Reviewer’s report

Title: Neuroprotective effects of amiodarone in a mouse model of ischemic stroke

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Reviewer: W. Scott Jellish

Reviewer’s report:

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The manuscript, "Neuroprotective effects of amiodarone on a mouse model of ischemic stroke", assesses the effect of a dose of amiodarone 50 mg/kg on mice that were given a focal cerebral insult by occlusion of their left middle cerebral artery. The mice had to have a > 85% decrease in cerebral blood flow on the left side to be included in the study. The amiodarone was given either 1 hour prior to MCA occlusion in one group or immediately after MCA occlusion in another. Hemodynamics were measured in all animals 1 hour before occlusion, at MCAO, 1 hour after and 48 hours after the insult. Behavioral tests including body asymmetry and corner tests were performed 48 hours after MCAO and then the brains were harvested and infarct volume analysis was performed and compared against control that had saline administered 1 hour before and immediately after MCAO.

1. Heart rates were lower in all animals that received amiodarone either before or after MCAO compared to control. Blood pressures were not significantly different between groups.

2. The mice that received amiodarone 1 hour before MCAO occlusion had reduced infarct volume compared to control or amiodarone post treatment.

3. The pretreated mice also had lower asymmetry body swing rates and reduced left turn on the corner test compared to control or post treatment.

4. The authors conclude that amiodarone pretreatment attenuates ischemic brain injury and improves functional outcome compared to post treatment.

5. An interesting and well-designed study which demonstrates the neuroprotective effect of amiodarone. There have been no studies that I am aware of that examine amiodarone's effect directly on the brain during an ischemic event.

6. Other studies have shown that amiodarone is associated with an increased risk of stroke (Medicine 2015; 94:1-6). However, this was mostly associated in patients with non-
valvular atrial fibrillation and was probably associated with an increased risk of emboli, especially since this was also associated with the use of digoxin.

7. Methods: Please describe in more detail a positive motor asymmetry test and what it represents. Please also describe in greater detail the corner test and what a positive test is and the meaning of this test.

8. Table 1: Header over HR in mmHg should be BPM or beats per minute.

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

Yes

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

Yes

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

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
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I am able to assess the statistics

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