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Research Article

A Critical Analysis of Lumbar Puncture in the Emergency Management of Febrile Seizures: A Cross-Sectional Study

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Abstract

Purpose: Meningitis is the most important differential diagnosis in children with a febrile seizure, and lumbar puncture for cerebrospinal fluid (CSF) collection may be a necessary procedure for establishing a differential diagnosis in cases in which bacterial meningitis is suspected. Nevertheless, since it has been shown that febrile seizure is rarely predictive of meningitis and in even fewer cases is it the only symptom of this pathology, performing CSF collection in pediatric patients presenting with febrile seizures remains a controversial issue. This study evaluated the profile of children with a febrile seizure submitted to CSF collection at a referral hospital for meningitis in northeastern Brazil between January 2013 and May 2014.

Patients and Methods: A cross-sectional, descriptive study in which the records of children of 6 months to 5 years of age presenting with a febrile seizure and submitted to CSF collection were analyzed. Cases with a traumatic lumbar puncture, cases with incomplete data, and patients with a different diagnosis were excluded from the study.

Results: A total of 126 patients were included, 25.40% of 6 - 12 months of age, 34.13% of 1 - 2 years of age and 40.48% of 2 - 5 years of age. Seventy-five (59.52%) were boys and 51 (40.48%) were girls. In 72 children (57.14%), the seizure occurred in the first 24 hours of fever. Associated symptoms were: vomiting (n = 46; 36.51%), altered sensorium (n = 25; 19.84%) and impaired general condition (n = 21; 16.67%); however, in 56 patients (44.44%), there were no other associated signs or symptoms. Signs of meningeal irritation were rare, with neck stiffness being found in 4 patients (3.17%) and headache in 3 (2.38%). CSF findings were normal in 125 children (99.21%) and only one patient presented with viral meningitis.

Conclusion: In children with a febrile seizure, clinical observation could reduce the practice of unnecessary lumbar puncture for CSF collection.

Keywords: *Febrile Seizures; Lumbar Puncture; Emergency; Children*

Introduction

Fever, a rise in body temperature that occurs as a response of the hypothalamic thermoregulatory center to certain situations, may be an adaptive mechanism of the organism to stimulate the immune system [1]. Although there are major differences of opinion in the literature with respect to what constitutes normal temperature in children, axillary temperature is generally considered normal at levels ranging from 36.0°C in the morning to 37.7°C in the evening, with any value above that being considered abnormal. Seizures induced by fever have long been known [1].

Febrile seizures are the most common type of seizure in childhood and account for a number of visits to the emergency department [2]. Around 2 - 5% of children in Europe and North America and 8% in Japan are affected [3]. While 70% of these children will have only one seizure and 20% will have two, 10% are likely to go on to have recurrent episodes.

The terminology febrile seizure was first adopted in 1990 by the International League Against Epilepsy(ILAE) however, this clinical condition is also referred to as febrile convulsion, since motor symptoms are not always involved [4]. Occasionally, these seizures can be atonic or, alternatively, the only symptoms may be loss of consciousness (complex partial seizures or absence seizures). Although the ILAE recommends that the term febrile convulsion should be avoided and replaced by febrile seizure, the former terminology continues to be widely used by pediatricians and neurologists [5]. The ILAE publication emphasizes that the term convulsion is unspecific and that the word seizure is preferable, since it describes the epileptic nature of the condition, i.e. the fact that it is associated with cortical epileptic lesions (excess neural activity). Therefore, since fever is capable of triggering epileptic seizures, it is actually febrile seizures that occur [6].

A febrile seizure is defined as a convulsive seizure accompanied by fever occurring in children from 1 month to 5 years of age with no sign of infection or inflammation of the central nervous system (CNS), in the metabolic alteration and in the history of any previous non-febrile seizures.

