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LETTER

Refractory status epilepticus: Is there room for grading refractoriness?

To the Editors:,

We read with interest the work by Dr Beuchat and colleagues, and we congratulate them for providing insights into the outcome of status epilepticus (SE) at successive treatment steps and for clinically confirming the notion of refractory SE (RSE).[1]

In a post hoc analysis of the SENSE (Sustained Effort Network for treatment of Status Epilepticus) cohort study, the likelihood of SE cessation significantly decreased between the first two and the third treatment lines and remained relatively stable afterward.[1] These findings are clinically relevant because they highlight the possibility of controlling seizure activity after different treatment failures. Similarly, the case fatality and the likelihood of good functional outcome at discharge were significantly different across treatment steps; these findings were explained by the difference between the first two and the third attempts, with no significant difference thereafter.[1] It is, however, worth noticing that there was a tendency toward less favorable outcomes with increasing number of treatments failed; whereas 8% of people with SE responsive after the first two treatments died and 75% had a good functional outcome, the corresponding figures for those treated with more than five antiseizure medications (ASMs) were 26% and 38%.[1]

The lack of analyses based on the types of treatments (i.e., ASMs vs. general anesthesia) did not allow exploration of whether differences exist according to the use of anesthetic agents. In a real-world cohort of routine-care SE management based on a stepwise approach, subjects with RSE that resolved with subsequent ASMs had a similar mortality, but a higher rate of poor functional outcome at discharge compared to subjects with responsive SE. Additionally, subjects with RSE that resolved with anesthetic agents were at higher risk of death and worsening of functional status at discharge compared to subjects with RSE that resolved with ASMs.[2] In a large, administrative dataset containing medication data, the cohorts of low (i.e., treatment with none or one intravenous ASM and no intravenous anesthetics), moderate (i.e., treatment with more than one intravenous ASM and no intravenous anesthetics), and high refractory SE (i.e., treatment with at least one intravenous ASM and at least one intravenous anesthetic) were defined.[3] High refractory SE was associated with a higher in-hospital mortality compared to moderate and low refractory SE, and the composite endpoint of in-hospital mortality and discharge to hospice was significantly more common in high (25.3%) than moderate (13.6%) and low (7.9%) refractory groups.[3]

The currently available evidence, despite the limits that allow inferring associations but not causation, suggests that different degrees of refractoriness may better suit the heterogeneity of SE and the spectrum of SE burden and outcome.[4] Additional, ideally prospective studies including participants matched for their disease rather than treatment preferences and controlling for the effects of potential confounders like etiology[5] and semiology[6,7] are needed to identify the best framework of SE refractoriness.

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CONFLICT OF INTEREST STATEMENT

S.L. has received speaker or consultancy fees from Angelini Pharma, Eisai, GW Pharmaceuticals, Medscape, and UCB Pharma and has served on advisory boards for Angelini Pharma, Arvelle Therapeutics, BIAL, Eisai, GW Pharmaceuticals, and Rapport Therapeutics outside the submitted work. S.M. has received research grant support from the Ministry of Health and the nonprofit organization Fondazione Cassa di Risparmio di Modena; and has received personal compensation as a scientific advisory board member for UCB, Jazz Pharmaceuticals, and Eisai outside the submitted work. 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.

Simona Lattanzi[1]
Stefano Meletti[2,3]

[1]*Neurological Clinic, Department of Experimental and Clinical Medicine, Marche Polytechnic University, Ancona, Italy*
[2]*Neurology Unit, OCB Hospital, AOU Modena, Modena, Italy*
[3]*Department of Biomedical, Metabolic, and Neural Science, Center for Neuroscience and Neurotechnology, University of Modena and Reggio Emilia, Modena, Italy*

Correspondence
Simona Lattanzi, Neurological Clinic, Department of Experimental and Clinical Medicine, Marche Polytechnic University, Via Conca 71, 60020 Ancona, Italy.
Email: alfierelattanzisimona@gmail.com

ORCID
Simona Lattanzi https://orcid.org/0000-0001-8748-0083
Stefano Meletti https://orcid.org/0000-0003-0334-539X

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