

Risk Factors of Recurrence of Febrile Seizures in Children in Southwest China: A Three Year Follow up Study

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Abstract: *Objectives:* Risk factors associated with recurrent febrile convulsions in children in southwest China were the main objective of this study. To summarize the effect of telephone follow-up continuous nursing on preventing recurrence after hyperthermia in emergency children. To study the influencing factors and preventive measures of febrile convulsion recurrence in children. *Methods:* This study was carried out in the pediatrics department of the Affiliated Hospital of Yunnan University of Traditional Chinese Medicine, which is prospective and longitudinal. Children aged 6 months to 6 years who had febrile convulsions for the first time and were seen between October 2016 and September 2019 were included in the study and followed up for recurrence. From The clinical data of 290 children with febrile convulsion were analyzed retrospectively, and the influencing factors of recurrence were analyzed by single factor analysis. Patients were randomly divided into control group and experimental group with 47 cases in each group. The control group was given routine discharge guidance, and the experimental group was given continuous telephone follow-up nursing. *Results:* Of the 1728 children, 605 (35.1%) had recurrences and 1123 (64.9%) had single febrile convulsions. The recurrence rate was higher in children <6 months of age (41.3%) than in children ≥6 months of age (24.1%). The recurrence rate was 52.5% in children with a temperature of 38°C at the time of the attack, compared to 17.2% in children with a temperature ≥105°F. There was a significant downward trend in the recurrence rate as the temperature increased. Children with a family history of febrile convulsions (45.5%) were more likely to have a relapse than those without a family history of febrile convulsions (27.8%). Multiple logistic regression analysis showed that younger age at onset, lower temperature at onset, shorter time between fever and onset, and family history of febrile convulsions were risk factors for recurrence of febrile convulsions in children. After nursing, the recurrence rate of children in the experimental group within 0.5 years was significantly lower than that in the control group (4.26% vs 21.28%, $P < 0.05$); Compared with the control group, the test group had the highest knowledge score, and the difference was significant ($P < 0.05$). *Conclusion:* The main risk factors of recurrent febrile attacks in children are young age of onset, short febrile time before the first febrile attack, low body temperature at onset, and family history of febrile attacks. Age < 3 years old, family history of high fever convulsion, season of onset < 6 months, onset temperature ≥39°C, frequency ≥2, complex onset and duration ≥3 min are all risk factors for recurrence of high fever convulsion. Prevention should be conducted against the above risk factors to avoid recurrence of convulsion.

Keywords: Febrile Convulsion, Telephone Follow-Up, Continuous Nursing, Recurrence Related Factors

1. Introduction

Febrile convulsions in the absence of prior febrile

convulsions and in children 6 months to 5 years of age who are inadequate (<15 minutes) during febrile illness that is not caused by acute neurological disease, do not recur within 24

hours, and do not have neurological deficits are defined as febrile convulsions. The most common type of seizures seen in children are febrile seizures [1]. Febrile convulsion in children is one of the common diseases in pediatric clinic, with infants aged 6 months to 4 years as a predisposing group. according to the results of relevant investigation reports, the incidence rate is 2%~8%, and the recurrence rate after the first attack is 30%~40%. Repeated seizures of febrile convulsion can cause brain damage in children, and some children can also have secondary epilepsy and mental decline, which seriously affects the quality of life of children and their families [2-3]. The recurrence of febrile convulsion in children is related to many factors, and understanding its influencing factors plays a vital role in prevention and the implementation of prognostic measures. Therefore, how to take a series of corresponding measures to improve the prognosis of children has important clinical significance. At present, continuous nursing is a commonly used model for out-of-hospital nursing of patients with various chronic basic diseases [4-6]. This study mainly analyzes the related factors and preventive measures of children with febrile convulsion, which are reported as follows. Assessing the risk factors associated with recurrent febrile convulsions in Chinese children was the main thrust of this study.

2. Methods

2.1. Setting and Design

This study was carried out in the pediatrics department of the Affiliated Hospital of Yunnan University of Traditional Chinese Medicine, which is prospective and longitudinal. Children aged 6 months to 6 years who had febrile convulsions for the first time and were seen between October 2016 and September 2019 were included in the study and followed up for recurrence. The ethical approval was obtained from the Institutional Ethics Committee of the Affiliated Hospital of Yunnan University of Chinese Medicine.