Meningitis is the most important differential diagnosis in children with a febrile seizure [7], although studies show that less than one-third of children with meningitis have a seizure (13 - 30%) [8]. Nevertheless, it is essential to rule out the possibility of meningitis in a child with a diagnosis of a febrile seizure. The possibility of meningitis occurring without the presence of meningeal signs (neck stiffness, Brudzinski's sign, Kernig's sign) is well known and this phenomenon is more common in infants younger than 18 months; however, it may also occur in older children and even in adults [9]. In view of the seriousness of meningitis, lumbar puncture for cerebrospinal fluid (CSF) collection is performed in cases in which this diagnosis is suspected [3]. Notwithstanding, lumbar puncture is not a completely innocuous procedure and can often be traumatic (> 500 red blood cells/ml of CSF). In addition, the procedure causes the child discomfort and pain. In rare cases, brain herniation and even death may occur.

In 1996, the American Academy of Pediatrics (AAP) [10] published an initial consensus "strongly" recommending that lumbar puncture be considered in children younger than 12 months following an initial febrile seizure, even in the absence of signs or symptoms of a CNS infection, and in children of 12 - 18 months in whom these manifestations may be indeterminate. In patients over 18 months old with a first episode of febrile seizure, lumbar puncture should not be performed as routine, but, rather, the patient should be kept under clinical observation for signs and symptoms suggestive of a central nervous system infection [10].

In 2011, this recommendation was reevaluated and the AAP went on to defend lumbar puncture only in the following cases: (1) for children of any age with a febrile seizure and meningeal signs and symptoms (impaired general condition, neck stiffness, Kernig's sign and/or Brudzinski's sign) (Recommendation B); (2) lumbar puncture is considered optional for children of 6 - 12 months of age with a febrile seizure, but recommended for those who did not receive scheduled immunizations for *Haemophilus influenzae* type b (Hib) or *Streptococcus pneumoniae*, or whenever immunization status cannot be determined, since these situations result in an increased risk of bacterial meningitis (Recommendation D); (3) additionally, lumbar puncture is an option for children previously treated with antibiotics, because antibiotic treatment can mask the signs and symptoms of meningitis. (Recommendation D) [11].

Would these new guidelines, restricting the indication of lumbar puncture in children with a seizure and fever, lead to missed diagnoses of meningitis?

A study published in 2012 showed that doctors tended not to follow the 1996 AAP recommendations and would indicate lumbar puncture based exclusively on clinical findings, with apathy/lethargy being the principal indication [2]. Those authors detected no cases of meningitis in a cohort of 278 children who had a febrile seizure between January 2007 and December 2009, even in those who were not submitted to lumbar puncture.

An earlier editorial, published in the 1980s, already suggested that lumbar puncture was being performed as routine in children with a febrile seizure due to the finding that in children meningitis may be indistinguishable from a simple febrile seizure; in other words, the possibility that other clinical criteria for bacterial meningitis could be absent, particularly in infants younger than 18 months, was contributing to the excessive number of cases of lumbar puncture [2]. This is a subject of continuous debate, since studies have shown that a febrile seizure is rarely predictive of meningitis and in even fewer cases is it the only symptom of this pathology [2].

Another study reviewed 503 cases of meningitis in two referral hospitals and showed that cases of bacterial meningitis in which the only manifestation is a febrile seizure are extremely rare or non-existent and that even when there are no meningeal signs, other suggestive findings such as altered sensorium, an abnormal neurological examination or a toxic appearance are typically present both in adults and children with meningitis [9]. That same study included reviews of 709 lumbar punctures and found that the presence of lethargy is a better predictor of meningitis than meningeal signs. On the other hand, a study showed that the younger the patient, the greater the possibility of meningitis occurring without the presence of meningeal signs and that lumbar puncture is therefore vital in younger age groups with no meningeal signs. More recent studies have questioned this recommendation, emphasizing not only the low frequency of meningitis in patients in whom the only manifestation is a febrile seizure, but also the importance of other clinical indicators, even in infants younger than 18 months [12,13].

Even the presence of a complex febrile seizure is of little positive predictive value when there are no other signs of meningitis [2,3,14,15]. Indeed, a recommendation of lumbar puncture remains controversial in cases of complex seizures [13,16].

