

Clinical Spectrum, Treatment Response and Outcomes in Children with Febrile Infection Related Epilepsy Syndrome (FIRES) : A Case Series from India

Ramya Bandi¹, Lokesh Lingappa¹, Vivek Jain², Ravi Sharma², Ramesh Konanki¹,

1. Rainbow Children's Hospital, Hyderabad, India, 2. Santokbha Durlabhji Memorial Hospital, Jaipur, India

INTRODUCTION

- Febrile infection-related epilepsy syndrome [FIRES] is a term proposed by Van Baalen et al in 2010 to address the spectrum of acute onset refractory seizures with a background febrile illness in children.
- Even after a decade of its conception, the knowledge gap in pathophysiology and especially, in treatment is evident.
- Hence, we would like to present our experience of **41 children** treated with FIRES.

METHODOLOGY

- This was a retrospective observational study.
- Children aged 2 to 18 years fulfilling the diagnosis of FIRES, seen at **two tertiary care** Pediatric Neurology Centers in India, seen between **July 2015 to November 2020**, were recruited.

Clinical Data

- Data was collected from patient files, electronic medical records and EEG database from January 2016 to May 2018 and prospectively thereafter.

Outcome

- Functional outcome was measured with **Clinical Assessment Scale in Autoimmune Encephalitis (CASE)** at discharge and latest follow-up.
- Good outcome was defined as either a return to premorbid functional baseline or as a final CASE of 5 or less.

RESULTS

- 41 Children (**27 male, 10 female**) with mean age of **7.2 yr (2 - 14)** were included.
- The mean interval from febrile illness to seizure onset was 4.2 days (Range: 1-14).

RESULTS

- After admission the mean time to start anesthetic drugs from the day of illness was 6.1 days (1-9).
- Most common seizure was unilateral clonic focal (n-16, 39%).
- First MRI brain was normal in 51% (n-21) and 46% (n-19) had abnormalities.
- Temporal lobe abnormalities(9/19) were commonest followed by multilobar abnormalities (5/19).
- **Predominant EEG** findings were focal spike wave/ sharp wave discharges in frontotemporal region (n-24, 57%).
- Of note, 2 children who had ictal suppression pattern died.
- **CSF examination** was normal in 23 children (57%), abnormal in 17 (42%) and could not be performed in one child.
- Only one child had rickettsial species positivity.
- **Mycoplasma IgM** was positive in 8 children but the causal role could not be established.
- Mean duration of starting anesthesia from the day of illness was 6.2 days (1-16).
- Mean number of AEDs used were 7 (Range: 2-12).
- **Midazolam** was used in all children as the first anesthetic infusion. It was restarted/cycled in 19 children.
- **Inhaled Isoflurane** was used in 13 children.
- All children received pulse dose of methyl prednisolone.
- **IVIG** was given in 26 children. Plasmapheresis was done in two children.
- **Rituximab** was used in 13 children at a dose of 375 mg/m², two doses one week apart. None of them required additional doses.
- **Cyclophosphamide** was also used in 13 children.
- **Ketogenic diet (KD)** was used in 23 children with definitive response in one child.
- Of note 6 children had diarrhea after starting KD.
- Deep venous thrombosis was seen in 14 children as a result of intensive and high end care. Average duration of hospital stay was 35.9 d (3-135).

Outcome

- **Fourteen** (33.3%) children died.
- Mean follow-up duration was **37 months** (9-96) in 27 children.
- At the latest follow-up **13 children had CASE scale of <5** and 15 had >5.
- Seizure recurrence after discharge was seen in all except 2.
- Majority of seizures recurred during the first few months (1-4) after discharge.
- Epilepsy was well controlled (no seizures for past 3 months) in 9 children and 3 children were off-AEDs.

Drug	Children Received (n=41)	Average Maximum Dose Given	Mean Duration Given	Good Response (%)	Poor Response (%)
Midazolam	41	16(4-25) mcg/kg/min	17.8 d (1-90)	12(29)	29(70.7)
Ketamine	33	1.6 mg/kg/h (0.5-7)	8.4 d (0.25-30)	7(21)	26(78)
Thiopentone	18	5.3(2.5-10) mg/kg/hr	8.1d (0.3-41)	3(16)	15(83)

DISCUSSION

- In concordant with previous findings, all children had **typical development** prior to illness. Majority were boys
- There was **no significant correlation** of various parameters such as time to start anesthetic, number of anesthetics, type of drugs used, MRI abnormalities, CSF findings, duration of stay to the outcome of children.
- **MRI brain was normal in half** of the children
- Among survivors, half of them had good outcome

CONCLUSION

- Severity of disease and poor response to treatment (**early and high requirement of CI**), were significantly negatively associated with bad outcome implying that aggressive treatment during the critical window could alter the outcome.
- **Ictal suppression pattern** in EEG is associated with poor outcome.
- After an average **follow-up period of 3 years** in 27 children, 3 children were off AED and 9 have well controlled epilepsy. These outcomes are **a ray of hope** in this gloomy condition.

REFERENCES

1. Van Baalen, A., Häusler, M., Boor, R., Rohr, A., Sperner, J., Kurlmann, G., Panzer, A., Stephani, U. and Kluger, G. (2010), Febrile infection-related epilepsy syndrome (FIRES): A nonencephalitic encephalopathy in childhood. *Epilepsia*, 51: 1323-1328.
2. Lim J, Lee S, Moon J, Jun J, Kim T, Shin Y, et al. Development of the Clinical Assessment Scale in Autoimmune Encephalitis. *Ann Neurol* (2019) 85(3):352-8.
3. Lee HF, Chi CS. Febrile infection-related epilepsy syndrome (FIRES): therapeutic complications, long-term neurological and neuroimaging follow-up. *Seizure*. 2018 Mar 1;56:53-9.