2.2. Inclusion Criteria

Children 6 months to 6 years of age presenting with epilepsy accompanied by fever, i.e. core body temperature 38.5°C, no central nervous system infection, and parents signed written informed consent were the subjects of our study.

2.3. Exclusion Criteria

Children with previous febrile convulsions, non-induced convulsions and intracranial infections were excluded from the study. In addition, those children who did not have parental consent were also excluded. Non-provoked seizures were seizures that occurred in the absence of a precipitating factor and could be caused by a static injury (distal symptomatic seizures) or a progressive injury (progressive symptomatic seizures).

2.4. Methods

Parents of children participating in the study are invited to sign written informed consent. The parents and children were given pre-designed and tested questionnaires. The questionnaire was administered by a pediatric nurse to all participants in the study. Each child was followed for 3 years. The follow-up period was until September 2019. Of the 3,156 children who had seizures, 562 had neurocysticercosis, 381 had meningoencephalitis, and the remaining 485 had cryptogenic uninduced seizures. Only 1,728 children met the inclusion criteria to be included in the study. The general conditions of the children included mode of delivery, sex, nature of the first seizure, history of the immediate family, time of the first seizure, body temperature at the first seizure.

2.5. Follow-up Methods

The children were followed up regularly after the treatment of outpatient or ward in our hospital. The follow-up method was telephone follow-up, once every 3 months, the follow-up time was 3 years, and the follow-up deadline was September 2019. The control group received routine discharge guidance as follows: first, receiving standardized treatment and nursing in the emergency department; second, introducing disease knowledge to children and parents, advocating dietary health guidance, matters needing attention, correct execution methods of thermometer and physical cooling, emergency measures to deal with diseases, etc.; finally, waiting for the child to be cured, receiving the time of parents' active return visit on the basis of keeping the child's case, telephone consultation.

On the basis of routine discharge guidance, the experimental group carried out telephone follow-up continuous nursing, as follows: (1) set up a continuous nursing group, including two nurses, deputy director nurse, head nurse and head nurse, each with rich clinical experience, strong responsibility and communication skills, as well as solid nursing knowledge; (2) design a continuous nursing plan, the nurse is mainly responsible for collecting, sorting out the personal information of children and their parents, and then by the group combined with the information content of parents to assess the degree of awareness of disease knowledge, needs, and develop a targeted, individualized nursing program; (3) Establish a follow-up file to ensure that each child has a nursing follow-up record with personal information (name, condition.); (4) Continuous nursing implementation, detailed introduction of out-of-hospital follow-up, household thermometer, antipyretic sedation drugs need, importance, strive for understanding, cooperation: continuous care program as a guide, using their own professional causes to introduce disease-related knowledge to children's parents, so that they know the child's condition, at the same time guide parents to provide children with a light, digestible nutrition diet, as well as provide children with a clean, quiet ward, and often open windows ventilation, as far as possible to maintain indoor air circulation, and depending on weather changes, increase or decrease clothing, avoid children cold, aggravate the condition; To help

children drink more water and drink juice, such as watermelon and apple, to maintain water and electrolyte balance, strictly forbid to eat irritant food.

The correct dosage and method of the medicine. To observe the changes of body temperature, face, consciousness and so on. Once the body temperature $\geq 38^{\circ}\text{C}$, see a doctor immediately. Telephone follow-up time, first, second after 1 d, and every three months after the third, to ensure that continuous care is carried out in a planned and systematic manner, thereby continuously and dynamically assessing the child's care situation. In addition, solve the problems raised by the parents in time, and provide corresponding solutions. For a few difficult questions to answer clearly, accurately recorded in the follow-up records, and by the group through the organization of meetings to analyze, discuss, to get a unified, satisfactory answer, in the

form of telephone communication to parents.

Observation indexes observed the recurrence rate of the two groups in half a year and the knowledge of the children's families. (The questionnaire was designed by our hospital, and the disease inducing factors, treatment measures and preventive measures were investigated by telephone follow-up.