The infections most commonly associated with febrile seizures are those of the upper airways, pneumonias, gastroenteritis and urinary tract infections [15,17]. Studies show that the incidence of febrile seizure increases in winter when viral infections are more common [16,18,19]. It is also important to emphasize that an indication for lumbar puncture is not only related to performing a differential diagnosis in cases in which bacterial meningitis is suspected, but may also be associated with other extrinsic factors such as the doctor's fear of being sued (a defensive medicine practice that leads to unnecessary excesses), a young doctor's lack of confidence, and extremely busy healthcare services where it is difficult to keep the child under observation for the time required to enable reexamination to be performed after a febrile seizure when the patient's temperature has returned to normal.

Objective of the Study

The objective of the present study was to evaluate the profile of patients submitted to CSF collection at a referral service for meningitis following a febrile seizure.

Materials and Methods

A descriptive, cross-sectional study was conducted at the Correia Picanço Hospital, a referral hospital for meningitis in the city of Recife, Pernambuco, Brazil. The hospital's pediatric emergency department has 13 beds, with an additional two isolation beds and 5 intensive care beds.

Investigators collected the data from medical charts referring to children of 6 months to 5 years of age with a diagnosis of febrile seizure who had been submitted to CSF collection. The study period was from January 2013 to May 2014. Patients for whom laboratory data on CSF were unavailable, cases of traumatic lumbar puncture, cases in which another diagnosis was suspected and children with a neurological disease were excluded from the analysis.

The initial sample consisted of 149 patients who had had a seizure. Of these, 8 were excluded because they had had a non-febrile seizure. Of the 141 remaining cases, CSF was not collected in 2 cases because the children were clinically well; in another case it was not known why CSF collection was not requested and in 5 cases collection was not performed for a variety of reasons. Of the 133 remaining cases, 4 patients were excluded because of a traumatic lumbar puncture and 3 because their clinical condition was suggestive of another diagnosis. Therefore, 126 patients were included in the study. The exclusion process is depicted in the flow chart in figure 1 and the reasons for exclusion are provided in table 1.

