neurological sequelae [1, 2]. Advances in medicine, particularly the development of vaccines and antibiotics, have led to a reduction in both the incidence of, and mortality due to, meningitis. Mortality has decreased from 50–80% at the turn of the 20th century to the present rates of 1–8% beyond the neonatal age group [3]. The neurological sequelae resulting from childhood meningitis can be persistent and debilitating [4, 5].

Most in-hospital deaths from meningitis occur within the first 48 h of admission to the pediatric intensive care unit (PICU) [6, 7].The occurrence of neurological or hemodynamic impairment prompts admission to the PICU, often necessitating invasive cardio-respiratory monitoring and support [7–12]. The timely institution of intensive care may improve survival from meningitis and shock [8–10]. Singhi et al. reported a 50% decrease in mortality from childhood meningitis with the introduction of PICU services at their institution [7]. In a study of adult patients with purulent meningitis, while keeping the therapeutic regimen otherwise unchanged, a four-fold increase in the use of mechanical ventilation over a 10-year period was associated with a decrease in adjusted mortality by 50% [9]. Although judicious use of assisted ventilation in patients with meningitis has been associated with improved survival, few studies have evaluated the use of other invasive medical devices, such as intracranial pressure (ICP) monitors, in childhood meningitis [13, 14].

This study was performed to describe patient characteristics, the use of intensive care technology and mortality in a cohort of children with meningitis treated in the PICU.

Materials and methods

We conducted a retrospective cohort study using the Pediatric ICU Evaluations (PICUEs) database. The PICUEs is a system for monitoring the performance of participating PICUs, providing standardized mortality ratios, length of stay and efficiency rates. The database contains prospectively collected data obtained from PICUs that voluntarily participate and pay a fee for annual standardized reports. At the time of the study, the database had approximately 20,000 records collected from 15 PICUs. Our study population included all PICU admissions with a diagnosis of meningitis, recorded within the primary or secondary acute diagnoses fields in the database (n=559) over a 6-year period from 1995 to 2000. The study was approved by the University of Michigan institutional review board for human subject research.

The data included physiologic and demographic variables, Pediatric Risk of Mortality III (PRISM III) scores, patient co-morbidities, patient disposition and information on the use of medical devices, such as mechanical ventilators, central venous/arterial catheters and intracranial pressure (ICP) monitors.

Measures

The study outcome was PICU mortality. Meningitis was diagnosed by cerebrospinal fluid analysis and classified into bacterial (Gram-positive and Gram-negative), fungal, viral and “other”. For the purpose of this study, the etiology of meningitis was analyzed in two groups: bacterial or non-bacterial. Certain definitions were made a priori. Invasive medical devices were defined as mechanical ventilators, ICP monitors, arterial catheters, central venous catheters (CVC) and infusion of vasoactive medications. These devices were assessed individually. Coma was defined as a Glasgow coma score of less than 8 within the first 12 h of PICU admission, as previously reported in the literature [6, 7, 13]. The diagnosis of shock was made by the physicians caring for the patients. The most abnormal physiologic values (highest or lowest) during the first 12 h of admission to the PICU were used in the analyses, including lowest systolic blood pressure and highest heart rate. Since hemodynamic or neurological impairments in children with meningitis are widely observed indications for PICU admission and bacterial etiology is associated with poorer outcomes, we described the characteristics of patients, use of invasive medical devices and mortality within the entire cohort and, subsequently, among the patients based on etiology, coma or shock status at PICU admission.

Statistical analysis

Descriptive analyses were performed to characterize the study population. Median values and inter-quartile ranges are reported. Bivariate analyses were conducted to assess the association of individual factors with mortality and, thereafter, to compare patient characteristics, use of invasive devices and outcome based on etiology, coma or shock status. We used Pearson’s chi-square test for categorical variables and the Mann-Whitney test for continuous variables, with an α-level of 0.05. All variables associated with mortality with a p value of 0.30 or less were included in multivariate logistic regression models. Two models were fit, initially with the PRISM III score as an independent variable and then without the score in order to include variables routinely incorporated within the PRISM III score. All analyses were conducted using Stata 7 for Windows (Stata; College Station, Texas).

