Reviewer's report

Title: Does burst-suppression achieve seizure control in refractory status epilepticus?

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Reviewer: Alain Lekoubou

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Does burst-suppression achieve seizure control in refractory status epilepticus?

This is an interesting study evaluating the relationship between the achievement of burst-suppression using Midazolam and seizure control in refractory status epilepticus. They analyzed data collected from a retrospective database in a single hospital. This is a common problem in neuro-critical care units. Seizure control was defined as the absence of breakthrough seizure or withdrawal seizure. They concluded that achieving burst-suppression was safe and associated with fewer breakthrough seizures but was not associated with an increased rate of intrahospital complications or long-term outcomes.

As a general comment, I will encourage the authors to focus on the main objective of the study which is the efficacy (seizure control) of Midazolam in a population of patient of refractory status epilepticus not related to non-anoxic brain injury. The title should also reflect this objective by include referring to "non-anoxic encephalopathy"

Abstract:

The purpose of the study is not clearly enunciated.

Can the author clarify for the reader what pre-compiled causal diagram mean?

Introduction

Please add a subtitle for Introduction

Please correct the typo in the sentence "Midazolam has been shown to have a wide margin of safety, a board therapeutic index, and be easy to use..." 

The sentence "The fact is that no study has established the effects of EEG-BS in
midazolam-treated RSE patients" may sound contemptuous and offending to authors who have addressed this question in the past. I suggest changing it to "There is a scarcity of study assessing the effects of EEG-BS in midazolam-treated RSE patients…"

The following sentence "Our study was conducted using systematically-collected retrospective data to analyze the effect of midazolam-induced BS on the occurrence of..." should appear in the methods section. Also the authors may want to explain how data can be systematically collected retrospectively?

Methods and Statistical analysis:

Please provide a brief description of the guidelines cited in the methods section.

It seems that definition of seizure freedom was based on EEG and clinical findings. This need to be clearly stated. The authors may want to provide references from the literature to support the definitions of breakthrough seizure and withdrawal seizure provided here. I imagine that some of the outcomes were observed more than once i.e. a patient will have a breakthrough seizure and placed back on burst suppression and later have another breakthrough seizure. The same is true for withdrawal seizure. The authors would like to clarify how these outcomes were counted.

Inclusion criteria may be redundant. Patients fulfilling criteria 2) automatically fulfill criteria 1)

What is the primary endpoint? What are the secondary endpoints? It seems that the following were endpoints: 1) presence of breakthrough seizure, 2) withdrawal seizure, 3) in-hospital complications, and functional outcome at three months. What is the primary independent variable? What is/are the dependent variable(s). What are other covariates included in the modes? It would stand to the readers that these important details should be clearly presented.

Results:

A selection tree/diagram would be useful in summarizing the selection process.

The relationship between the outcome variables and the burst-suppression are presented as incidence rate ratio. The use of incidence rate ratio is misleading in this case. Incidence rate ratio is the ratio of the incidence rate between the exposed group and the non-exposed group in the cohort. The incidence rate is the number of event divided by the unit-time of exposure. It seems
that the authors did not compute these estimates to be able to derive an incidence rate ratio. It rather appears that the authors have reported on the cumulative incidence rate during the period of hospitalization extending from June 2005 through April 2016. The incidence rate ratio is likely the incidence risk ratio which is the ratio of the cumulative incidence in the exposed group vs. the control group.

It is not clear if the measure of association provided is adjusted or not.

Discussion:

A word should be say on the exclusion of anoxic brain injury

Limitations:

The significance of some results may also be due to random variations in this small sample.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

No

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review
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