continued from use in cardiac surgery and replaced with either tranexamic acid or epsilon-aminocaproic acid as a cost-effective alternative.

References


The authors of the original paper [1] were invited to comment on this Letter to the Editor but declined the offer.

* Corresponding author. Tel.: +81 22 293 1111; fax: +81 22 291 8114. E-mail address: sakuraim@snh.go.jp.

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Letter to the Editor

Which cell does apoptosis induce?

Masahiro Sakurai*

Department of Cardiovascular Surgery, National Hospital Organization Sendai Medical Center, 2-8-8, Miyagino, Miyagino-ku, Sendai 983-8520, Japan

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Keywords: Cell damage; Temporal profile

We read with interest the article by Pastuszko and associates titled ‘The effect of hypothermia on neuronal viability following cardiopulmonary bypass and circulatory arrest in newborn piglets’ [1]. We agree that the protection by hypothermia was observed in the striatum by decreasing the expression of Bax and caspase3. However, it is unclear whether each of these proteins was induced in the neurons. In the experimental model of brain protection, the main concern has been the selective vulnerability of neurons. Therefore, a histological study is important and some researchers have counted the number of neurons following ischaemia [2,3]. In addition, the authors have described only the results of the Western blot analysis. However, there are several components in the central nervous system, such as the neurone, glia and vessels. Yanagisawa et al. demonstrated the protective effects of DJ1 following brain ischaemia with temporal profiles of nitrtyrosine [2]. Furthermore, our previous report has demonstrated that local cooling enhanced and prolonged the HSP72 protein levels in motor neurons, and saved the neuronal cells from lethal ischaemia [3]. Both quantitative and qualitative analyses are essential for evaluating brain damage. Therefore, the authors should demonstrate the temporal profiles of Bax, caspase3 and Bcl2 in histochemical study or in an in situ hybridisation study.

References


* Corresponding author. Tel.: +81 22 293 1111; fax: +81 22 291 8114. E-mail address: sakuraim@snh.go.jp.

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Reply to the Letter to the Editor

Reply to Sakurai.

Brain injury in cardiopulmonary bypass surgery

Peter Pastuszko a,*, William J. Greeley b, David F. Wilson c, Anna Pastuszko c

a Department of Surgery, University of California at San Diego, San Diego, CA, USA
b The Children’s Hospital of Philadelphia, Department of Anesthesiology and Critical Care Medicine, Philadelphia, PA, USA
c Department of Biochemistry and Biophysics, Medical School, University of Pennsylvania, Philadelphia, PA, USA

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Keywords: Alpha-stat; Apoptosis; Cardiopulmonary bypass; Circulatory arrest; Oxygen; pH-stat

The authors thank Dr Sakurai for his comments [1] concerning their study.

It has long been recognised that survivors of heart surgery involving deep hypothermic cardiac arrest (DHCA) face a variety of central nervous system deficits and the identification of neuroprotective strategies that would guard the brain from the negative sequelae of DHCA is therefore of great importance. To test for the protection of the brain we have made a rather deliberate decision to measure the critical regulators of programmed cell death by using the Western blot analysis. The accumulating evidence indicates that the increased expression of Bcl-2 provides protection against
apoptosis and ischaemic neuronal death, whereas an increase in the pro-apoptotic protein Bax has been shown to promote cell death by caspase activation. Our observation that mild hypothermia increases the Bcl-2/Bax ratio following DHCA is consistent with cerebral protection via decreased apoptotic cell death.

Dr Sakurai is thinking ahead—given that there is protection, what cell types would be affected? In the experiments reported, we did not attempt to determine whether neurons were the primary site of brain injury but focussed on whether hypothermia can decrease the injury [2]. The extensive literature on this subject shows that cardiopulmonary bypass and deep hypothermic circulatory arrest induce neuronal injury. In our publication, we discussed neuronal injury; however, our data did not distinguish among the different cell types.

In an identical experimental protocol, we used the terminal dUTP nick-end labelling to detect apoptotic cells (TUNEL) stain on the perfused piglet brain following 6 h of post-bypass recovery (unpublished data). We observed that there were increased numbers of TUNEL-positive cells following DHCA but, because of the short recovery period, the numbers were too low to allow testing for an effect of hypothermia. While TUNEL cannot distinguish apoptosis from necrosis, it is a valuable marker of neuronal cell damage. Experiments using 12-h recovery periods, where the number of TUNEL-staining cells is substantially higher, are in progress. TUNEL measurements are being combined in our long-term experiments (12-h recovery) with haematoxylin and eosin (H&E) staining to analyse the morphological characteristics of cell death and with immunohistochemical staining for caspase-3. The preliminary results indicate that there is an increase of caspase-3 immunostaining in different regions of the brain, and this effect is diminished by mild hypothermia, particularly in the striatum.

We are aware that it is possible to observe the distribution of Bax, Bcl-2 or other proteins involved in cell injury or protection in tissue slices as well as through other measurements suggested by Dr Sakurai. We have used in situ hybridisation and autoradiograms to show that hypoxia induces expression of the 72-kDa heat-shock protein (hsp72) mRNA in different regions of the newborn piglets' brain and that this was significantly diminished, particularly in striatum, by the depletion of dopamine prior to hypoxia [3]. In another model of hypoxia—repetitive apnoea—we have shown that striatum of apnoeic piglets has a larger number of fluoro-Jade-positive neurons than that of sham-operated animals [4]. Such studies can identify the type of cells affected and the regional specificity of the injury, but at the expense of quantification.

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References


Letter to the Editor

Fatal rupture of splenic artery mycotic aneurysm after mitral valve replacement for infective endocarditis

Nicholas A. Charokopos*, Christophoros N. Foroulis, Efthymia G. Rouska, Christos Papakonstantinou
Aristotle University Medical School, AHEPA University Hospital, Department of Thoracic and Cardiovascular Surgery, Thessaloniki, Greece

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Keywords: Infective endocarditis; Intra-abdominal bleeding; Mycotic aneurysm; Septic emboli; Splenic artery aneurysm

We appreciate and read with great interest the article by Winears et al. reporting a rare case where the diagnosis of Enterococcus faecalis endocarditis was established after intra-abdominal bleeding due to rupture of the spleen [1]. We recently experienced a case of a sudden, fatal, massive intra-abdominal bleeding from splenic artery rupture due to a mycotic aneurysm. A 52-year-old man presented with high-grade fever and malaise. Clinical examination revealed a generalised abdominal tenderness and a long systolic cardiac murmur. A trans-thoracic echocardiogram confirmed severe mitral valve regurgitation with vegetation on the posterior mitral valve leaflet (1.3 cm x 1.1 cm). Blood cultures on admission were positive for Staphylococcus aureus, and therefore intravenous antibiotic treatment was commenced. An abdominal computed tomography (CT) scan revealed multiple, small, acute infarcts in the liver and spleen, consistent with septic emboli, as well as an intramural haematoma in the stomach. At the same time, the patient became unstable and inotropic support was needed. Thus the decision for an emergency operation was made, and an urgent mitral valve replacement was performed using a 31-mm Carbomedics (SORIN BIOMEDICA CARDIO S.r.l., Saluggia, Italy) mechanical valve. Following surgery, the patient recovered and was discharged from the intensive care unit on the