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LETTERS

Comment on Epilepsy in cerebrovascular diseases: Review of experimental and clinical data with meta-analysis of risk factors

To the Editors:

I read with interest the review by Ferlazzo et al.[1] on epilepsy in cerebrovascular disease. One given aim of the paper was to review data concerning the prognosis of post-stroke epilepsy (PSE). Based on a literature search, the authors state that PSE has a good prognosis and that clinical studies indicate that seizure freedom rates are high following antiepileptic drug (AED) administration. The article addresses important issues, but some comments are needed regarding the prognosis of PSE. At least in my opinion, a more complex picture emerges from the literature.

Ferlazzo et al. state in their results that "In general, PSE has a good prognosis, being well controlled by AEDs." However, the two real-life observational studies cited report seizure-freedom rates of 54% (n = 36) and 67% (n = 46), respectively.[2,3] These seizure-freedom rates are not remarkable compared to those seen in epilepsy from other causes. On their own, they hardly motivate a label of good prognosis. In a more recent small, single-center study (n = 35), we found that only 55% of patients with PSE at a tertiary center in Sweden had achieved seizure freedom with the first or second AED at last follow-up.[4] Other retrospective studies exist, but report older cases and may not reflect current clinical practice.[5,6] The findings in real-life observational studies contrast markedly with the excellent efficacy of different AEDs seen in monotherapy clinical trials. In clinical trials cited in the review, seizure freedom rates of >70% are not uncommon.[7–10]

The authors are justified in their conclusion that clinical studies indicate that seizure-free rates are high following AED administration, if by studies one means clinical trials and by administration one means treatment delivered in a setting comparable to a clinical trial. Biologically, PSE seems to be treatment-responsive in many cases. Unfortunately, the literature suggests that this favorable characteristic of PSE is not translated into clinical practice. There is not a great deal of evidence to support the notion that PSE has a favorable prognosis outside of clinical trials.

The discrepancy between real-life data and clinical trials becomes evident in thorough high-quality reviews, like the one by Ferlazzo et al. Such work is therefore of great importance. In my opinion, the review demonstrates that ambitions need to be raised in the treatment of PSE. The reasons for treatment failure may be several: perhaps neurologists are not even consulted and patients therefore deprived of routine epilepsy care—a tailored selection of AED followed by therapy revision until seizure freedom is achieved.

DISCLOSURE

The author has no conflicts of interest to disclose. I confirm that I have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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Response to Comment on Epilepsy in cerebrovascular disease: Review of experimental and clinical data with meta-analysis of risk factors

To the Editors:

We thank Dr. Zelano for his kind interest in our work.[1] We agree that results of clinical trials on post-stroke epilepsy (PSE) may be different from those of "real-life" studies. However, a number of considerations should be pointed out. First, generally speaking, observational studies have known methodologic limitations: they are often conducted in tertiary centers, generating a selection bias toward more severe epilepsy patients, and they lack a control group. Second, in our opinion, the observational studies[2,3] cited in our paper and in that of Zelano[3] do not challenge the notion that PSE carries a good prognosis. Indeed, the study by Semah et al.[2] was conducted on patients with focal lesional epilepsy, and PSE had the best prognosis when compared to symptomatic epilepsy from other causes. In the work by Stephen et al.[3] on localization-related epilepsies, almost 70% of patients with cerebral infarction achieved seizure freedom. This percentage was only inferior to the proportion of seizure-free patients with arteriovenous malformation. Moreover, data from another retrospective study[4] confirm that drug resistance is rare (5%) among patients with PSE. Finally, the chance to achieve seizure freedom with low doses of antiepileptic drugs in most patients with late-onset epilepsy (including PSE)[5] supports the notion of a favorable prognosis of this condition. In conclusion, we believe that the evidence from clinical trials and observational studies is adequate to conclude that PSE has a good prognosis when compared to other forms of focal epilepsy.

