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Efficacy of High-Dose Oral Steroids in Children With Epileptic Spasm

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We read with interest, the recent article by Gonzalez-Giraldo and colleagues.[1] These authors retrospectively studied the effect of high-dose oral steroids in children with epileptic spasms. We wish to add a few points.

We in the developing countries use synthetic adrenocorticotropic hormone, which has good efficacy and a one-month treatment cost of around $120 when compared with $100,000 in the United States. However, we agree with the authors that repeated daily intramuscular injection may increase the treatment cost. In India, the most common underlying etiology of West syndrome is perinatal insult or hypoglycemic brain injury that is more common in poor families because of inadequate access to the health care facilities.[2] The one-month cost of oral prednisolone is around $9, and the high cost of adrenocorticotropic hormone can lead to poor compliance or discontinuation of therapy.

In the study, all the children were treated initially with 40 to 45 mg/day of steroids and the dose was escalated to 60 mg/day if there was persistent spasm after one week of therapy. The authors have included children aged from one to 32 months, and the average weights of healthy one-month and 32-month-old children are 3 and 15 kg, respectively. If we convert the steroid dose (40 to 45 mg/day) that was given in the study to per kilogram of body weight, then it would be around 3 to 13 mg/kg/day, which would be a very high dose for younger children and can lead to adverse effects of steroid toxicity.

This study included children aged between zero to 24 months, but according to Table 1, the authors included children aged up to 32 months. The median time between spasm onset and steroid initiation was 28 days, but the age range is different in the result text and Table 1 (one day to 10 months and one day to 12 months, respectively). They included children who were on a ketogenic diet and switched to oral prednisolone if there was no response within one to two weeks. The antiepileptic effect of ketogenic diet usually takes four to 12 weeks,[3] and the switchover to steroids was too early.

References

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Reply to Sharawat et al. "Efficacy of High-Dose Oral Steroids in Children With Epileptic Spasms"

We appreciate these comments on our article. We completely empathize with the cost issues between these two therapies in India, as well as the United States.

We recognize the concerns about a very young infant (as young as one month old in our series) receiving a dose of steroids as high as theoretically ~8 mg/kg/day. In reality, of course, most patients were approximately 10 kg and therefore received no higher than 6 mg/kg/day. In the United Kingdom Infantile Spasms study, which led to our center's original decision to use oral prednisolone instead of adrenocorticotropic hormone, the protocol dosed 40 mg of prednisolone daily (10 mg four times a day) with an increase to 60 mg (20 mg three times a day) if spasms continued.[1] In their series, children also could be quite young (two to 12 months inclusion age). In their important article, the authors stated in the discussion "most adverse events due to steroids are not dose-dependent. We did not want to use too small a dose and miss an important effect." They continued "No evidence has suggested that a per-kg dose is appropriate for prednisolone." We agree with their opinion that, for a potentially devastating condition such as infantile spasms, a higher dose is needed, safe, and strongly warranted. Steroid-related side effects absolutely may (and do) occur; all these infants should be closely monitored, and the dose should be lowered if necessary. Clinical judgment is paramount.

The comments also do point out an error in Table 1 (the range of the delay to steroid treatment was as long as 10 months, not 12). The authors are, however, incorrect regarding the time frame necessary for the ketogenic diet to show a therapeutic effect. Improvement with ketogenic dietary therapy occurred after a median of two weeks in one study, and it has been used for short term in multiple studies

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for status epilepticus.[2] When attempting the ketogenic diet for *new-onset* (not refractory) infantile spasms, we feel strongly that two weeks is an absolute ethical and realistic maximal time frame.[3] If it is ineffective, infants should be switched immediately to a therapy with more published evidence for new-onset infantile spasms (prednisolone or vigabatrin). Allowing 12 weeks for the ketogenic diet to take effect, as suggested, would be inappropriate.

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