

## DRUGS

# Factors associated with response to ACTH treatment in infantile spasms, a Chinese study

Yan Chen MD, Wei Yu MD, Qiongxiang Zhai MD, Jian Xiang Liao MD PhD

Epilepsy Center, Shenzhen Children's Hospital, Shenzhen, Guangdong, China

Address correspondence to: Dr JX Liao, Epilepsy Center, Shenzhen Children's Hospital, Shenzhen, 518026 China. E-mail: liaojianxiang@sina.com

*Introduction:* Although adrenocorticotrophic hormone (ACTH) is widely used as first-line drug for infantile spasm, there is still no agreement on the dosage and duration of treatment. We investigated the response to short duration, low dose ACTH treatment in a group of Chinese infants.

*Methods:* We retrospectively reviewed 155 patients admitted to our Center from January 2000 to June 2007, who fulfilled the ILAE diagnostic criteria for infantile spasm, and were treated with ACTH. The inclusion criteria of this study were: Onset age <12 months; newly diagnosed IS or patients' control of epileptic spasms failed with other antiepileptic drugs, whose dosage was not changed during ACTH treatment; patients previously not treated with ACTH or other steroids; hypsarrhythmia or modified hypsarrhythmia on EEG before treatment. CT or MRI scan of the head was performed before treatment. A second awake and sleep video-EEG  $\geq 2.5$  hours was performed within 2 weeks after the ACTH treatment. Inborn errors were screened with GC-MS method.

The natural ACTH was manufactured by the First Shanghai Biochemistry Pharmaceutical Limited Company, China. It was infused intravenously for more than 8 hours at 20-25IU daily for 2 weeks. Oral prednisone at 1.5-2mg/kg per day was continued for another 2-4 weeks, and was tapered off over 2-4 weeks. The parents or caregivers were asked to count the number of spasm during the treatment period.

The primary clinical outcome was cessation of spasms and the electroclinical outcome was cessation of spasms and resolution of hypsarrhythmia. Cessation of spasms denote that no clinical spasms have been witnessed within 14 days of commencement of ACTH and for at least 4 weeks from the last witnessed spasms. Responders were patients who had cessation of spasms and resolution of hypsarrhythmia.<sup>1</sup>

*Results:* 74 patients (male 47, female 24) fulfilled the criteria of the study. Age of onset was < 3 months in 18 patients; treatment lag (interval between onset of spasms and initiation of ACTH treatment) was < 2 months in 36 patients; age at initiation of ACTH was < 3 months in 7 patients; positive family history of epilepsy in 10 patients; 49 patients were symptomatic, and 25 patients cryptogenic.

Typical hypsarrhythmia was seen in 26 patients, modified hypsarrhythmia in 48 patients. After ACTH treatment, 47 patients had resolution of hypsarrhythmia. The overall response rate with both cessation of spasms and resolution of hypsarrhythmia was 56.8%. Response rates were: cryptogenic (76%), symptomatic (46.9%,  $X^2=5.696$ ,  $P=0.017$ ); treatment lag < 2 months (75.0%), > 2 months (39.5%,  $X^2=9.506$ ,  $P=0.002$ ); age of onset of spasm < 3 months (33.3%), > 3 months (64.3%,  $X^2=5.317$ ,  $P=0.021$ ); age at initiation of ACTH treatment < 3 months (42.9%), > 3 months (58.2%,  $X^2=0.144$ ,  $P=0.705$ ); males (57.4%), females (55.6%,  $X^2=0.025$ ,  $P=0.874$ ); positive family history of epilepsy (40.0%), negative family history (59.4%,  $X^2=1.323$ ,  $P=0.250$ ). The rate of cessation of spasms was 74.3%, resolution of hypsarrhythmia was 63.5%. On multivariate unconditional logistic regression model, treatment lag and the etiology were significant factors affecting response ( $P=0.029$ , 0.004; odds ratio 4.56, 3.54; 95% CI 1.62-12.84, 1.13-11.09 respectively). There was significant correlation between cessation of spasms clinically and resolution of hypsarrhythmia after ACTH treatment ( $X^2=15.264$ ,  $P<0.001$ ,  $r=0.44$ ). In

the infants whose hypsarrhythmia resolved, cessation of spasms occurred in 89.4% patients. In infants with cessation of spasm, resolution of hypsarrhythmia was seen in 76.4% patients.

*Conclusion:* Our study shows that 2-weeks low-dose ACTH treatment is effective in the treatment of infantile spasm. Symptomatic patients and infants with treatment lag >2 months have worse outcome. There was correlation between cessation of spasms and resolution of hypsarrhythmia.

### **Reference**

Lux AL, Osborne JP. A proposal for case definitions and outcome measures in studies of infantile spasms and West syndrome: consensus statement of the West Delphi group. *Epilepsia* 2004; 45(11):1416-28.