2.6. Statistical Analysis

Data were collated using Microsoft Excel and analysed using SPSS version 21.0.

Categorical variables were analysed using percentages and Chi-square tests. Multiple logistic regression analysis was used to determine risk factors for recurrence of febrile convulsions. $p < 0.05$ was considered a statistically significant difference.

3. Results

Post-discharge phone call follow-up questionnaire		
Patient Name : _____		
Follow up phone call made to : <input type="checkbox"/> Family <input type="checkbox"/> Patient		
Follow up day post-discharge (0-8day) : _____		
Questionnaire	Yes	No
1.How old was your child when he first had febrile seizures?		
2.What was the temperature at the first attack? What's the temperature this time?		
3.How long does the fever convulsion last for the first time? How long did the attack last this time?		
4.Do you have recurrent febrile seizures in one day?		
5.Is there a history of febrile convulsion or epilepsy in your family?		
6.Do you have a history of iron deficiency anemia in your family? Did your child have any trace elements deficiency?		
7.What are the causes of fever in children? Is it a respiratory infection?		
8.Do you have physical cooling or oral antipyretic, after high fever?		
9.Any abnormalities in previous EEG?		
10.What's the mood of the parents?		
Current overall condition: <input type="checkbox"/> Excellent <input type="checkbox"/> Good <input type="checkbox"/> fair <input type="checkbox"/> Poor		
Follow up:Appointment Number	Date	Time
1.		
2.		
3.		
Additional Comments		

Figure 1. The following is a sample of the telephone follow-up questionnaire. In addition to what is described in this form, special emphasis is placed on pregnancy history and parental mood.

Of the 1728 children, 605 (35.1%) had recurrences and 1123 (64.9%) had single febrile convulsions. The recurrence

rate was higher in children < 6 months of age (41.3%) than in children ≥ 6 months of age (24.1%). The mean age of the

study participants was 32.3 ± 2.7 months. The recurrence rate was 33.5% in female children and 28.9% in male children, but the difference was not statistically significant ($p = 0.102$). Recurrence of febrile convulsions was not associated with a child's history of religious or neurodevelopmental disorders.

The recurrence rate was higher in children <6 months old (41.3%) than in children ≥ 6 months old (24.1%), with a statistically significant difference ($p < 0.0001$).

The recurrence rate was 56.4% in children with seizures ≥ 15 min compared to 43.6% in children with seizures <15 min, a statistically insignificant difference ($P = 0.075$). The recurrence

rate was 52.5% in children with a temperature of 101°F at the time of onset and decreased significantly with increasing temperature, while in children with a temperature $\geq 105^\circ\text{F}$ the recurrence rate was only 17.2% ($P = 0.001$). Children with a family history of febrile convulsions (45.5%) were more likely to have a recurrence than children without a family history of febrile convulsions (27.8%) and children with a family history of epilepsy (78.6%) than children without a family history of epilepsy (31.7%). Recurrence of febrile convulsions was not associated with the type of convulsion, history of vaccination or iron deficiency.

Table 1. Factors associated with recurrence of febrile seizures.