Results

Of 559 patients with meningitis, 58% were male. The median age was 19 months (interquartile range [IQR]: 4–92) and the median PRISM III score at 12 h was 3 (IQR: 0–8). Five percent of the patients had an underlying chronic illness. At the time of admission to the PICU, 14% of the patients were comatose and 11% were in shock. The median PICU length of stay was 2 days (IQR: 1–4) and a bacterial etiology for meningitis was found in 334 (60%) patients. In the entire cohort, the overall frequency of use of invasive medical devices varied from 6% (ICP monitors) to 32% (CVC) (Table 1). Two hundred and fifty (45%) patients had at least one medical device in situ, while 175 patients (31%) had two or more devices used during their PICU stay.

Thirty-nine (7%) patients died in the PICU. Survivors and non-survivors were similar in age and gender and had similar PICU lengths of stay (Table 1). Non-survivors were sicker upon PICU admission, with significantly higher PRISM III scores, a higher proportion of patients with bacterial meningitis (87 vs 58%, p<0.01), coma (59 vs 10%, p<0.01) or shock (33% vs 9%, p<0.01) at PICU admission. Invasive devices were used more often in the patients who eventually died.

Patients in shock at the time of admission to the PICU had significantly higher use of invasive medical devices (except ICP monitors), longer length of stay in the PICU, more physiologic instability and higher mortality; compared to patients not in shock at the time of admission to the PICU (Table 2). The predicted mortality was higher in the patients with shock compared to the patients not in shock (7.7% vs 0.8%, p<0.01).

Patients in coma at the time of admission to the PICU had a statistically significant higher use of invasive medical devices. They also had higher PRISM III scores, longer length of stay in the PICU and higher mortality (Table 3). The predicted mortality was higher in the comatose patients compared to the non-comatose patients (10.5% vs 0.7%, p<0.01). Having bacterial meningitis was associated with higher PRISM III scores, shock,

Table 1 Demographic and clinical characteristics of patients with meningitis admitted to a PICU

	All	Survivors	Non-survivors	*p*
	n=559	*n*=520	*n*=39	
Age in months, median (IQR)	19 (4, 92)	19 (4, 90)	34 (5, 97)	0.71
Male gender, *n* (%)	321 (58)	302 (58)	19 (49)	0.25
Coma on admission, *n* (%)	76 (14)	53 (10)	23 (59)	<0.01
Shock on admission, *n* (%)	61 (11)	48 (9)	13 (33)	<0.01
Bacterial meningitis, *n* (%)	334 (60)	300 (58)	34 (87)	<0.01
Length of stay in days, median (IQR)	2 (1, 4)	2 (1, 4)	2 (1, 5)	0.99
PRISM III, median (IQR)	3 (0, 8)	2 (0, 7)	22 (16, 32)	<0.01
Highest HR (beat/minute) Median (IQR)	156 (128, 180)	154 (127, 178)	181 (158, 208)	<0.01
Lowest systolic BP (mmHg), median (IQR)	91 (80, 101)	92 (81, 102)	75 (60, 91)	<0.01
Central venous catheter, *n* (%)	181 (32)	150 (29)	31 (80)	<0.01
Arterial catheter, *n* (%)	140 (25)	110 (21)	30 (77)	<0.01
ICP monitor, *n* (%)	34 (6)	26 (5)	8 (21)	<0.01
Mechanical ventilator, *n* (%)	165 (30)	131 (25)	34 (87)	<0.01
Vasoactive medications, *n* (%)	116 (21)	86 (17)	30 (77)	<0.01

PRISM III Pediatric Risk of Mortality score III, *BP* blood pressure, *HR* heart rate, *ICP* intracranial pressure
Vital signs are reported as the most abnormal values during the first 12 h of PICU admission.
Median values and the interquartile range (IQR) are reported as median ($25^{th}\%$, $75^{th}\%$).

