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Letters to the Editor

Letter to the Editor

About the neuroprotective effects of FK-506, L-carnitine and azathioprine on spinal cord ischemia-reperfusion injury

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Keywords: Spinal cord ischemia; FK-506; L-Carnitine; Azathioprine

I read with interest the article of Akgun et al. [1] about the neuroprotective effects of FK-506, L-carnitine and azathioprine on spinal cord ischemia-reperfusion injury.

Although this paper has reproduced in part the work done by myself and other authors and published 2 years ago [2], I have major concerns about the validity of that study. Thus, the rats have not been ventilated throughout the surgical procedure and there is no mention of oxygen saturation recorded in any part of the text, therefore I wonder whether the spinal cord injury might have been related to hypoxia rather than ischemia. Moreover, all rats have been anesthetized with ketamine, a well-known neuroprotective agent that can mitigate the effects of other neuroprotective drugs [3]. Therefore, the conclusion that FK-506, L-carnitine and azathioprine improve neurological outcome after transient spinal cord ischemia is not supported by that experiment.

As the authors state that two catheters were placed into the aorta and femoral arteries to monitor proximal and distal aortic blood pressures, it is difficult for me to understand how they could manage to place vascular clamps on the abdominal aorta and aortic bifurcation with the catheters in. Was the supra-renal aorta catheterized through midline laparotomy?

Regarding the histopathological analysis, it is not clear whether most of spinal cord injury in control animals was due to necrotic or apoptotic cell death. In this type of animal model, most neurons in central gray matter die through a necrotic process rather than by apoptosis. That study differs from most other published in the literature since more than 75% of neurons died apparently from apoptosis. As most of spinal cord damage was due to apoptosis in this study, it would have been interesting to evaluate neurological status after 4 or 5 days, because FK-506, L-carnitine and azathioprine might just have delayed spinal cord injury, as it has been reported with ketamine pre-treatment [3].

Finally, I would like to remember the authors of this article that plagiarism is not permitted by the European Association of Cardio-thoracic Surgery and I was surprised to find a paragraph in their discussion copied word for word from one article published by myself and collaborators in Anesthesia and Analgesia in 2001 [2].

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Reply to the Letter to the Editor

Reply to Lang-Lazdunski

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We thank Dr Lang-Lazdunski for his comments and concerns regarding our article [1]. We are familiar with the valuable research articles of Dr Lang-Lazdunski about spinal cord protection. As a matter of fact we cited his article in our manuscript [2]. However, we tried to compare the effects of two new agents which had not been studied

previously with FK-5O6. Also there were no published articles comparing L-carnitine and azathioprine in spinal cord protection models. We think that this reflects the originality of our paper.

In our study, we did not entubate or ventilate any of the rats. We can conclude that the spinal cord injury was related to ischemia because if it were not so, the specimens of the sham group would not be fully normal and there would be necrotic changes in the histopathological examination of this group.

We agree that ketamine is a neuroprotective anesthetic agent. We think that ketamine anesthesia did not create a bias in our study since we anesthesized all the rats with ketamine. As you know, ketamine is one of the agents used for anesthesia in this type of animal models and its neuroprotective effects are not concerned so much [3,4].

The monitorization of the blood pressure of the proximal aorta was performed through a catheter placed in suprarenal aorta after midline laparotomy. Aortic cross clamp was placed just below the level of the catheterization site. Distal aortic pressure was measured through the femoral artery cannulation and there was no difficulty in the management of these procedures.

There are so many studies about the spinal cord ischemia reperfusion injury. Neuronal death in gray matter might be due to both necrosis and apoptosis. The results of our study suggest that 75% of neurons died due to apoptosis. This result may be due to the method that we used for detection of apoptosis in our study. The anti-PARP p85 fragment pAb was used for detection of apoptosis. PARP (human poly(ADP-ribose) polymerase) is a nuclear DNA-binding protein that detects DNA strand breaks. It is particularly important in DNA repair. Activation of the PARP is one of the earliest stages in apoptosis. Anti-PARP p85 fragment pAB specifically recognizes an 85 kDa band of PARP from the cells that are induced to undergo apoptosis. Thus, this antibody provides an early detection of apoptosis because cleavage of PARP occurs before DNA fragmentation that is detected by the use of TUNEL assays [5,6]. But further studies are required to confirm this result.

We did use the paragraph mentioned by Dr Lang-Lazdunski but as the information it contained was general knowledge about the pharmacological effects of FK-506, we did not think it was necessary to recitate Dr Lang-Lazdunski. Of course we should have and we are sorry for this oversight.

As a summary the conclusion of our study is not only the neuroprotective effects of FK-506 but also the neuroprotection by L-carnitine and azathioprine on spinal cord ischemia reperfusion injury with comparison.

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Letter to the Editor

Surgical assistants and working time directives

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Keywords: Surgical nurse assistant; Working time directive; Training

We commend Alex and co-workers for raising the important, and sometimes overlooked, issue of the impact of working time directives on training cardio-thoracic surgeons [1].

The authors have carried out a retrospective review of two non-randomised groups of patients. Their aim was to ascertain whether the harvest of saphenous vein graft by a qualified and fully trained surgical assistant had a negative impact on outcomes when compared with a junior surgical trainee performing similar tasks. They conclude that although surgical nurse assistants can be used effectively in low-risk cases without compromising postoperative results, they can compromise the training needs of junior surgical trainees.

We agree with the first statement, but disagree with the second. In their conclusion they also implicitly affirm