Risk factors	Children with nonrecurrent febrile seizures (n=354), n (%)	Children with recurrent febrile Seizures (n=174), n (%)	Total children (n=528)	P
Gender				
Male	143 (71.1)	58 (28.9)	201	0.116
Female	211 (64.5)	116 (35.5)	327	
Age at first seizure (months)				
<6	159 (58.7)	112 (41.3)	271	<0.0001*
≥ 6	195 (75.9)	62 (24.1)	257	
Duration of fever (h)				
<1	47 (42.7)	63 (57.3)	110	<0.0001*
≥ 1	307 (64.2)	171 (35.8)	478	
Temperature ($^\circ\text{C}$)				
38 $^\circ\text{C}$	19 (47.5)	21 (52.5)	40	0.001*
38.1-38.5 $^\circ\text{C}$	68 (63.6)	39 (36.4)	107	
38.5-39 $^\circ\text{C}$	106 (68.4)	50 (36)	139	
39 $^\circ\text{C}$ -40 $^\circ\text{C}$	72 (82.8)	49 (31.6)	155	
40 $^\circ\text{C}$		15 (17.2)	87	
Family history of febrile seizures				
Present	73 (54.5)	61 (45.5)	134	0.00034*
Absent	281 (71.3)	113 (28.7)	394	
Family history of iron deficiency				
Present	31 (56.4)	24 (43.6)	55	0.075
Absent	323 (68.3)	150 (31.7)	473	
History of vaccination				
Present	230 (67.6)	110 (32.4)	340	0.692
Absent	12 (15.8)	64 (84.2)	76	
Treatment after fever				
Yes	15 (88.20)	2 (11.8)	17	0.054
No	332 (65.9)	172 (34.1)	504	
Respiratory tract infection				
Yes	34 (59.6)	23 (40.4)	57	0.208
No	320 (67.9)	151 (32.1)	371	
EEG stating				
Normal	173 (67.8)	82 (32.2)	255	0.706
AbNormal	181 (66.3)	92 (33.7)	273	
Parent's Emotionally				
Nervy	3 (21.4)	11 (78.6)	14	0.0002*
Anxiety	351 (68.3)	163 (31.7)	514	
Irritable				

* $p < 0.05$ is significant

Table 2. Multiple logistic regression analysis to identify risk factors for recurrence of febrile seizures.

factor	Beta coefficient	or	Lower 95 % CI	Lower 95 % CI	P
Gender (reference = female).	0.05	0.95	0.42	2.15	0.897
Age of first onset (reference ≤ 18 months).	0.93	0.39	0.17	0.94	0.037*
Temperature (per or Fahrenheit).	1.09	0.34	0.15	0.76	0.009*
Duration of fever (reference = 1 h).	0.99	0.36	0.13	0.99	0.040*
Family history of febrile seizures (reference = absence).	1.31	3.72	2.27	6.10	0.001*
Family history of epilepsy (reference = none).	0.25	1.29	0.13	12.19	0.820

* $p < 0.05$ indicates Significant. The reference category for the dependent variable is non-recurrent febrile seizures in subjects. OR = Odds ratio. CI= confidence interval

It was observed that younger age at onset, lower temperature at onset, shorter time from fever to onset, and family history of febrile convulsions were significantly associated with recurrence of febrile convulsions in children. The risk of recurrence was 0.39 times lower in children ≥ 6 months of age than in children < 6 months of age. The risk of recurrence was greatest in children with a body temperature of 38°C at the time of the seizure, with a 0.34-fold reduction in the risk of recurrence for every 1°C increase in temperature. The risk of recurrence was 0.13 times lower in children with a duration of ≥ 1 hour compared with children with a duration of > 1 hour. Gender and family history of epilepsy were not significantly associated with seizure recurrence.

4. Discussion

Febrile convulsion in children belongs to the common type of infantile convulsion, accounting for 40%–60% of infantile convulsion. It belongs to the abnormal discharge of cerebral cortical neurons in the event of acute infection of the non-central nervous system [7-9]. It can cause involuntary contraction of local muscle or whole body muscle in children. The recurrence rate is which is 30%–40%, mostly related to infection.

At the same time, it is related to the physiology of the brain in children, the development of the brain in children is immature, and the differentiation of cortical cells is not complete, so fever can cause excessive synchronous discharge of cerebral cortical neurons to lead to the occurrence of convulsion, and there is a tendency to relapse.

This study analyzed the mode of delivery, type of the first febrile seizure, immediate family members, history of febrile seizure, age of the first seizure, and the factors related to the body temperature of the first seizure. [10] Mode of delivery of children: the results of this study showed that the recurrence rate of natural delivery of children is low, and its physiological mechanism still needs to be studied. [11] The type of onset of first febrile convulsion in children: complex febrile convulsion can easily lead to brain injury in children, and at the same time can also cause abnormal development of the original nervous system, more likely to cause recurrence, resulting in a vicious circle. [12] Genetic factors of children: at present, most febrile convulsions are polygenic, and a few are autosomal dominant with incomplete exsertion. Children with a family history of febrile convulsions and epileptic seizures are more likely to relapse. [13] The child age: the first is related to infant brain development maturity, brain development is mature and brain development is extremely mature children are not easy to happen, this age is related to the patient's immune system, the age of 6 months to 2 years old of children's own immune system has not been developed but gradually disappear from the mother's immune antibody, therefore susceptible to infectious diseases, recurrence of the thermal induced convulsion. 5 children with first onset temperature: when onset, high fever for infants and young