Table 2 Patient characteristics, invasive device use and outcome, according to shock status at PICU admission

	In shock	Not in shock	*p*
	(*n*=61)	(*n*=498)	
Length of stay, median (IQR)	3 (2, 7)	2 (1, 4)	<0.01
PRISM III, median (IQR)	11 (5, 19)	2 (0, 7)	<0.01
Highest HR (beat/minute), median (IQR)	185 (158, 207)	153 (126, 178)	<0.01
Lowest systolic BP, median (IQR)	83 (72, 96)	92 (81, 102)	<0.01
Central venous catheter, *n* (%)	44 (72)	137 (28)	<0.01
Arterial catheter, *n* (%)	35 (57)	105 (21)	<0.01
ICP monitor, *n* (%)	5 (8)	29 (6)	0.46
Mechanical ventilator, *n* (%)	33 (54)	132 (27)	<0.01
Vasoactive medications, *n* (%)	44 (72)	72 (15)	<0.01
Death, n (%)	13 (21)	26 (5)	<0.01

PRISM III Pediatric Risk of Mortality score III, *BP* blood pressure, *HR* heart rate, *ICP* intracranial pressure
Vital signs are recorded as the most abnormal values during the first 12 h of PICU admission.
Median values and the interquartile range (IQR) are reported as median ($25^{th}\%$, $75^{th}\%$).
Chi Square and Mann-Whitney tests used for bivariate comparisons

higher use of invasive devices and higher mortality (Table 4). In multivariate analysis, patients had 1.26 higher odds of mortality for each unit increase in PRISM III score (odds ratio 1.26, 95% confidence interval: 1.19–1.34), while adjusting for etiology, the presence of shock and gender.

In a separate model without the PRISM III score, the presence of coma at PICU admission and a diagnosis of bacterial meningitis were associated with, respectively, 10-fold and 3-fold higher odds of mortality. Each unit increase in the lowest systolic blood pressure had a nominal protective effect (Table 5). Eleven (14%) of the comatose patients had ICP monitors inserted, compared to 23 (5%) of the non-comatose patients (Table 3) ($p<0.01$). The latter group of non-comatose patients who had ICP monitors placed was significantly less ill, with a lower median PRISM III score (5 vs 12, $p<0.01$). However, they were sicker than the non-comatose patients who did not have an ICP monitor placed (median PRISM III score of 2, $p<0.01$).

The use of ICP monitors varied widely between the various PICUs. Of the 15 centers, 4 did not insert ICP monitors in their comatose patients with meningitis (non-use centers), 4 inserted them less than half the time (low-use centers) and 6 centers inserted them more than half the time (high-use centers). One center had no patients with meningitis in coma on admission to the PICU. Of the 23 patients without coma who had ICP monitors placed, 20 patients (87%) had the monitors placed in the high-use centers. There was no difference in the survival of patients between centers with high, low or non-use of ICP monitors, with mortality rates of 5.0%, 8.5% and 8.4%, respectively (chi-square 2.61, p=0.27). Comparison of mortality between high-use centers and all other centers

Table 3 Patient characteristics, invasive device use and outcome according to coma status at PICU admission

	Comatose	Non-comatose	p
	(n=76)	(n=483)	
Length of stay, median (IQR)	3 (1, 6)	2 (1, 4)	<0.01
PRISM III, median (IQR)	12 (7, 19)	2 (0, 5)	<0.01
Highest HR, median (IQR)	163 (133, 195)	156 (128, 178)	0.04
Lowest systolic BP, median (IQR)	88 (70, 102)	91 (81, 101)	0.06
Central venous catheter, *n* (%)	47 (62)	134 (28)	<0.01
Arterial catheter, *n* (%)	41 (54)	99 (21)	<0.01
ICP monitor, *n* (%)	11 (14)	23 (5)	<0.01
Mechanical ventilator, *n* (%)	54 (71)	111 (23)	<0.01
Vasoactive medications, *n* (%)	33 (43)	83 (17)	<0.01
Death, *n* (%)	23 (30)	16 (3)	<0.01

PRISM III Pediatric Risk of Mortality score III, *BP* blood pressure, *HR* heart rate, *ICP* intracranial pressure
Vital signs are recorded as the most abnormal values during the first 12 h of PICU admission.
Median values and the interquartile range (IQR) are reported as median (25^{th}%, 75^{th}%).
Chi Square and Mann-Whitney tests used for bivariate comparisons

