

In reply to ‘‘Animal models for neurotoxicity assessment in cardiac arrest’’



Respuesta a «Modelos animales para evaluar la neurotoxicidad en el paro cardíaco»

Dear Editor,

Thank you very much for your interest¹ in our work showing that amiodarone does not affect cerebral injury in a rat model of transient forebrain ischemia.² We appreciate your valuable comments. As you pointed out, the high mortality rates in the cardiac arrest models might have been improved by skillful nice works. However, we wish to resolve some misunderstandings on this point. Regarding the reproducibility of cardiac arrest due to cessation of circulation and breathing, the article you cited certainly indicates that it is reproducible. However, the article does not say anything about successful resuscitation or survival.³ Another report you cited indicated a survival rate in the control group of only 55%,⁴ which did not match our target survival rate. The transfer of laboratory techniques from skilled to unskilled laboratories is often challenging. As suggested by Sanderson and Wider,⁵ it is true that the cardiac arrest models are still associated with a high mortality rate in other laboratories similar to ours. We chose a more reliable and reproducible model in terms of the survival rate because other models require more skill to stabilize the variability of outcomes. In addition, as you suggested, each animal model of neurocritical pathology has advantages and disadvantages, so that none is ideal. Therefore, we think that our model was suitable to investigate amiodarone neurotoxicity in the ischemic brain, which requires a certain period of survival after ischemic injury to evaluate the effects.

However, it is true that bilateral carotid artery occlusion does not truly mimic the brain ischemia caused by cardiac

arrest. Therefore, further investigation with a more appropriate approach is required to draw firm conclusions about amiodarone's application in cardiac arrest.

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References

- Rodríguez-Rodríguez A, Boyero L, Sempere L, Vilches-Arenas A. Animal models for neurotoxicity assessment in cardiac arrest. *Med Intensiva*. 2018, <http://dx.doi.org/10.1016/j.medin.2018.09.009>
- Yamakana K, Inoue S, Naito Y, Kawaguchi M. Amiodarone does not affect cerebral injury in a rat model of transient forebrain ischemia. *Med Intensiva*. 2018, pii: S0210-5691(18)30183-9 [Epub ahead of print].
- Barouxis D, Chalkias A, Syggelou A, Iacovidou N, Xanthos T. Research in human resuscitation: what we learn from animals. *J Matern Fetal Neonatal Med*. 2012;25:44–6.
- Zhu J, Liu K, Huang K, Gu Y, Hu Y, Pan S, et al. Metformin improves neurologic outcome via AMP-activated protein kinase-mediated autophagy activation in a rat model of cardiac arrest and resuscitation. *J Am Heart Assoc*. 2018;7.
- Sanderson TH, Wider JM. 2-Vessel occlusion/hypotension: a rat model of global brain ischemia. *J Vis Exp*. 2013;76:50173.

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