children belong to the strong stimulation, infants and young children can cause alarm, but because of infant neurodevelopmental immature, in low temperature convulsions in the system of the patients did not cause alarm, at the same time also prompted children have different degree of potential lesions in the brain or central nervous system is not stable, bring down surprised threshold is low, the thermal more sensitive feeling, more easy to relapse.

In the present study, 32.9% of children aged 6 months to 6 years presented with febrile seizure recurrences. Some researchers have observed a 15-70% risk of recurrence within the first 2 years after the initial febrile seizure. In this study, young age at onset, low temperature at onset, short time from fever to onset, and family history of febrile seizures were found to be risk factors for febrile seizure recurrence. In this study, recurrences were more common in children < 6 months of age (41.3%) compared to children ≥ 6 months of age (24.1%).

In the present study, the recurrence rate was 52.5% in children with a temperature of 101°F at the time of seizure, compared to 17.2% in children with a temperature greater than or equal to 105°F . There was a significant downward trend in the recurrence rate of febrile convulsions ($p=0.001$).

In our study, children with a fever < 1 hour before their first seizure (57.3%) were at significantly higher risk than children with a fever ≥ 1 hour before their first seizure (35.8%). The results of this study showed that a family history of epilepsy was not associated with recurrence. These observations found that children with a family history of epilepsy had a greater risk of febrile seizure recurrence. In our study, iron deficiency was associated with the recurrence of febrile seizures in children. In another study, the incidence of iron deficiency was almost twice as high in children with febrile seizures compared to children with epileptic seizures. However, the relationship between iron deficiency and recurrence has been studied. There are some limitations to this study. The follow-up period was 3 years, which may have resulted in study participants missing recurrent episodes later in life. Iron deficiency anaemia was assessed using haemoglobin and peripheral blood smears, while assessment of iron stores requires a more accurate estimate of iron deficiency. In this study, multiple logistic regression analysis showed that younger age at first convulsion, lower body temperature at the time of convulsion, shorter time between fever and first convulsion, and family history of febrile convulsions were significantly associated with recurrence of febrile convulsions in children [14]. In another study in southern China, risk factors for recurrent febrile convulsions were: younger age of onset, convulsions with low-grade fever, chronic fatigue syndrome, multiple febrile convulsions, febrile convulsions or a positive family history of epilepsy. Recurrent febrile convulsions can have a negative impact on the quality of life of the family, as parents may feel anxious and fearful whenever their child has a fever. This fear is known as 'fragile child syndrome' and includes a range of behaviours that are thought to be caused by excessive

parental anxiety. This excessive parental fear of fever and febrile convulsions can have a negative impact on daily family life, parental behaviour and parent-child interaction [15]. This fear and anxiety can be alleviated by appropriate education and counselling about febrile convulsions. Parents and carers should be provided with specific information on how to care for their children. For doctors, identifying risk factors for recurrence may lead them to consider intermittent oral valium during febrile episodes and possibly even long-term prevention. The risk factors and prognosis for recurrent febrile convulsions need to be further investigated with a longer follow-up period.

The following preventive measures can be taken: (1) the risk factors for recurrence of children are evaluated while active treatment is carried out, and the children with caesarean section, first febrile convulsion are followed up as complicated febrile convulsion, the immediate family has a history of convulsion, the first seizure age is 6 months to 2 years old, the first seizure temperature $<39.5^{\circ}\text{C}$ are included in the key management population of febrile convulsion recurrence, the records of febrile convulsion are established, and the relevant data are sent to the corresponding community health service health network, and follow up, and appropriate guidance is given. (2) To give a lecture on the prevention of febrile convulsion to the families of the children, and to inform them of the main influencing factors and protective measures of febrile convulsion recurrence. To improve the knowledge and health level of the children's families and the nursing skills of the children, if the family members do not know the disease completely, it is easy to lead to the treatment is not timely, when serious will not only cause irreversible brain damage to the children, but also endanger the lives of the children. (3) To promote breast-feeding of children, to instruct their families to strengthen their nutrition, to carry out vaccination on time, to actively protect against chronic diseases, to improve their disease resistance, to observe the abnormal reactions of children in their daily life, to detect abnormalities in time and to detect their body temperature, and to take antipyretic drugs at home, to take them promptly and to control them. Child body temperature below 38°C .