Table 4 Patient characteristics, invasive device use and outcome, according to etiology of meningitis

	Bacterial	Non-bacterial	p
	(n=334)	(n=225)	
Length of stay, median (IQR)	2 (1, 4)	2 (1, 4)	0.21
PRISM III, median (IQR)	4 (0, 9)	2 (0, 6)	<0.01
Highest HR, median (IQR)	162 (132, 184)	148 (120, 176)	<0.01
Lowest systolic BP, median (IQR)	90 (79, 102)	92(82, 100)	0.45
Central venous catheter, *n* (%)	129 (39)	52 (23)	<0.01
Arterial catheter, *n* (%)	99 (30)	41 (18)	<0.01
ICP monitor, *n* (%)	27 (8)	7 (3)	0.02
Mechanical ventilator, *n* (%)	105 (31)	60 (27)	0.23
Vasoactive medications, *n* (%)	89 (27)	27 (12)	<0.01
Coma, *n* (%)	49 (15)	27 (12)	0.37
Shock, *n* (%)	48 (14)	13 (6)	<0.01
Death, *n* (%)	34 (10)	5 (2)	<0.01

PRISM III Pediatric Risk of Mortality score III, *BP* blood pressure, *HR* heart rate, *ICP* intracranial pressure
Vital signs are recorded as the most abnormal values during the first 12 h of PICU admission.
Median values and the interquartile range (IQR) are reported as median (25^{th}%, 75^{th}%).
Chi Square and Mann-Whitney tests used for bivariate comparisons

Table 5 Multivariate logistic regression analyses of the predictors of outcome

	Variables	Adjusted OR	95% CI	p
Model 1				
r^2=0.49, −2Log	PRISM III score	1.26	1.19–1.34	<0.01
likelihood	Bacterial etiology	2.90	0.90–9.29	0.07
=143.80	Shock on admission	0.57	0.18–1.79	0.33
	Female gender	0.86	0.34–2.15	0.74
Model 2				
r^2=0.31, −2Log	Coma on admission	10.43	4.84–22.47	<0.01
likelihood	Shock on admission	2.47	0.99–6.17	0.05
=196.15	Bacterial etiology	3.43	1.24–9.47	0.02
	Lowest systolic BP	0.98	0.95–0.99	0.03
	Highest HR	1.01	0.99–1.02	0.06
	Female gender	1.14	0.53–2.49	0.74

PRISM III Pediatric Risk of Mortality score III, *BP* blood pressure, *HR* heart rate, *95% CI* 95% confidence interval, *OR* odds ratio revealed similar findings that were not statistically significant (chi-square-Mantel-Haenszel 2.59, p=0.11). After adjusting for PRISM score using logistic regression with the PICU outcome (dead or alive) as the dependent variable and the center use of ICP monitors as the independent variable, the odds ratio (OR) for death in high-use centers versus other centers was 0.65 (95% confidence interval 0.25–1.69, p=0.37).

Discussion

This study describes the immediate outcome in the largest cohort to date of children with meningitis admitted to US PICUs. We report a mortality rate of 7% in our cohort, consistent with published mortality rates of 1–8%, for childhood meningitis beyond the neonatal period [3, 6]. Severity of illness, marked by the presence of hemodynamic or neurological impairment at the time of PICU admission, was associated with higher predicted and observed mortality in this cohort of children admitted to the PICU with meningitis.

A median PRISM III score of 3, with a predicted mortality of 1% in the entire cohort, suggests the likelihood of the admission of some less sick patients into the PICU for monitoring of physiologic status rather than for intensive PICU management. We therefore described the characteristics of patients, invasive device use and outcome based on the presence of either coma or shock at the time of PICU admission, since such complications should ideally prompt PICU admission. We also characterized patients based on etiology, as bacterial meningitis is associated with poorer outcomes. We observed higher mortality in patients with bacterial meningitis, and hemodynamic or neurological impairment at the time of PICU admission.

