Journal Pre-proof

Real-life data comparing the efficacy of vigabatrin and oral steroids given sequentially or combined for infantile epileptic spasms syndrome

Pavone Piero, Falsaperla Raffaele

PII: S1090-3798(24)00014-X

DOI: https://doi.org/10.1016/j.ejpn.2024.02.007

Reference: YEJPN 3136

To appear in: European Journal of Paediatric Neurology

Please cite this article as: Piero P, Raffaele F, Real-life data comparing the efficacy of vigabatrin and oral steroids given sequentially or combined for infantile epileptic spasms syndrome, *European Journal of Paediatric Neurology*, https://doi.org/10.1016/j.ejpn.2024.02.007.

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2024 European Paediatric Neurology Society. Published by Elsevier Ltd. All rights reserved.



Real-life data comparing the efficacy of vigabatrin and oral steroids given sequentially or combined for infantile epileptic spasms syndrome

Pavone Piero and Falsaperla Raffaele. Section of Pediatrics and Child

Neuropsychiatry, Department of Clinical and Experimental Medicine, University of

Catania, 95124 Catania, Italy.

Editorial commentary

Infantile Epileptic Spasm Syndrome (IESS) is a quite rare epileptic encephalopathy that occurs within the first two years of life, and manifesting with epileptic spams usually in cluster, electroencephalographic anomaly mostly hypsarrhythmia pattern, and developmental arrest or regression. IESS are etiologically classified in symptomatic and cryptogenic. Nowadays there is no general agreement on the treatment of the IESS as hormonal therapy, oral steroid, ketogenic diet and modified Atkins, pyridoxine, anticonvulsants drugs including vigabatrin (VBG), valproate, levetiracetam, topiramate, and benzodiazepines have been proposed to be used individually, sequentially, or in combination. (1) Prompt diagnosis and appropriate treatment in IESS are maintained useful to improve the cognitive course of the disorder. As known, the IESS outcome is related to etiological factors and to precocious treatment. (2)

We have read the interesting article on IESS treatment published in this Issue by Dozieres-Puyravel et al. (3) The authors report the results of a comparative study on the treatment carried on two real-life IESS children of similar cohorts. Retrospective cohorts of 40 children treated with VGB followed in addition by steroids (sequential therapy-ST) were compared to prospective cohorts of 58 children treated with VGB and steroids in combination (combined therapy-CT). At the day 14 from the initial treatment, significant differences were found comparing the rate of children spasms-free between the ST (27,5%) and CT (64%) (pc 0.0004) cohorts as significant differences were also found on day 30 with 55 % in ST group compared to 76 % in the CT cohorts. With exception of increase in appetite, high blood pressure found in three children, and support of hydrocortisone supplementation for several months no severe side-effects were reported by the authors as regard the administration of VGB and steroids. The authors suggest the use of VGB and steroids in combination as first-line treatment for infants with IESS.

In the treatment of IESS previous studies affirmed the efficacy of hormonal therapy and VGB in combination. A multicentre, open-label randomized trial study was conducted by O'Callaghan et al. (4) in 766 infants affected by IESS. A selected group of 377 were randomly selected and among these 186 infants were treated with hormonal therapy and VGB in combination and 191 with hormonal therapy alone. At days 14 and 42, resolutions of spasms in comparison between the two groups were reported in 133 (72%) infants out 186 with ACTH and VGB treatment in combination

and in 108 (57%) out 191 IESS children treated with hormonal therapy alone.

(difference 15-0%, 95% CI 5.1-24.9, p=0.002). Severe side-effects were reported in 16 children on hormonal therapy alone and in 17 children with hormonal and VGB in combination.

The results obtained by the study of Dozieres-Puyravel et al. (3) showed new advances on the efficacy of combined hormonal therapy with VGB in the treatment of children with IESS, to note in absence of severe side effects. In the treatment of IESS, the efficacy of the combination of hormonal therapy with anticonvulsants drugs has been confirmed by this study. (3) It has been advanced the hypothesis that the efficacy of combined treatment may be linked to a different mechanism of action of the second drug. (5) Undoubtedly improvement in the treatment of children with IESS has been reached, however prognosis remains still unsatisfactory as various harmful factors influence the outcome of these children.

References

- Pavone P, Polizzi A, Marino SD, Corsello G, Falsaperla R, Marino S, et al. West syndrome: a comprehensive review. Neurol Sci. 2020 Dec;41(12):3547-3562.
 doi: 10.1007/s10072-020-04600-5. Epub 2020 Aug 22. PMID: 32827285;
 PMCID: PMC7655587.
- 2) Lux AL, Edwards SW, Hancock E, Johson AL, Kennedy CR, Newton RW, et al. The United Kingdom Infantile Spasms Study comparing vigabatrin with prednisolone or tetracosactide at 14 days. A multicentre, randomized controlled trial. Lancet 2004 Nov 364(9447):1773-8, doi:10.1016/50140-6736(04)17400-X.
- 3) Dozieres-Puyravel B, Nasser H, Mauvais FX, De Saint Martin A, Perriard C, Di Meglio C, et al. Real-life data comparing the efficacy of vigabatrin and oral steroids given sequentially or combined for infantile epileptic spasms syndrome. Eur J Paediatr Neurol. 2023 Nov 27;48:61-66. doi: 10.1016/j.ejpn.2023.11.009. Epub ahead of print. PMID: 38041897.
- 4) O'Callaghan FJ, Edwards SW, Alber FD, Hancock E, Johnson AL, Kennedy CR, et al. Safety and effectiveness of hormonal treatment versus hormonal treatment with vigabatrin for infantile spasms (ICISS): a randomised,

Journal Pre-proof

multicentre, open-label trial. Lancet Neurol. 2017 Jan;16(1):33-42. doi: 10.1016/S1474-4422(16)30294-0. Epub 2016 Nov 10. PMID: 27838190.

5) Knupp KG, Leister E, Coryell J, Nickels KC, Ryan N, Juarez-Colunga E, et al;
Pediatric Epilepsy Research Consortium. Response to second treatment after
initial failed treatment in a multicenter prospective infantile spasms cohort.
Epilepsia. 2016 Nov;57(11):1834-1842. doi: 10.1111/epi.13557. Epub 2016 Sep
12. PMID: 27615012; PMCID: PMC5863234.

Pavone Piero and Falsaperla Raffaele. Section of Pediatrics and Child Neuropsychiatry, Department of Clinical and Experimental Medicine, University of Catania, 95124 Catania, Italy.