Finding the Best: Corticosteroids for the Treatment of West Syndrome

West syndrome (WS) is one of the common and severe epilepsies of early childhood, accompanied by unfavorable long-term neurodevelopmental outcomes in most cases, especially in cases of structural or genetic etiology. Structural lesions due to perinatal insult, intrauterine infections, cortical malformations, and neuro infections are the most common cause of WS in India. Besides the underlying etiology, early diagnosis and prompt initiation of effective treatment determine the long-term seizure and development outcomes. Delayed treatment portends a poor long-term prognosis. Corticosteroids are the most effective first-choice medications for treating WS, irrespective of etiology, except in cases of tuberous sclerosis complex where vigabatrin is preferred as the first-line medication.[1,2] There has been intense debate about which corticosteroid preparation is superior in this regard; still the search is ongoing to find the best corticosteroid for the treatment of WS. For many decades daily injections of adrenocorticotrophic hormone (ACTH) for one to three months were prescribed widely in view of literature evidence. However, there are many disadvantages noted with ACTH injections, including pain associated with intramuscular injections, high direct and indirect costs, and logistical difficulties associated with procuring, storing (cold-chain), and getting daily intramuscular injections by a qualified person. In addition, medication errors during the administration of ACTH injections are common.

Recent systematic reviews and meta-analyses demonstrated that the efficacy of high-dose oral prednisolone is comparable to ACTH for the electro-clinical remission of infantile spasms in WS.[3,4] In addition, low-dose ACTH was found to have comparable effectiveness but a lower incidence of adverse effects. Thus, high-dose oral prednisolone is currently widely used as the first-choice medication for the treatment of WS as the short-, medium-, and long-term seizure, and development outcomes have been found to be similar compared to ACTH. Recently, various other forms of corticosteroids (both oral and intravenous) were compared to oral prednisolone or ACTH for efficacy in the treatment of WS.[5,6] Not surprisingly, there were no significant differences found between different steroid preparations in terms of short-term efficacy. But there were significant differences in the sustained long-term seizure remission rate and relapse rate, which generally favored oral prednisolone.[5]

We read with great interest the article published in the current issue of this journal, "Oral dexamethasone versus prednisolone for management of children with West syndrome: An open labelled randomized controlled pilot trial" by Deswal *et al*.[7] This pilot study demonstrated comparable efficacy and safety between oral dexamethasone and high-dose oral prednisolone in the short-term electro-clinical remission of infantile spasms on day 14. Despite having limitations and a convenient sample size of 20 patients in each group, this is the first study to demonstrate the efficacy and safety of oral dexamethasone in WS in a randomized controlled design, to the best of our knowledge. The authors highlighted that efficacy of oral dexamethasone was comparable to oral prednisolone in terms of proportion of children achieving spasms cessation, electroclinical remission, greater than 50% reduction of spasms, and time to spasms cessation. However, this study is not powered to find the noninferiority or equivalence due to the convenient sample size. Though adverse effects profiles between the groups were comparable, again, the study is underpowered for this outcome as well. The high incidence of irritability in dexamethasone groups needs further research to find the correct dose of dexamethasone in terms of efficacy and the least adverse effects.

Dexamethasone is orally effective, inexpensive, and widely available in many developing countries which makes it an attractive alternative to oral prednisolone. Dexamethasone has favorable pharmacokinetics when given orally with ready absorption from the gastrointestinal tract resulting in good bioavailability (81%).[8] It protects the brain from hypoxic-ischemic injury by suppressing neuronal maturation and delays myelination by suppressing gene expression related to glial function.[9,10] Dexamethasone is a long-acting glucocorticoid compared to prednisolone.

Another significant problem in the treatment of WS is the recurrence of infantile spasms once corticosteroids are tapered off; up to 30%–50% of the patients show recurrence. The addition of vigabatrin to the steroids is preferred whenever there is only a partial response to initial treatment or there is recurrence. Sodium valproate, clobazam, nitrazepam, topiramate, lamotrigine, and zonisamide are some of the anti-seizure medications which are effective as second-line treatment for patients with WS resistant to initial treatment.

To conclude, the preliminary findings of this study need to be reassessed in a larger multicentric trial that is adequately powered to find the small effect size, especially about medium-term seizure outcomes, adverse effects, and long-term neurocognitive outcomes. Until then, high-dose oral prednisolone will remain the widely used first-choice medication for treating WS.

Lakshminarayanan Kannan, Lokesh Saini[1]

Advanced Centre for Epilepsy, Gleneagles Global Health City, Chennai, Tamil Nadu, [1]Department of Pediatrics, All India Institute of Medical Sciences, Jodhpur, Rajasthan, India

Address for correspondence: Dr. Lakshminarayanan Kannan, Advanced Centre for Epilepsy, Gleneagles Global Health City, No 439, Cheran Nagar, Perumbakkam, Chennai – 600 100, Tamil Nadu, India.
E-mail: drklnaiims@gmail.com

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