Physiologic instability, evidenced by the presence of coma, shock and tachycardia, was associated with mortality among the entire cohort. These indices signify severe disease and are components of the PRISM III score, a tool used to predict the risk of mortality in children admitted to the PICU [15]. We found higher odds of mortality with increment in severity of illness scores. In a single-center PICU study to describe the functional status of survivors of bacterial meningitis, Madagame et al. [16] similarly reported severity of illness on admission as a significant predictor of both mortality and impaired functional status on follow-up. It is important to note, however, that the PRISM III score is not a tool intended for assessment of individual patient outcomes.

We also describe the use of technology among the study cohort. The delivery of care within the PICU is complex and medical devices may not improve outcome on their own but are incorporated into the processes of ICU care. Mechanical ventilators, when used judiciously, have been shown to improve outcome for select patients with meningitis [9]. As expected, the use of invasive monitoring devices, as a whole, was higher among the more severely ill patients and we observed a significant difference in the use of invasive medical devices by etiology, coma and shock status.

Intracranial pressure (ICP) is a crucial determinant of cerebral perfusion and is important in the outcome of meningitis in children. It is frequently elevated in patients with clinical meningitis, with the maximal elevation occurring within the first 24–48 h after diagnosis [13, 17]. Increased ICP, with resultant compression of the brain stem and impairment of cerebral circulation, is an important cause of neurological damage and death in patients with meningitis. No guidelines presently exist for the use of ICP monitors in patients with meningitis and medical opinion differs as to whether ICP monitoring as a process of care alters outcome. Some clinicians do not consider elevated ICP a treatable complication and, consequently, aggressive monitoring and treatment of elevated ICP is often not pursued in children with meningitis [17]. Others, as shown in studies by Pesso et al. [14] and Grande et al. [18], have demonstrated improved prognosis with ICP monitoring and management in both children and adults with severe bacterial meningitis. Some clinicians consider monitoring ICP in children in whom there is clinical or radiographic evidence of increase in ICP [17], while others have reported the lack of correlation between findings on cranial tomography and the risk of cerebral herniation in children with meningitis [6].

As our data show, ICP monitoring is not routinely performed in children with meningitis, even among the subset of patients in coma. Thirty-four patients (6%) in our study cohort had an ICP monitor placed, two thirds of whom were not comatose on admission to the PICU. Madagame et al. [16] reported that only 2 patients out of their cohort of 32 patients had ICP monitors inserted, even though 6 of these patients underwent endotracheal intubation and mechanical ventilation for the treatment of elevated ICP. We also observed significant variation in the use of ICP monitors among the various PICUs in the study cohort. PICUs that used ICP monitors more frequently in meningitis had lower, though statistically insignificant, mortality rates in comparison to those with less frequent, or non-use, of ICP monitors. Variation in the use of various therapies in the PICU setting has been previously reported and could contribute to the differences in outcomes of pediatric critical illness [19, 20]. The authors advocate adequately powered prospective studies to study further the association between "center use" of ICP monitors and outcome of meningitis, particularly in those patients comatose at admission into the PICU.

This study has limitations. The specific etiologic bacterial organisms were not reported in the database. A description of the specific bacterial organisms might have shed light on the impact of meningitis from vaccinepreventable invasive bacterial disease in this cohort of children with meningitis treated in the PICU. Another limitation stems from the fact that the diagnoses within the data set were made within 24 h of PICU admission and the delineation of bacterial versus non-bacterial meningitis might be unclear at this time. To address this limitation, characteristics of patients with and without bacterial meningitis were described, highlighting the patient-level characteristics, use of technology and outcome.

The actual indication for each PICU admission was unknown and some patients had low PRISM III scores suggesting minimal impairment of physiologic status. To address this limitation, analyses were conducted based on coma and shock status, well-recognized complications of meningitis that often prompt admission to the PICU. The indications for the use of invasive devices in each individual patient were based on individual provider judgement; hence the reasons for device placement, including ICP monitor placement, in our cohort were unknown and might not have been consistent. We were therefore unable to determine which patients received therapy for intracranial hypertension or which had ICP monitored with a ventricular drain that would provide a means for cerebrospinal fluid drainage.

Meningitis, especially bacterial meningitis, leads to significant morbidity [4, 5]. Due to the retrospective nature of our study design, the functional status of the survivors within our cohort could not be assessed. Also, functional status was measured at the time of PICU discharge in only 13% of the survivors, making the information not generalizable to all the survivors in the cohort.