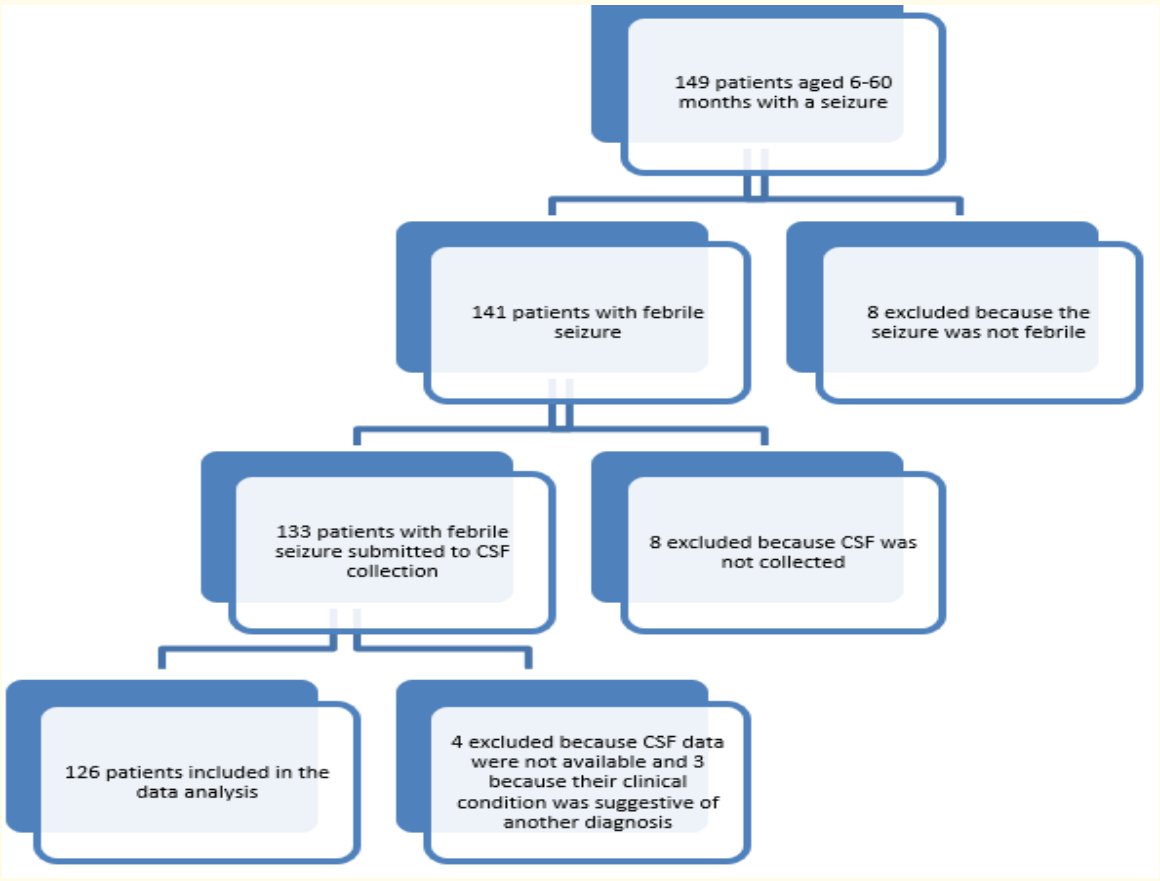

Figure 1: *Flowchart depicting the exclusion process.*

Reason for exclusion	Number of Cases
Seizure without fever	8
Clinically well; CSF was not collected	2
CSF was not collected; reason unknown	1
CSF was not collected; various different reasons	5
Missing data on CSF examination	1
Missing data on CSF due to a traumatic lumbar puncture	3
Clinical condition suggestive of other diagnosis	3

Table 1: *Cases excluded from the study according to pre-established criteria.*
CSF: Cerebrospinal Fluid.

The children's sociodemographic variables (sex and age) were evaluated as well as clinical variables such as the type of seizure, body temperature during fever, time between the onset of fever and the seizure, possible sources of infection and other associated symptoms, CSF findings, and final outcome.

The data collected were processed on an Excel spreadsheet and analyzed using Epi Info version 7.0 (Centers for Disease Control and Prevention, Atlanta, GA, USA). Proportional frequencies were verified, and the chi-square test and Fisher's exact test were used, as appropriate. A margin of error of up to 5% was considered admissible.

The study was conducted in accordance with Resolution 466/12 of the National Health Council. The internal review board of the Faculdade Pernambucana de Saúde (AECISA) approved the study protocol on October 9, 2014 under reference 35957314.0.0000.5569 (CAAE). Since this study consisted exclusively of a review of hospital records and since the identity of all the participants was maintained confidential, the need for signed informed consent was waived.

Results

A total of 126 patients with a febrile seizure who were submitted to CSF collection were included in the study. The sociodemographic and clinical characteristics of the patients are described in table 2. Overall, 59.52% of the sample was male. For the purposes of analysis, the patients were divided into three age groups: 6 - 12 months (25.40%), 1 - 2 years (34.13%) and 2 - 5 years (40.48%). Table 3 describes the patients according to the characteristics of the infection and CSF results.

	Absolute frequency n	Relative frequency %
Sociodemographic characteristics		
Age group		
6 - 12 months	32	25.40
1 - 2 years	43	34.13
2 - 5 years	51	40.48
Sex		
Male	75	59.52
Female	51	40.48
Clinical characteristics		
Type of seizure		
Simple	97	76.98
Complex	29	23.02
Time between onset of fever and seizure		
< 24 hours	72	57.14
≥ 24 hours	32	25.40
Data missing	22	17.46
Associated signs and symptoms		
Bulging fontanelle	0	0
Vomiting	46	36.51
Altered sensorium	25	19.84
Impaired general condition	21	16.67
Neck stiffness	4	3.17
Brudzinski/Kernig/Lasègue sign	0	0
Headache	3	2.38
Cyanotic lips	1	0.79
Pupil miosis	1	0.79
None	56	44.44

