Author's response to reviews

Title: A pilot study of rivastigmine in the treatment of delirium after stroke; a safe alternative

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Author's response to reviews: see over
Dear editor,

We thank you and the reviewers for the constructive comments. The points raised by the reviewers are answered below.

Further we requested a registration at the “Nederlands Trial Register” and added the number in the abstract.

The points about the medical ethics committee and the Helsinki declaration are added in the method section line 17-20.

We hope that after these changes our paper is suitable for publication in your journal

Kind regards, also on behalf of the co-authors

Dr. Gerwin Roks

Reviewer 1.

1. As the mean age is 77 years, in 15% a pre-existent dementia will be available. Theoretical, the positive effect of rivastigmine in these patients is on the dementia. A relevant standard result is missing: An indication of the cognitive functions of the patients at discharge, par example using a MMSE score, can make this point more clear. We agree with the reviewer that undiagnosed dementia can play a role in the effect of rivastigmine on delirium. In the discussion section line 12- line20 we explained why we think this is not the explanation of the results we found. We used the IQCODE as an indicator of cognitive decline and not the MMSE score. For this reason we are not able to give MMSE scores at discharge

2. As only one patient seems to be a non-responder, please describe patient 11 more in detail. This has been done in line 20- line 26 in the result section

Some data are necessary before publication:

3. How long after CVA and how long after debut delirium is rivastigmine started. We added these data in the method section line 4 – line 5.

4. For further research, the novel titration scheme for rivastigmine has to be more specific. We described it more explicit in line 13 – line 14 of the methods section

5. The roles of other psychofarma as adjuvans need to be cleared out. This was added in line30 - line 32in the result section

6. If above data are available, abstract needs to be reviewed. Writing is acceptable. We made some adjustments in the abstract see comments reviewer 2
Page 5: Accept for the start day, the novel titration scheme for rivastigmine is not described in detail. Is rivastigmine given only b.i.d. or more frequent? How is the increased doses divided?
See point 4

Is antipsychotic medication allowed as adjuvans therapy of rivastigmine?
We allowed haloperidol in the protocol as one of the escape medication but this was only used in one patient after rivastigmine was stopped

Page 6: Which other psychofarmaca treatment were allowed and also given (for insomnia)?
See point 5

Page 11: Is possible to describe patient 11 (nor-responder) more in detail?
See point 2

How long after CVA and how long after debut delirium is rivastigmine started?
See point 3

Is possible to indicate the cognitive functions of the patients, par example using a MMSE score?
See point 1

Is possible to indicate the rate of Alzheimer’s disease in these patients?
We can only say that 2 out of 17 patients were in the range of dementia using the IQCODE. It is not possible to use this score to diagnose the subtype of dementia

Reviewer 2:
The abstract could be more explicit with the mention of:
definition of severe delirium
Added in line 8 of abstract
-dose range of orally administered rivastigmine
Added in line 10 of abstract
-average reduction in Delirium rating scale
Added in line 13 of abstract and also in line 14 – line 15 of the result section

One patient showed no response at all, despite a daily rivastigmine dose of 9 mg
(Detail why titration to 12 mg was not tried)
This was added in the patient description line 20- line 26 of the result section

Five patients needed additional medication because of insomnia (specify drugs and dosages if possible).
This was added in line 30 - line 32 in the result section