

Analysis of Prognostic Factors of Children with Intracranial Infection Coma

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Abstract

Objective: To investigate the prognostic factors of coma due to intracranial infection in children, in order to judge the prognosis of coma earlier and guide appropriate treatment. **Methods:** 1) Collecting the clinical data of 39 comatose children due to intracranial infection admitted into Department of Neurology in Children's Hospital of Chongqing Medical University from July to September 2007 and 2009, and analyzing their age and sex distribution, causes of coma, and laboratory examinations retrospectively. 2) Implementing the Glasgow coma score among these children immediately after admission, and collecting the serum and cerebrospinal fluid within 24 - 48 hours, and then measuring the NSE levels. 3) Following up these children 3 months after discharge, and analyzing the relationships among prognosis and age, sex, etiology, protein content in CSF, and NSE levels in Serum and CSF. **Results:** 1) In the cases studied, the age range was from 9 months to 14 years, the average age was (4.25 ± 2.82) years, and 9 months - 3 years, 3 - 5 years, 5 - 11 years, and ≥ 11 years were accounted for 33.3%, 30.8%, 30.8%, 5.1% respectively. There were 24 males and 15 females, and the gender ratio (male-to-female) was 1.6:1. 2) The group of 39 patients consists of Japanese encephalitis (23 cases, 59%), Viral encephalitis (5 cases, 12.8%), Tuberculous meningitis (5 cases, 12.8%), Acute disseminated encephalomyelitis (5 cases, 12.8%) and Purulent meningitis (1 cases, 2.6%). 3) CSF examination in 33 cases, protein elevated in 18 cases (54.5%), content between 0.47 and 4.33 g/L. 4) The statistical analysis showed that the causes, CSF protein content, serum and cerebrospinal fluid NSE levels were correlated with the prognosis, and that the age and sex had no correlation with the prognosis. **Conclusions:** 1) In this group of 39 patients, the incidence of children under 5 years old was the highest, and the incidence of boys was higher than girls. 2) Infectious diseases were the most common cause of coma in children. 3) Cerebrospinal fluid protein content was correlated with the prognosis, and the prognosis was worse as the protein content was higher. 4) NSE was a specific biochemical parameter of pathological damage nerve tissue; serum NSE levels could indirectly reflect the changes in CSF.

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Keywords

Coma, Clinical, Outcome, Intracranial, Infection

1. Introduction

Coma is a severe disturbance of consciousness, which is a common pediatric clinical department critical illness, and has a high mortality, its survivors often left with varying degrees of neurological sequelae. Children coma can occur at any age, but more common in children under 5 years of age [1]. The causes of coma are numerous. Non-traumatic coma is the most common in children; infection is the most common cause of non-traumatic coma in children, accounting for 38%. Other causes also include poisoning, long-term seizures, congenital malformations of the brain or heart, hypoxic-ischemic damage, metabolic diseases (e.g. diabetic ketoacidosis), etc. [2]. Coma prognosis depends largely on the extent of damage of primary disease and reasonable treatment. Therefore, detailed history, physical examination, laboratory and auxiliary examinations are crucial [3]. The prognosis of coma is determined primarily by clinical signs, Glasgow score and radiographic examination in clinical in the past, but it has poor accuracy, it cannot rely solely on clinical examination to determine the prognosis of coma [4] [5]. In this paper, age, gender, etiology, laboratory tests of 39 cases of children with coma were analyzed retrospectively and we analyzed the relationship among age, sex, etiology, cerebrospinal fluid protein, serum and cerebrospinal fluid NSE content and prognosis. The aim was to investigate prognostic factors of children with intracranial infection coma, facilitate early prediction coma prognosis and guide appropriate treatment.

2. Materials and Methods

2.1. The Research Object

Collected the clinical data of 39 comatose children due to intracranial infection admitted into Department of Neurology in Children's Hospital of Chongqing Medical University from July to September 2007 and 2009. All enrolled patients underwent Glasgow score, and confirmed $GCS \leq 8$ points.

2.2. Research Methods

2.2.1. Glasgow Coma Scale

Patients were hospitalized within 24 h on Glasgow Coma Scale score, the $GCS \leq 8$ points selected into the case group of children.

2.2.2. Clinical Data Analysis

The clinical data of 39 cases of coma in children were retrospectively analyzed, recording their age, sex, etiology, laboratory examination, analysis of coma patients' clinical and prognostic factors.

2.2.3. The Determination of NSE

1) Specimen collection: When children admitted to hospital blood 1 mL, 4°C, 3000r/min centrifugal 10 min, the serum stored at -20°C under test. 24 - 48 h after admission to complete lumbar puncture to collect cerebrospinal fluid 1 mL under sterile conditions, 4°C, 3000 r/min centrifugal 10 min, the supernatant was kept under test at -20°C. 2) NSE in serum and cerebrospinal fluid measurement: using ELISA ELISA, according to NSE-ELISA kit (R & D System Company) instructions, the instrument used by the US imported automatic microplate reader (model VARIOSKAN-FLASH).

