Letter to the Editor

Nicorandil cardioplegia or procaine cardioplegia?

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I read with interest the article by Steensrud and colleagues on myocardial protection with nicorandil cardioplegia [1]. The study investigates the protective efficacy of intermittent cold blood nicorandil cardioplegia compared with intermittent standard hyperkalemic cold blood and cold crystalloidal cardioplegia in pigs undergoing cardiopulmonary bypass and hearts subjected to 60 min global ischemia and 120 min reperfusion. Measurement of function and MVO₂ demonstrated improved protection with nicorandil cardioplegia compared to either of the hyperkalemic solutions, and it is concluded that nicorandil, as sole cardioprotective agent, provides superior preservation of LV contractility and myocardial energetics.

I disagree with the emphasis that the authors place on the importance of nicorandil in this study. The statement that nicorandil is the sole cardioplegic agent is incorrect; indeed, I suspect, in the context of their ‘nicorandil’ cardioplegia formulation, that nicorandil would only have a minor cardioprotective effect, if any, in this study. Steensrud et al. fail to acknowledge the effect of procaine, included in their solution (albeit only during the bolus initial infusion) at a concentration of 2.5 mmol/L, compared with the nicorandil concentration of 0.1 mmol/L. Procaine, a Na-channel blocker, has been used as the arresting agent in many cardioplegic solutions; a concentration of 3.7 mmol/L, shown to be optimal for recovery, is close to the procaine concentration used in this study. We have previously demonstrated [2] that Na-channel blockade (using 0.022 mmol/L tetrodotoxin), induces rapid arrest at a membrane potential of around −70 mV (thus inducing a polarized arrest) and this leads to significantly improved protection when compared with hyperkalaemia (depolarized arrest) in rat hearts subjected to 5 h cold (7.5 °C) global ischemia. Polarized arrest should reduce ionic imbalance and maintain myocardial high energy phosphates (as the myocardium requires less energy expenditure to attempt to correct ionic changes); we have shown [2,3] that this does indeed occur in the polarized arrested heart compared to the depolarized heart arrested by hyperkalaemia.

We have also examined the protective effects of pinacidil (a KₐTP-channel opener) as an arresting agent. Interestingly, we showed [4] that, in hearts from various species (rat, rabbit and guinea pig), pinacidil was unable to induce arrest even when infused over prolonged periods (30 min) at concentrations up to 1.0 mmol/L. Complete arrest in guinea pig hearts could only be induced by a combination of pinacidil (at 0.3 mmol/L) and procaine (at 1.0 mmol/L); this combination maintained the membrane potential during arrest at approximately −70 mV and induced protection that was significantly better than hyperkalemic arrest [4]. Studies by Sato and coworkers [5] have shown that nicorandil, at 0.1 mmol/L (the same concentration of nicorandil used by Steensrud et al. [1]) did not influence the sarcolemmal KₐTP-channels, although mitochondrial flavoprotein oxidation (indicative of mitochondrial KₐTP-channel activation) did occur; a 10-fold higher concentration was required before sarcolemmal KₐTP-channels were opened. It is difficult to envisage, therefore, how nicorandil (at the concentration used in the study by Steensrud et al. [1]) can be exerting any effect on the sarcolemmal KₐTP-channels sufficient to induce a ‘hyperpolarization’ that would lead to myocardial arrest.

I believe that these authors are incorrect in suggesting that nicorandil acts as the sole arresting agent in their ‘nicorandil’ cardioplegia and that, by employing the term nicorandil cardioplegia, they are misleading the readership of the journal.

References


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