Clobazam in Adjunctive Therapy in Children with Infantile Spasms

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INTRODUCTION

Infantile convulsions represent a severe epileptic disorder that typically occurs in infancy and has a variable etiology. Cognitive impairment occurs in 75-87% of patients with infantile spasm, and this condition is exacerbated by failure of spasm control. Although standard treatments (vigabatrin, adrenocorticotropic hormone (ACTH), and steroids) are well established, seizures do not respond to these medications in 27–62% of patients. Initial treatment failed to control seizures in 59% of children with infantile spasm, according to a recent multicenter cohort study. However, convincing evidence for alternative second-line treatments is still lacking, and preference varies by institution or clinician (1).

Clobazam is the benzodiazepine most widely used in the long-term treatment of epilepsy. It is recommended by the National Institute for Health and Care Excellence as an adjunctive treatment for all drug-resistant epileptic disorders and has shown remarkable efficacy in treating all types of seizures. Several studies have shown that clobazam is effective in 54-85% of pediatric patients; this is defined as a reduction in seizure frequency of at least 50% when clobazam is used as adjunctive therapy in refractory epilepsy (2,3).

OBJECTIVES

In approximately half of children with infantile spasms, seizures do not improve with initial treatment attempts. We examined the effectiveness of clobazam as adjunctive therapy in patients whose seizures failed to respond to initial regimens of standard treatment for infantile spasms.

MATERIALS AND METHODS

All patients from 2018-2023 that received clobazam as adjunctive treatment for infantile spasms were selected for the study. The diagnostic criteria of infantile spasms were as follows: (1) clinical epileptic spasms manifested between 3 months and 2 years of age and (2) characteristic findings on EEG, such as hypsarrhythmia or modified hypsarrhythmia. Only those patients whose seizures failed to respond to treatment with one or more standard antiepileptic drugs (AEDs) for infantile spasms (i.e., vigabatrin, ACTH, and steroids) and who had no alterations in the other AED regimens during 2 weeks of clobazam treatment were included in this study. In terms of treatment response patients were classified as follows: Complete response in patients with disappearance of convulsions within 2 weeks after administration of clobazam and the patients became spasm-free during four weeks.

RESULTS

In all,70 patients included for the analysis. Clobazam was administered after the usage of 2 (median) AEDs that were not effective. Clobazam was added at the mean age of 12 months. After clobazam therapy was initiated, 22(31.4%) patients became spasm-free ≥ 2 weeks and total 51 (72.8%) of patients had decrease more than fifty percent in spasms. Patients with different etiologies and had recevied or not received prior ACTH/steroids were similar complete spasm control ratio. Patients who had fewer (one and less) prior exposures to AEDs were more likely to have complete spasm control (47.3%) than the others (25.4%). Adverse effects were minor, and only 4 (5.7%) patients experienced. The adverse events observed were sedation, hipotonia.

CLINICAL PARAMETERS	COMPLETE RESPONDERS (N = 41) 58,6%	PARTIAL OR NONRESPONDERS (N = 29) 41,4%	P-VALUE
SEX			0,58
FEMALE	13 (54,2%)	11 (45,8%)	
MALE	28 (60,9%)	18 (39,1)	
ETİOLOGY			0,98
UNKNOWN	10 (58,8%)	7 (41,2%)	
KNOWN	31 (58,5%)	22 (41,5%)	
AGE AT SPASM ONSET (MONTHS)			0,82
PRİOR AEDS			0,28
ACTH OR STEROİDS	23	21	
VİGABATRİN AND/OR OTHER AEDS	28	30	
AGE AT CLOBAZAM İNİTİATİON (MONTHS)			0,68
TİME BETWEEN FİRST AED AND CLOBAZAM İNİTİATİON (MONTHS)			0,83
DURATİON OF CLOBAZAM USE (MONTHS)			0,55
MAİNTENANCE DOSE OF CLOBAZAM (MG/DAY)			0,87

CONCLUSIONS

Clobazam may be an effective and safe alternative treatment option in patients whose seizures do not respond to initial standard treatments for infantile spasms (2). Clobazam is particularly effective as adjunctive therapy in Lennox-Gastaut syndrome, an epilepsy disorder seen in 20-50% of patients experiencing infantile spasms (3). Clobazam may be considered as adjunctive therapy in status epilepticus; Sustained infantile spasms have been shown to occur as a unique form of status epilepticus in young infants (1). Therefore, the potential use of clobazam in patients with infantile spasm needs to be evaluated. Further prospective studies focusing on specific groups with good responses and the long-term results of clobazam in infantile spasms are needed.

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