Table 2: *Sociodemographic and clinical characteristics of patients with a febrile seizure submitted to cerebrospinal fluid collection, Recife, PE, Brazil, 2016.*

	Absolute Frequency n	Relative Frequency %
Possible source of infection		
Common cold/flu	20	15.87
Otitis	2	1.59
Gastroenteritis	13	10.32
Skin manifestations	2	1.59
No source identified	5	3.97
Data missing	84	66.67
CSF laboratory findings		
Normal	125	99.21
Viral	1	0.79
Bacterial	0	0
Final outcome		
Referred back to service of origin	85	67.46
Referred to other service	7	5.56
Hospitalized	1	0.79
Data missing	33	26.19

Table 3: *Infection sources, laboratory characteristics and final outcome of the patients with a febrile seizure who were submitted to CSF collection, Recife, PE, Brazil, 2016.*

Correlations were sought between age (6 - 24 months and 24 - 60 months) and the following variables: type of seizure (simple or complex); time between the onset of fever and the seizure (< 24 hours or > 24 hours) and altered sensorium. No statistically significant correlations were identified ($p > 0.05$). In addition, a correlation was sought between the sex of the child and the type of seizure; however, again, no statistically significant correlation was found. These analyses are shown in table 4.

Age			**Coefficient ***
	Type of Seizure		
	Simple	Complex	
6-24 months	56	19	p = 0.59
24-60 months	41	10	
	Time between onset of fever and seizure		
	< 24 hours	**≥ 24 hours**	
6-24 months	40	21	p = 0.45
24-60 months	32	11	
	Altered sensorium		
	Yes	**No**	
6-24 months	16	59	p = 0.77
24-60 months	9	42	
Gender			**Coefficient ***
	Type of seizure		
	Simple	**Complex**	
Male	62	13	p = 0.104
Female	35	16	

Table 4: *Clinical and demographic correlations as a function of the characteristics of the febrile seizure, Recife, PE, Brazil, 2016.*

** Chi-square test*

In 72 children (57.14%), the seizure occurred in the first 24 hours of fever. Data on the possible source of infection were available for only 42 patients; however, the most common sources identified were: the common cold in 20 patients (15.87%) and gastroenteritis in 13 patients (10.31%).

In 56 patients (44.44%), the febrile seizure was the only symptom present. In those patients with other associated symptoms, the most common were vomiting (n = 46; 36.51%), altered sensorium (n = 25; 19.84%) and impaired general condition (n = 21; 16.67%). No cases of bulging fontanelle were recorded. With respect to specific signs of central nervous system involvement, neck stiffness was recorded in 4 patients (3.17%) and headache in 3 cases (2.38%). There were no registered cases of any specific signs of meningeal irritation.

Alterations to the child's general state of health were defined as the presence of hypoactivity (recorded in 5 cases) and intense crying (recorded in 14). In another 2 patients, there was a record of impaired general condition; however, no further details were provided. A search was also made for possible cases of altered sensorium, with irritability being registered for 13 patients and somnolence for 12. There were no records of torpor or lethargy in any of the children.

In relation to the CSF findings, results were normal in 125 cases (99.21%), with only one exam showing characteristics of viral meningitis.

Regarding the final outcome of the patients seen in the emergency department, 85 (67.46%) were referred back to the healthcare service of origin or discharged following CSF examination. Seven children were referred to another hospital for further testing and/or treatment. One patient was hospitalized. In 33 cases, no data were available on final outcome.

Discussion

Febrile seizures constitute a motive of concern both for the family and for the attending physician and represent a condition that has an important emotional impact. Defining whether a febrile seizure is associated with severe infections of the central nervous system such as meningitis is the principal question when seeing these patients.

According to the literature, there are controversies between seizures classified as simple or complex and their association with the presence of meningitis [13-16]. In the present study, 77% of the patients had a simple febrile seizure. No statistically significant associations were found when the type of seizure was correlated with age and sex.

