Letters to the Editor

Mortality manifesto: a meta-analysis of aprotinin and tranexamic acid mortality

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Later and colleagues presented the results from a non-sponsored, double-blind, randomised trial comparing the clinical outcomes for tranexamic acid and aprotinin [1]. They report that aprotinin significantly reduced bleeding in comparison with tranexamic acid, but there was no difference in the number of packed red blood cells. With regard to outcomes, they report no significant differences, but negate the twofold difference in mortality. This issue of comparative mortality with anti-fibrinolytic agents has been unresolved as yet. For this reason, we updated our head-to-head meta-analysis to determine the safety of aprotinin over tranexamic acid with regard to mortality.

We conducted a review of the published randomised control trial since our last meta-analysis comparing mortality rates in head-to-head trials between aprotinin and tranexamic acid [2]. We found three additional adult cardiac surgery trials: Fergusson (BART), Dietrich and Later (2008–2009). BART was the first large-scale head-to-head trial comparing aprotinin with lysine analogues, tranexamic acid and epsilon–aminocaproic acid (N = 2331), reporting a significant increased risk of 30-day mortality among patients randomised to aprotinin compared with either lysine analogue (RR: 1.53; 95% confidence interval (CI): 1.06–2.22) [3]. Dietrich reported on a smaller trial (N = 220) of patients randomised to aprotinin (two deaths) or tranexamic acid (one death) with no significant difference [4]. Later reported no significant difference in mortality, but observed a twofold difference. We calculated a pooled estimate on mortality for aprotinin compared with tranexamic acid (Fig. 1). Aprotinin had a significant 50% increased risk of death compared with tranexamic acid (RR: 1.50; 95% CI: 1.04–2.17).

As a result of Later’s results and other recent randomised trials, we must conclude that the mortality risks do in fact outweigh the benefits of aprotinin and should be discon-
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.

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Letter to the Editor

Which cell does apoptosis induce?

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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 protein 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


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Reply to the Letter to the Editor

Reply to Sakurai.

Brain injury in cardiopulmonary bypass surgery

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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