The Use of Steroids in Epilepsy: Time for a Reappraisal?

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KEY WORDS: epilepsy, absence seizures, corticosteroids

IMAJ 2010; 12: 176–177

Epilepsy is a heterogeneous disease with multiple etiologies, either acquired or congenital. The disease may be symptomatic to previous central nervous system insults or to acute brain derangement, or it can result from genetic causes at the molecular level [1]. Many epileptic patients, particularly children, can be classified into specific epilepsy syndromes. This approach allows for better understanding of the natural course and prognosis of the disease in a specific patient and helps determine the best treatment for the child [1,2]. Traditionally, the treatment of epilepsy has adopted a pragmatic approach aimed at reducing the number of seizures or their total elimination, without necessarily influencing the pathophysiology of the disease. Thus, anti-epileptic drugs are mostly prescribed for the sole purpose of controlling seizures [1].

As one-quarter of epilepsy patients do not respond satisfactorily to AEDs, different therapeutic approaches have been introduced, either as seizure-prevention treatments such as the ketogenic diet [3] and vagus nerve stimulation [4] or, whenever possible, to cure the disease by surgical means [5]. Corticosteroids, well known for their anti-inflammatory and anti-immune properties, have been used with variable results in different epilepsy types [6].

AEDs = anti-epileptic drugs

The use of steroids in epilepsy began as far back as the 1960s [7]. Prednisolone, ACTH (adrenocorticotropin), methylprednisolone, hydrocortisone and deflazacort have been prescribed for different epileptic syndromes, namely, those types of epilepsies that are characterized not only by seizures but, most importantly, by the cognitive dysfunction and/or deterioration noted in these patients. This group of epilepsies, known as encephalopathic epilepsies, mostly affects infants and children and includes infantile spasms (West syndrome), Landau-Kleffner syndrome, Lennox-Gastaut syndrome, myoclonic epilepsies, and myoclonic-astatic epilepsy (Doose syndrome) [6,8]. The reported efficacy of steroids in these syndromes varies among the different reports [9-13]. However, of all these conditions, infantile spasms (especially those cases with no previous brain structural damage or not caused by a severe inborn error of metabolism) is the only syndrome that consistently shows an excellent response to steroids, namely ACTH [14].

Apart from their use in epileptic encephalopathies, steroids have been used with varying success in other epilepsy syndromes for which there is evidence or suspicion of inflammatory or immune mechanisms. Rasmussen encephalitis, a severe progressive focal epilepsy with cognitive and motor deterioration [15] and ESES (electrical status epilepticus in sleep) [16], are two examples of such syndromes. Corticosteroids are only partially effective in most cases, although dramatic improvement in specific patients may occur.

Although many pediatric neurologists and epileptologists do use steroids in encephalopathic epilepsy syndromes with anecdotal success, a recent Cochrane Review based on a search for randomized controlled trials found no evidence for the efficacy or safety of corticosteroids in treating childhood epilepsies [6].

Childhood absence epilepsy (petit mal) is characterized by brief absence seizures with a distinct electroencephalographic pattern. In its classic form it is believed to be a genetic condition. Most patients are cognitively normal and the disease tends to resolve spontaneously within months to a few years. While the majority of children respond to AEDs [17], some children depict an atypical course characterized by either lack of response to medications, a tendency to develop absence status epilepticus, or an evolution to severe forms of epilepsy, including convulsive seizures [18-20].

In this issue of *IMAJ*, Lichtenfeld et al. [21] report on the successful use of methylprednisolone in a 7 year old girl with a 2 year history of typical petit mal. However, despite the expected good response to AEDs and good prognosis, her absences had proved refractory to four very effective AEDs. A brief trial of the ketogenic diet was stopped as the child had major difficulty complying with this strict diet. Hence, methylprednisolone as pulse therapy was administered with marked clinical and EEG improvement within days. An intermittent course of oral prednisone was then implemented for 6 weeks. By the time of the report, the patient had remained seizure-free for 8 months. As the authors rightfully point out, the effective use of glucocorticoids in childhood absence epilepsy has not been previously reported.

The marked success of methylprednisolone in this case should be interpreted with caution. First, as previously

mentioned, most typical cases of petit mal respond to conventional AEDs. Therefore, the likelihood of this child representing an atypical case is quite high. Second, although the etiology of many atypical childhood absence cases is unknown, it is quite likely that an autoimmune or an inflammatory process plays a role in this particular case, leading to an impressive clinical response to steroids. Cases misinterpreted as primary (genetic) generalized epilepsies have indeed been associated with autoimmune, steroid-responsive conditions such as Hashimoto thyroiditis [22] and antiphospholipid antibody syndrome [23]. Nevertheless, this is an important report since it broadens the therapeutic armamentarium for children with atypical/refractory absence epilepsy.

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