2.2.4. Follow-Up

Follow-up clinical outcomes of children after they discharge for 3 months, clinical outcomes were divided into 5: Level I: fully recovered; II level: mild disability, but can live independently; Grade III: severe disability, the need to take care of daily life; class IV: persistent vegetative state; V class: death. Which clinical outcomes included in Class I and Class II calculate the prognosis is good, III level, IV and V grade level classified as poor prognosis calculations.

2.2.5. Statistical Methods

SAS 9.0 using statistical package for statistical analysis, count data using χ^2 test and Fisher's exact probability calculation, measurement information and data to $X \pm S$ said, using t test or rank sum test and Spearman rank correlation analysis, $P < 0.05$ considered the difference statistically significant.

3. Results

3.1. Age and Sex

In the cases studied, the age range was from 9 months to 14 years, the average age was (4.25 ± 2.82) years, 9 months-3 years, 3 - 5 years, 5 - 11years, ≥ 11 years were accounted for 33.3%, 30.8%, 30.8%, 5.1% respectively. There were 24 males and 15 females, and the gender ratio (male-to-female) was 1.6:1.

3.2. Cause of Disease

The group of 39 patients include Japanese encephalitis (23 cases, 59%), Viral encephalitis (5 cases, 12.8%), Tuberculous meningitis (5 cases, 12.8%), Acute disseminated encephalomyelitis (5 cases, 12.8%) and Purulent meningitis (1 cases, 2.6%).

3.3. Laboratory Tests

In this group, 33 cases of children with Bank of cerebrospinal fluid examination, leukocytosis 15 cases (45.5%), white blood cell count was $16 \times 10^9 - 1182 \times 10^9$ L, protein increased 18 cases (54.5%), the content of 0.47 - 4.33 g/L.

4. Analysis of Prognostic Factors

39 cases in this group of children in a coma, the success of follow-up in 23 cases, of which 18 cases with good prognosis (fully recovered nine cases, nine cases of mild disability), accounting for 78.3%. Poor prognosis five cases (all deaths), accounting for 21.7%.

4.1. Etiology and Prognosis

In the follow-up of cases, four cases of viral encephalitis are good prognosis; Japanese encephalitis 13 cases, 11 cases with good prognosis, 2 deaths; tuberculous meningitis, 3 cases were dead; purulent meningitis 1 cases, the prognosis is good; two cases of acute disseminated encephalomyelitis, both good prognosis. The statistics, etiology and prognosis correlated ($P < 0.05$).

4.2. CSF Protein and Prognosis

In this group of patients checking CSF 33 cases, 18 cases of elevated protein content between 0.47 - 4.33 g/L. In the follow-up to the 23 cases in children, children with normal protein content of 9 cases were good prognosis; 0.45 - 1 g/L total of seven cases, six cases the prognosis is good, and 1 died; greater than 1 g/L total of four cases, 1 case with good prognosis, three deaths. The statistics, CSF protein levels correlated with prognosis ($P < 0.05$) (Table 1).

4.3. The Relationship between NSE Levels in Serum and CSF and Prognosis

In this group of patients, NSE levels in the serum and CSF of children with death were significantly higher than 16 cases of children with a good prognosis, the statistics in the serum and CSF NSE levels were correlated with prognosis ($P < 0.05$) (Table 2). Spearman rank correlation analysis showed that serum and CSF NSE levels showed a significant positive correlation ($r = 0.768$, $P < 0.01$).

5. Discussion

Coma is one of the common clinical pediatric critical illness with high mortality, the etiology of Coma is range, can occur at any age, 5 years of age for the onset of the peak in this group of patients, about 64%, consistent with similar reports in the literature [1]. The patients were female ratio was 1.6:1, by unconscious gender statis-

Table 1. The relationship between protein content in CSF and prognosis.

CSF protein content (g/L)	n	Prognosis is good			Poor prognosis		P values
		Fully recovered	Mild disability	Vegetative	Death		
0.15 - 0.45	9	4	5	0	0	<0.05	
0.45 - 1	7	4	2	0	1		
≥1	4	0	1	0	3		

Table 2. The relationship between NSE content in serum and CSF and prognosis.

Groups	n	Serum NSE content (μg/L)	NSE levels in CSF (μg/L)
Prognosis is good	16	8.46 ± 0.65	7.32 ± 0.51
Death	5	12.02 ± 3.29	10.80 ± 3.16
P values		<0.05	<0.05

tics in this group of children, age was no correlation with prognosis.