Appropriate preventive use of anticonvulsant drugs can reduce the recurrence of convulsion, children with risk factors of recurrence under the guidance of a physician appropriate use can prevent the recurrence of febrile convulsion in children. Febrile convulsion has a rapid onset and severe symptoms, so it must be accurately and quickly detected and normally diagnosed as well take effective measures here to avoid danger. With the rapid development and improvement of current medical level and nursing operation technology, most children with febrile convulsion can obtain good clinical effect and good long-term prognosis after corresponding treatment and nursing, but there is a high recurrence rate of the disease, once the recurrence, if the isnot treated in time, nursing, there will be repeated attacks. directly affect the brain development of children, which is not conducive to the healthy growth of children [16].

Therefore, we should pay more attention to the implementation of timely and effective nursing measures while paying attention to the clinical treatment of children, and further prevent and cure the recurrence phenomenon. Continuous nursing is a new type of nursing model, which refers to the continuation from hospital to home, which can ensure that children continue to receive continuous follow-up after discharge, as well as standardized nursing guidance. Among them, telephone follow-up belongs to one of the various forms of continuous nursing follow-up, which takes information tools as the medium to improve the health of children as the goal, and promotes the nurses, children and parents to form a purposeful interaction [17]. Continuous nursing by telephone follow-up can effectively track the changes of children's condition after discharge, provide professional nursing guidance, and achieve the purpose of reducing complications and improving prognosis. In view of this, this article used telephone follow-up nursing for children with febrile convulsion in our hospital, the results showed that the recurrence rate of the children in the experimental group within 0.5 years was lower than that in the control group, and the score of the parents' knowledge in the experimental group was higher than that in the control group. As far as children are concerned, parents are the first members to find out the changes of the disease, so, guide parents to correctly grasp the knowledge of the disease, especially the fever omen and its treatment measures, emergency treatment when convulsion attack, conducive to the recovery of the prognosis of children. This paper carries out continuous nursing in the form of telephone follow-up, mainly through carrying out disease knowledge and health education to children according to their actual condition, parents' psychology, knowledge and so on, according to the principle of stratification and step by step, so that they can fully realize the harm of disease recurrence, and know the recurrence inducing factors and their treatment countermeasures, so as to achieve the purpose of reducing recurrence rate [18]. It can be seen that telephone follow-up continuous nursing has the characteristics of simple operation, economic and effective, on the one hand, it can save manpower and material resources, on the other hand, it can improve the working efficiency of nursing staff.

5. Conclusion

This study found that younger age at first convulsion, lower body temperature at the time of convulsion, shorter time between fever and first convulsion and family history of febrile convulsions were significantly associated with recurrent febrile convulsions in children. These risk factors should be kept in mind, physicians, while dealing with children suffering from febrile seizures. Caregivers of children at risk should be advised on long-term prevention and increased vigilance for children with each fever to prevent recurrences. Continuous telephone follow-up can help to deepen the relationship between parents and children. Disease awareness, which can help children to obtain good care

measures, reduce recurrence.

Ethical Statement

This study was carried out in accordance with the recommendations of “Ethics Review Committee of Affiliated hospital of yunnan university of traditional Chinese medicine.” with written informed consent from all subjects. All subjects gave written informed consent in accordance with the Declaration of Helsinki. The protocol was approved by the “Ethics Review Committee of Affiliated hospital of yunnan university of traditional Chinese medicine.

Author Contributions

ZC: study design and draft the work; WJ: picture editing and data analysis; YJ: revising it critically for important intellectual content. All the authors read and approved the final manuscript.

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