Disclosure

None of the authors has any conflict of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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Announcements

32nd International Epilepsy Congress

2–6 September 2017
Barcelona, Spain
Congress website: www.epilepsybarcelona2017.org

Regional Congresses

3rd African Epilepsy Congress

5–7 May 2017
Dakar, Senegal

12th Asian and Oceanian Epilepsy Congress

21–24 June 2018
Bali, Indonesia
Website: www.epilepsybali2018.org

13th European Congress on Epileptology

26–28 August 2018
Vienna, Austria
Website: www.epilepsyvienna2018.org
Call for session proposals

Upcoming Chapter Congresses

Annual Meeting of the Austrian and German Society for Epileptology and the Swiss Epilepsy-League

3–6 May 2017
Vienna, Austria
Website: www.epilepsie-tagung.de

Other Congresses

Joint Meeting of Nordic Congress of Clinical Neurophysiology & Kuopio Epilepsy Symposium

15–17 March 2017
Kuopio, Finland
www.uef.fi/fi/web/kuopioepilepsysymposium

The 11th World Congress on Controversies in Neurology (CONy)

23–26 March 2017
Athens, Greece
www.comtecmed.com/cony/20176-8 April 2017

Treatment Strategies in Pediatric Epilepsies First International Training Course – EPIPED

29 March–1 April 2017
Girona, Spain
Course Directors: Victoria San Antonio, Jaume Campistol, Alexis Arzimanoglou
Website: www.epiped-course.com | Program

6th London-Innsbruck Colloquium on Status Epilepticus and Acute Seizures

6–8 April 2017
Salzburg, Austria
www.statusepilepticus.eu

1st North American Workshop on Neuropathology and Epilepsy Surgery

27–30 April 2017
Presented by Cleveland Clinic Epilepsy Center
Cleveland, OH, USA
Flyer

4th Residential International Course on Drug Resistant Epilepsies

7–13 May 2017
Tagliacozzo (AQ), Italy
Announcement | Programme | Application Form

Brain Plasticity in Epilepsy

13–16 May 2017
Leuven, Belgium
www.epilepsy2017.com

First International Training Course on Neuroimaging of Epilepsy

18–21 May 2017
Montreal Neurological Institute of McGill University, Canada
Sponsored by ILAE Neuroimaging Task Force
Poster | Information
Website: www.neuroevents.mcgill.ca

XXVI European Stroke Conference (ESC)

24–26 May 2017
Berlin, Germany
Website: www.eurostroke.conventus.de

10th International Epilepsy Colloquium

15–18 June 2017
South Beach, Miami Beach, FL, USA

12th EPNS Congress

21–24 June 2017
Lyon, France
Lifelong course of diseases of the child's nervous system.
Sponsored by the European Paediatric Neurology Society
Website: www.epns2017.com

3rd Summer School on Imaging in Epilepsy (SuSIE)

9–12 July 2017
Rauischholzhausen Castle, Marburg, Germany
Website: www.imaging-in-epilepsy.org

Advanced International Course: Bridging Basic with Clinical Epileptology – 6

17–28 July 2017
San Servolo (Venice), Italy
Course Directors: Giuliano Avanzini and Marco de Curtis
Information

7th International Summer School for Neuropathology and Epilepsy Surgery (INES 2017)

22–25 July 2017
State University of Campinas – UNICAMP, Brazil
Flyer

11th Baltic Sea Summer School on Epilepsy (BSSSE 11)

6–11 August 2017
Tartu, Estonia
Clinically oriented, and focused on comprehensive aspects of diagnosis and treatment of epilepsy.
Announcement: Program, fees, and more information | Past BSSSE Schools | Website: www.epilepsiestiftung-wolf.de

XIV Workshop on Neurobiology of Epilepsy (WONOEP) 2017

28 August–1 September 2017
Mon St Benet, Barcelona, Spain
Announcement | WONOEP Report

XIII World Congress of Neurology

16–21 September 2017
Kyoto, Japan
Website: www.2017.wcn-neurology.com/

7th Eilat International Educational Course: Pharmacological Treatment of Epilepsy

15–20 October 2017
Jerusalem, Israel
Website: www.eilatedu2017.com

European Congress of NeuroRehabilitation 2017

24–27 October 2017
Lausanne, Switzerland
Website: www.ecnr-congress.org

2018 Congresses

31st International Congress of Clinical Neurophysiology (ICCN)

1–6 May 2018
Washington, DC, USA
ICCN 2018 Website: http://iccn2018.acns.org/

4th International Congress on Brain and Mind

3–5 May 2018
Brno, Czech Republic
Read about the previous Brain and Mind congress

6th Global Symposium on Ketogenic Therapies for Neurological Disorders: Embracing Diversity, Global Implementation and Individualized Care

5–8 October 2018
Jeju, Korea
Website: www.ketoconnect.org

ERRATUM

Epilepsia, 58(3):509–510, 2017
doi: 10.1111/epi.13714

Ceulemans B, Schoonjans A-S, Marchau F, Paelinck BP, Lagae L. Five-year extended follow-up status of 10 patients with Dravet syndrome treated with fenfluramine. *Epilepsia* 2016;57:e129–e134. doi:10.1111/epi.13407.