5.1. Cause of Disease

Numerous causes of coma can be divided into traumatic and non-traumatic categories, have been reported traumatic and non-traumatic coma incidence rates of about thirty hundred thousandths, but non-traumatic coma in children is more common [3]. Infection in children with non-traumatic coma is the most common cause, accounting for 38% [2]. Cai *et al.* [6] analysis 277 cases of children in coma, coma caused by infectious disease accounted for 66.7% of children, and poisoning, diabetes, epilepsy, only accounting for 1.4%, 1.1%, and 2.2% respectively,. To understand the prognostic factors of coma caused by infectious disease, we collect 39 cases of patients were analyzed. In this group of patients, Japanese encephalitis most common, accounting for 59% of the cases, considered in this group were collected mainly in the 7 - 9 month and 5 years of age is more common, since the 7 - 9 month for Japanese encephalitis epidemic season, 2- - 6-year-old is a good age for Japanese encephalitis. Therefore, in 7 - 9 months, pay attention to the group carried out JE prevention and control, can reduce the coma. After follow-up, three cases of tuberculous meningitis were died and 100% mortality, 13 cases of Japanese encephalitis death two cases, the mortality rate of 15.4%, four cases of viral encephalitis, two cases of acute disseminated encephalomyelitis, 1 case of purulent meningitis are good prognosis, some children to varying degrees left sequelae. The statistics, etiology and prognosis correlated ($P < 0.05$), for a clear cause coma in children as early as possible in order to facilitate minimizing the occurrence of poor prognosis.

5.2. Laboratory Tests

Related auxiliary examination can help diagnose the cause of coma; routine laboratory tests should include blood sugar, blood routine test and metabolism-related tests (such as electrolytes, liver and kidney function, blood ammonia, blood lactate, etc.) [3]. Hyperglycemia should be considered diabetes, hypoglycemia should be noted that hypoglycemia, Reye’s syndrome, and severe liver disease.CSF examination to clear coma etiology and differential diagnosis is particularly important, and more tips cerebral hemorrhage or subarachnoid hemorrhage when cerebrospinal fluid become yellowing bloody. White blood cells, protein and sugar quantitative changes in intracranial infection often occur. The group of 39 cases of children with coma, CSF examination 33 cases, 15 cases of leukocytosis (45.5%), white blood cell count was $16 \times 10^9 - 1182 \times 10^9$ L, protein increased 18 cases (54.5%), content 0.47 - 4.33 g/L. The statistics, CSF protein levels correlated with prognosis, the higher the protein content of the worse the prognosis.

5.3. NSE

Enolase is involved in a key enzyme in glycolysis, there $\alpha\alpha$, $\beta\beta$, $\gamma\gamma$, $\alpha\beta$, $\alpha\gamma$ five kinds of isoenzymes, which $\gamma\gamma$ specificity exists in neurons and neuroendocrine cells, so called neuron-specific of enolase (Neuron-specific enolase, NSE). NSE distributed in various body systems, but most of the distribution in the central nervous sys-

tem, accounting for 1.5% of the soluble protein in the brain [7]. Under normal circumstances, NSE levels in the body fluids were very low, but when the nervous system lesions appear, cause neuronal degeneration and necrosis, nerve myelin disintegration and destruction of blood-brain barrier, the neuronal cytoplasm NSE is released into the cerebrospinal fluid, and through impaired blood-brain barrier into the blood circulation, causing the cerebrospinal fluid and blood NSE levels increased. A large number of studies have shown that NSE is sensitive and specific markers of neuronal damage, in cerebrovascular disease, traumatic brain injury, hypoxic-ischemic brain injury and seizures and other neurological diseases will rise, which increases the degree of brain damage extent and prognosis [8]. Meynaar [9] studies comatose patients after hypoxia showed that the serum NSE concentration of the poor prognosis group in 24 hours and 48 hours (29.9 $\mu\text{g/L}$, 37.8 $\mu\text{g/L}$) was significantly higher than the good prognosis group (9.9 $\mu\text{g/L}$, 9.5 $\mu\text{g/L}$), and patient with serum NSE concentrations $> 25\mu\text{g/L}$ is often difficult to wake up. In this set of experiments, levels of NSE in serum and cerebrospinal fluid of poor prognosis group (12.02 $\mu\text{g/L} \pm 3.29 \mu\text{g/L}$, 10.80 $\mu\text{g/L} \pm 3.16 \mu\text{g/L}$) was significantly higher than the good prognosis group (8.46 $\mu\text{g/L} \pm 0.65 \mu\text{g/L}$, 7.32 $\mu\text{g/L} \pm 0.51 \mu\text{g/L}$), further confirmed the higher NSE content in serum or cerebrospinal fluid, the more severe the patient's condition, the worse the prognosis, which Shinozaki K [10], such as the consistent reports. Studies have shown [11], after the acute phase, serum NSE levels became normal in the group of good prognosis, but in the poor group serum NSE will continue to be maintained at a high level, it suggesting that neurons have sustained damage, the condition may worsen, so the dynamic NSE monitoring of serum or cerebrospinal fluid changes is value to determine the extent of brain damage and prognosis. NSE is specific biochemical indicators of nerve histopathological damage, appear elevated in a variety of neurological disorders [12], which is closely related to the brain injury and prognosis, its dynamic monitoring provides a new reference for the extent of brain damage and prognosis in children with coma.

6. Conclusion

Coma is a serious disturbance of consciousness. It can occur at any age in children, more common under 5 years old, and more common in boys than girls. Non-traumatic coma is the most common in children, and infection is the most common cause. Etiology, protein content in cerebrospinal fluid, NSE levels in serum and cerebrospinal fluid might have important roles in assessing the prognosis of coma due to intracranial infection.

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