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Neurodevelopmental and epilepsy outcome in children aged one to five years with infantile spasms—A North Indian cohort

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KEYWORDS
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Summary
Purpose: The present study was planned as there is paucity of outcome data of children with infantile spasms, from India where profile of patients is different from the western world. Moreover, most previous studies have either not used strict inclusion criteria or standardized psychometric tests for developmental outcome.
Methods: Ninety-five children, aged one-to-five years under follow up for more than six months in Pediatric Neurology Clinic of a tertiary care hospital with the diagnosis of infantile spasm were enrolled in this cross-sectional study if they had completed one or more years after the onset of spasms. The study period was January—December 2011. Neurodevelopment of each child was assessed using Development Profile 3 and Gross Motor Function Classification System. History regarding epilepsy frequency and control in the last one year was taken.
Results: Perinatal asphyxia was the commonest etiology in 43/95 children (45.2%). Favorable neurodevelopmental outcome was observed in 8/95 patients. Favorable epilepsy outcome in 58/95 (61.1%) patients was associated with treatment lag $\leq$ 3 months between apparent onset of spasms and institution of therapy {OR 2 (1.1—3.8)} and response to first line antiepileptic drug {5 (2.6—10)}.
Conclusions: The commonest etiology was potentially preventable perinatal cause. Early appropriate treatment may have a favorable epilepsy outcome.

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Introduction

Infantile spasms (IS) constitute an age dependent epileptic encephalopathy associated with many different underlying conditions. It is characterized by clinical spasms that occur in clusters, has its onset during first 2 years of life, usually during infancy and has a characteristic EEG pattern of hypsarrhythmia with or without psychomotor retardation (Lux and Osborne, 2004).

The psychomotor arrest and regression associated with this epileptic encephalopathy make it one of the main causes of cognitive deterioration during infancy. The onset of spasms is so subtle that it is often missed by parents. The cry associated with it may be misinterpreted by the physicians and parents alike as infantile colic!

The long-term implications of infantile spasm are significant, with frequent occurrence of cognitive impairment and persistent seizures in survivors, and increased incidence of early mortality.

The cost of health care services for these children is enormous. Also, there is scarcity of specialized pediatric neurologists for managing children with epilepsy in developing countries. Therefore there is a need to sensitize the physicians and public about the prevalence of this entity. The patient and treatment variables that seem to be associated with the neurodevelopmental and epilepsy prognosis also require further study.

Moreover, from clinical experience, profile of Indian patients appears to be different from the developed world. There are more patients with severe birth asphyxia, there is lack of awareness in community and physicians which leads to late diagnosis and inappropriate treatment. Most previous studies have not used strict inclusion criteria especially documented hypsarrhythmia (Singhi and Ray, 2005; Malik et al., 2012). Results of developmental assessments in previous studies were often based on clinical impression and school placement rather than standardized, age-appropriate psychometric testing (Lombroso, 1983; Hrachovy et al., 1991).

Therefore, the present study was planned to fill this gap in knowledge and to determine the neurodevelopmental and epilepsy outcome and factors associated with the outcomes in such children in a tertiary care setting who have been treated with the current standard treatment option.

Materials and methods

Patient enrolment

This was begun after obtaining institutional ethical committee clearance. The study center is located in New Delhi in North India. It is a tertiary care research, training and referral Institute situated in the national capital-New Delhi. The majority of patients (approximately 70%) attending this center are from the National Capital Region (NCR) and rest are referred from adjacent North Indian states of Haryana, Bihar, Uttar Pradesh, Rajasthan, etc. The referrals both from Delhi and adjacent regions (nearly 60%) were usually not for the spasms that were unrecognized but for management of associated cerebral palsy! The diagnosis of infantile spasms was based on clinical semiology and EEG pattern of classical or modified hypsarrhythmia. The children were enrolled in this cross-sectional study after obtaining written informed consent according to following criteria:

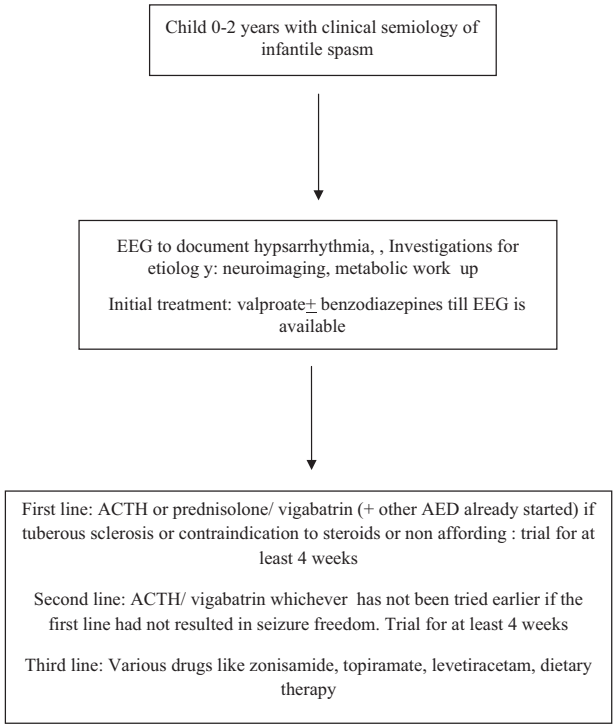

Figure 1 Treatment approach followed at study center for infantile spasm.

Inclusion criteria: The study subjects fulfilled all the following criteria namely, age between 1 and 5 years, history of or ongoing infantile spasms diagnosed on history or witnessed by physician, completion of 1 or more years after onset of spasms, EEG pattern of classical or modified hypsarrhythmia documented any time during treatment and under follow up for at least 6 months. The study period was January—December 2011.

Exclusion criteria: Patients with one or more of the following were excluded from the study: Significant systemic illness interfering with developmental assessment or non-availability of primary caregiver at the time of enrollment or non-availability of exact date of birth.

Treatment protocol

The treatment protocol followed at this center is depicted in Fig. 1. Treatment naïve patients were put on valproate ± benzodiazepines before EEG was available and baseline workup for infection and screening for tuberculosis was done. Most of the referred patients were on phenobarbitone/phenytoin which were tapered and the child was started on valproate. Four patients were on levetiracetam from a private practitioner which was continued till investigations became available. Injection Adrenocorticotrophic Hormone (ACTH) was used in the dosing regimen of 40 IU intramuscular once daily for 4 weeks followed by tapering over 4 weeks. Prednisolone was used in the