The finding that the febrile seizure had occurred in the first 24 hours of fever in the majority of the patients in the present study ratifies what is already known on the characteristics of febrile seizures in pediatric patients. No statistically significant correlations were found between the patient's age and the time between the onset of fever and the febrile seizure.

In agreement with data published in the literature, the principal infectious processes identified in the present sample were the common cold and gastroenteritis [3,15-19]. Few patients had any signs or symptoms that would support an indication for lumbar puncture and cerebrospinal fluid collection according to the 2011 AAP guidelines [11]. In fact, most of the children in the present study were between 2 and 5 years of age and in this age group the specific symptoms are the most relevant predictors.

CSF examination was normal in 99.20% of the patients in the present study, with results compatible with viral meningitis in only one child. This fact highlights the difficulty faced by duty doctors in referral hospitals in contraindicating CSF collection after the patient has been transferred from another healthcare service.

In this respect, the most important question to ask is whether the clinical criteria would not have been sufficient evidence to enable CSF collection to be avoided in these cases of febrile seizure.

As shown in the literature, the risk of bacterial meningitis associated with a simple febrile seizure when clinical examination is normal is extremely low [3,13,20], even in children younger than 18 months [13,14]. Therefore, lumbar puncture is of little use in these children. A meta-analysis showed that the number of lumbar punctures that would have to be performed to identify one single case of a central nervous system infection (the number needed to treat) is 1,109 for children with a first simple febrile seizure and 180 children with a first complex febrile seizure [3]. That same article concluded that careful clinical observation for a few hours after the seizure should be an acceptable strategy in these children. Patients who recover consciousness quickly should be kept under observation and the decision regarding lumbar puncture should be delayed [1]. Another similar paper emphasized that it is improbable that a first simple febrile seizure would be predictive of bacterial meningitis, since, although there is a possibility of occult bacteremia or bacterial meningitis, the phenomenon may also be a manifestation of some other febrile disease such as a viral respiratory infection. The incidence of severe bacterial diseases in children with a simple febrile seizure is low and similar to that of children with fever who have not had a seizure [16]. A more recent study emphasized that a febrile seizure may constitute a predictive factor for meningitis only when the patient is not within the usual age group for a febrile seizure (6 - 60 months) [2]. Performing lumbar puncture prematurely in children with a suspicion of bacteremia but without meningeal involvement may result in false-negative results, diagnostic errors, delayed treatment and an adverse outcome [16].

Febrile status epilepticus (>30 minutes' duration) occurs in 5% of children who have febrile seizures. However, prospective population-based studies have found that bacterial meningitis is present in up to 18% of children with febrile status epilepticus [21]. Therefore, in febrile status epilepticus, early parenteral antibiotics have been recommended, followed by a lumbar puncture when it is safe to do so [22,23].

Additionally, an important change occurred in the epidemiological profile of bacterial meningitis following universal vaccination against *Haemophilus influenzae*, *Streptococcus pneumoniae* and meningococcus C [13]. The incorporation of these vaccines in the USA, in Brazil and in many other countries has led to a significant reduction in bacterial meningitis caused by these principal etiological agents [15]. Furthermore, the AAP recommendations emphasize the importance of checking the child's vaccination diary prior to indicating lumbar puncture in children with a febrile seizure [11].

The results of this study and the literature review conducted highlight the importance of taking four parameters into consideration before indicating lumbar puncture for a child with a febrile seizure in an emergency room setting: the patient's clinical condition and age; the availability of an appropriate environment in which to keep the child under observation after the seizure; the child's current immunization status; and the experience of the attending physician in the management of such patients.

The fact that data collection was based on emergency medical records constitutes a limitation of this study and may have contributed to biases.

Conclusions

The results of this study reinforce that in the management of children with a febrile seizure and no other signs or symptoms, careful clinical observation may reduce the large number of unnecessary lumbar punctures.

Disclosure

The authors report no conflicts of interest associated with this work.

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