In the above mentioned article, two errors were published in Table 1. The errors appear in the right-most column presenting echocardiography observations. For patients 4 and 5 the published table indicates "slightly thickened aortic and tricuspid leaflets." For both patients the observation should be "slightly thickened AML and tricuspid leaflets."

These errors were not used in the interpretation of the results, and are not essential for the conclusion of the article. Below is a corrected version of Table 1.

Epilepsia, 58(3):509–510, 2017
doi: 10.1111/epi.13714

Table 1. Overview of all included patients with Dravet syndrome

Patient number[a]	Gender (M/F)	Mutation type SCN1A	Age at start FFA	Total duration of FFA treatment (years)	FFA dose at last FU	AED combined with FFA (at last consultation)	Therapy changes during the 5-year FU	Side effects at last FU	BMI (kg/m^2) at the last consultation	Echocardiography during 5-year FU
1	F	Nonsense c.2584C>T	2.17	27	2 × 5 mg 0.13 mg/kg/day	VPA + TPM	TPM ↑, VPA ↑	No	26.7	2012-Slight AML thickening 2014-Normal
2	F	Missense c.2644A>T	16	24	1 × 20 mg 0.27 mg/kg/day	VPA	No	No	30.4	2014-Normal
3	M	Missense (2×) c.4351C>G c.4467G>L	7	23	1 × 20 mg 0.27 mg/kg/day	VPA	No	Rigid behavior	20.8	2010–2014-Slightly thickened aortic and tricuspid leaflets, stable
4	M	Deletion (frameshift) c.2322-2324delCAC	4	21	1 × 20 mg 0.34 mg/kg/day	VPA + CLB + LTG + LEV	Start slowly tapering LTG (end of 2014)	No	20.1	2013–2014-Slightly thickened AML and tricuspid leaflets
5	M	Missense c.680T>G	1.33	21	5–10 mg 0.29 mg/kg/day	VPA + TPM + ethyl loflazepate	Trial stop ethyl loflazepate with exacerbation of seizures TPM ↑, VPA ↑, and FFA ↑	No	15.0	March 2014-slightly thickened AML and tricuspid leaflets Late 2014-Normal
6	F	–	13	14	2 × 10 mg 0.20 mg/kg/day	VPA + LTG	No	No	30.9	Normal at all examinations
9	F	Missense c.5534A>C	7	10	2 × 10 mg 0.31 mg/kg/day	STP + CLB + VPA	Stop ESM. Start STP, VPA ↑, Switch CLB → CZP → ethyl lofazepate → CLB	No	23.2	Normal at all examinations
10	M	Missense c.2792G>A	11	9	3 × 5 mg 0.25 mg/kg/day	VPA + TPM + ethyl loflazepate	TPM ↑, ethyl loflazepate ↑	Anorexia	19.0	2013-Slightly thickened AML 2014-Normal
11	M	Splice acceptor mutation c.4853-1 G>C	13	6	2 × 5 mg 0.19 mg/kg/day	VPA + TPM	VPA ↑	Anorexia, fatigue	16.6	2010–2013-Slightly thickened AML and tricuspid leaves 2014-Normal
12	F	Nonsense c.1738C>T	1.83	6	2 × 5 mg 0.46 mg/kg/day	VPA + TPM	Stop ethyl loflazepate VPA ↑, TPM ↑	Aggressive behaviour, increased appetite	17.5	Normal at all examinations

FU, follow-up; VPA, valproate; TPM, topiramate; LTG, lamotrigine; FFA, fenfluramine; CLB, clobazam; LEV, levetiracetam; STP, stiripentol; ESM, ethosuximide; CZP, clonazepam; AML, anterior mitral leaflet; BMI, body mass index; ↑, increased dose; →, switched treatment.

[a]Patient number is from original 2012 publication.[3] Patients 7 and 8 have discontinued treatment as described in Methods.