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EDITORIAL COMMENTARY

What Matters the Most for Hormonal Therapy in West Syndrome: Drug, Dosage, or Duration?

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West syndrome, a common infantile-onset developmental and epileptic encephalopathy, is characterized by epileptic spasms (mostly in clusters) and commonly associated with hypsarrhythmia in electroencephalogram. The treatment goals are enduring cessation of epileptic spasms and resolution of hypsarrhythmia. Hormonal therapy, in various forms [adrenocorticotropic hormone (natural, synthetic), oral steroids, intravenous pulse methylprednisolone] and dosage (high or low), has been used for its management with varying success [1]. Oral steroids are often preferred as the initial treatment considering the ease of administration and low-cost, especially during the coronavirus disease 2019 (COVID-19) pandemic [2]. In the United States of America, high-dose oral prednisolone (8 mg/kg/d) for 2 wk with subsequent tapering over the next 2 wk is preferred [3]. It is based on the premise that high-dose for short duration might successfully treat the underlying pathophysiological model of neuroinflammation, minimizing the adverse effects due to prolonged therapy. However, the relapses are known to occur (suggesting probable ongoing neuroinflammation), which often respond to a repeat course of hormonal therapy. Japanese child neurologists prefer a lower dose of hormonal therapy for a variable duration to minimize dose-dependent adverse events [4]. In India and many developing countries, a moderate dose of oral prednisolone (3–4 mg/kg/d) for 2 wk followed by tapering over 2–6 wk is commonly used [2]. Hence, a quest remains to find an appropriate dosage and duration of therapy.

The findings of the study by Kapoor and colleagues are particularly relevant in this context [5]. The authors compared intravenously administered methylprednisolone (30 mg/kg/d for 3 d) followed by short-course oral prednisolone tapered over 2 wk with oral prednisolone (4 mg/kg/d) for 2 wk followed by tapering over the next 2 wk. It was noticed that short-term response at 2 wk as a cessation of epileptic spasms was similar in both groups, but remission at 6-wk was better with oral steroids. Also, the proportion of children with remission at 6 wk in the oral steroid arm increased by nearly 30% (from that at day 14). The possible reasons for this include a late resolution of hypsarrhythmia (after day 14) with ongoing steroids (probable effect of duration or cumulative dose), an effect of second-line therapy which might have been added in nonresponders, and absence of early relapses after achieving electroclinical remission at day 14. However, in the methylprednisolone arm, 6 children relapsed after stopping therapy. Hence, the duration or cumulative dose of hormonal therapy might be crucial in achieving sustained remission at 6 wk and preventing early relapses between 2 and 6 wk. A further longer follow-up data are desirable to understand the long-term impact. It was also noted that the high-dose pulse methylprednisolone group experienced more adverse events in comparison with the group that received oral steroids. This highlights the dose-dependent adverse effects of steroid therapy in the given study.

There is a need to have an adequately powered, randomized, controlled trial with a longer follow-up to answer these concerns. Considering that a large number of children with

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West syndrome are being managed by pediatricians and pediatric neurologists in India, it is a challenge as well as an opportunity to conduct such studies and generate high-quality evidence in this regard.

Declarations

Conflict of Interest None.

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