In conclusion, in a large cohort of children admitted to the PICU with meningitis, higher severity of illness was significantly associated with increased mortality. Patients with bacterial meningitis or who were either comatose or in shock early in their PICU admission had a greater likelihood of dying despite higher use of invasive medical devices, suggesting the need for timely admission of this subset of patients with meningitis. In critically ill children with meningitis, the utilization of ICP monitors, the inter-institutional variation in their use and the relationship of ICP monitoring to clinical outcomes need further study.

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References

1. Wald E, Bergman I, Taylor G, Chiponis D, Porter C, Kubek K(1986) Long-term outcome of group B streptococcal meningitis. Pediatrics 77:217–221
2. Sell S (1983) Long term sequelae of bacterial meningitis in children. Pediatr Infect Dis J 2:90–93
3. Prober CG (2000) Central nervous system infections. In: Behrman (ed) Nelson textbook of pediatrics, 16th edn. Saunders, Philadelphia, p 756
4. Bedford H, deLouvois J, Halket S, Peckham C, Hurley R, Harvey D (2001) Meningitis in infancy in England and Wales: follow up at age 5 years. BMJ 323:533–536
5. Grimwood K, Anderson P, Anderson V, Tan L, Nolan T (2000) Twelve year outcomes following bacterial meningitis: further evidence for persisting effects. Arch Dis Child 83:111–116
6. Rennick G, Shann F, de Campo J (1993) Cerebral herniation during bacterial meningitis in children. BMJ 306:953–955
7. Singhi S, Singhi P, Baranwal A (2001) Bacterial meningitis in children: critical care needs. Indian J Pediatr 68:737–747
8. Zhukov V, Borzunov V, Egorov V (1997) Respiratory aid to patients with severe forms of suppurative meningitis. Anesteziol Reanimatol 1:28–31
9. Rasmussen N, Hansen B, Bohr V, Kristensen S (1988) Artificial ventilation and prognostic factors in bacterial meningitis. Infection 16:158–162
10. Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, Peterson E, Tomlanovich M (2001) for the Early Goal-Directed Therapy Collaborative Group: early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med 345:1368–1377
11. Van Deuren M, Brandtzaeg P, Van der Meer J (2000) Update on meningococcal disease with emphasis on pathogenesis and clinical management. Clin Microbiol Rev 13:144–166
12. Ceneviva G, Paschall JA, Maffei F, Carcillo JA (1998) Hemodynamic support in fluid-refractory pediatric septic shock. Pediatrics 102:e19
13. Minns RA, Engleman HM, Stirling H (1989) Cerebrospinal fluid pressure in pyrogenic meningitis. Arch Dis Child 64:814–820
14. Pesso JL, Floret D, Cochat P, Dumont C (1988) Suppurated pneumococcal meningitis in infants and children: complications and prognostic factors. Pediatrie 43:263–267
15. Pollack MM, Patel KM, Ruttimann UE (1996) PRISM III: an updated pediatric risk of mortality score. Crit Care Med 24:743–752
16. Madagame E, Havens P, Bresnahan J, Babel K, Splaingard M (1995) Survival and functional outcome of children requiring mechanical ventilation during therapy for acute bacterial meningitis. Crit Care Med 23:1279–1283
17. Goitien KJ, Tamir I (1983) Cerebral perfusion pressure in central nervous system infections in infancy and childhood. J Pediatr 103:40–43
18. Grande P-O, Myhre EB, Nordstrom C-H, Schliamser S (2002) Treatment of intracranial hypertension and aspects on lumbar dural puncture in severe bacterial meningitis. Acta Anaesthesiol Scand 46:264–270
19. Roberts JS, Bratton SL, Brogan TV (2002) Acute severe asthma: differences in therapies and outcomes among pediatric intensive care units. Crit Care Med 30:581–585
20. Tilford JM, Simpson PM, Yeh TS, Lensing S, Aitken ME, Green JW, Harr J, Fiser DH (2001) Variation in therapy and outcome for pediatric head trauma patients. Crit Care Med 29:1056–1061