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LETTERS TO THE EDITOR

Animal models for neurotoxicity assessment in cardiac arrest

Modelos animales para evaluar la neurotoxicidad en el paro cardíaco

Dear Editor:

We have read the article by Yamanaka et al.[1] entitled ''Amiodarone does not affect cerebral injury in a rat model of transient forebrain ischemia'' with great interest. Authors conclude that the administration of amiodarone after transient forebrain ischemia do not contribute to additional neuronal damage in rats. These results encourage authors to cautiously propose that same results would be appreciated in amiodarone use for resuscitation in patients with cardiac arrest, and hence suggest that its current application is appropriate.

Although authors recognize it is not a real model of cardiac arrest, they justify its use based on variability and mortality rate of cardiac arrest models. However, we have found in literature very refined and reliable cardiac arrest models that achieve high reproducibility and, therefore, are established and widely used for resuscitation and neurological injury research after cardiac arrest.[2] Cardiac arrest models are characterized by reproducing the cessation of circulation and breathing, generating a true global ischemia that affects all organs, including the brain, followed by restoration of blood flow. Thereby, global cerebral ischemia during cardiopulmonary resuscitation affects anterior and posterior circulation. Nevertheless, arterial occlusion models, such as the one described in the article, do not normally guarantee some trickle flow from the posterior circulation of the Willis circle to the forebrain of the rat.[3] Additionally, Yamanaka et al.[1] do not describe pulseless activity.

Although the model originally described by Sanderson et al.[4] couples bilateral carotid vessel occlusion with reduced systemic mean arterial blood pressure (30 mmHg) for generating brain ischemia, this scenario is not appropriate to reproduce many brain ischemia clinical situations, especially in a drug test context. In particular, after liver ischemia, which is not mimicked in the model but highly probable in cardiac arrest, the clearance of amiodarone could be decreased, fact that could increase cerebral toxicity risk, as Yamanaka et al.[1] already recognize.

Despite high mortality rates are inherent in cardiac arrest models ought to their own pathophysiology, much work is being done to improve these rates. In fact, in a recent paper of cardiac arrest model, authors report a 7-day survival rate of up to 85%.[5]

The study of the neurocritical pathology results extremely complex due it's own nature. The use of animal models to analyze this kind of injury results very useful, but in many cases these models are far from patient's reality. Neurocritical pathologies are very heterogeneous, since patients have associated comorbidities and the mechanisms of injury are diverse. Therefore, multiple animal models have been developed for the study of the neurocritical pathology. Each model has its advantages and disadvantages, but none is ideal.

For all these data, we consider Yamanaka et al.[1] paper very interesting in the context of amiodarone neurotoxicity analysis in cerebral ischemia animal model, but we do not consider it appropriate to draw conclusions about its application in cardiac arrest.

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A. Rodriguez-Rodriguez[a], L. Boyero[a,*], L. Sempere[a], A. Vilches-Arenas[b]

[a] *Laboratorio de Neurocríticos, U.G.C. Cuidados Críticos, H.U. Virgen del Rocío-IbiS, Spain*
[b] *Unidad Medicina Preventiva y Salud Pública. H.U.V. Macarena-Universidad de Sevilla, Spain*

[*] Corresponding author.
E-mail address: lboyero@hotmail.com (L. Boyero).

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