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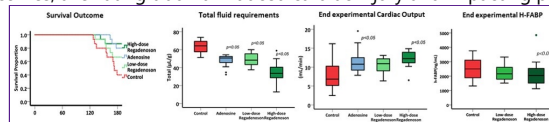
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## Rescuing Cardiac Dysfunction Following Traumatic Haemorrhagic Injury

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### Abstract:

Cardiac dysfunction (CD) is a significant cause of delayed deaths in trauma-haemorrhagic shock patients. It is associated with poor outcomes and no treatments are available. Adenosine, via the mediation of its A<sub>2A</sub> receptor, could potentially alleviate such CD. This study investigates the efficacy of adenosine and regadenoson, an adenosine A<sub>2A</sub> receptor agonist, as a novel cardiovascular protective resuscitation approach in a preclinical trauma-haemorrhage model. A murine pressure-controlled haemorrhagic shock model was dosed with adenosine (54 µg/g) or regadenoson (10 or 30 µg/g) during the initial post-injury echocardiography-guided resuscitation (1h post-injury) (n=15/group). Cardiovascular function (Echocardiography/MAP) and lactate were assessed up to 3 hours post-injury and terminal samples were analysed for myocardial injury markers. A control group was only dosed with crystalloid. Animals receiving adenosine and regadenoson (30 µg/g) demonstrated significant improvement survival outcomes and the maintenance of cardiac output, compared to controls (80% and 87% vs 40%, and 11.64 ± 3.4 mL/min, 12.05 ± 2.2 mL/min vs 7.66 ± 3.8 mL/min, all p<0.05). Additionally, these animals also required lower volumes of resuscitation fluid to restore stroke volume (47.9 ± 7.0 µL/g and 34.9 ± 10.8 µL/g vs 63.8 ± 7.5 µL/g, p<0.05), improving systemic perfusion with lower lactate levels (4.6 ± 0.9 mmol/L and 4.4 ± 1.5 mmol/L vs 6.6 ± 2.6 mmol/L, p<0.05). Animals receiving high-dose regadenoson showed a significant lower cardiac injury biomarker h-FABP level (1548.8 ± 442.6 vs 2465.0 ± 650.2 ng/mL, p<0.05). It also significantly reduced infiltration of neutrophils and apoptotic myocardial injury (0.5 ± 0.1% vs 0.8 ± 0.3 Ly6G, p=0.038 and 0.63 ± 0.24% vs 2.50 ± 1.17% Caspase 3, p = 0.0224). In conclusion, the administration of regadenoson during resuscitation improves physiological outcomes, alleviating trauma-induced cardiac injury and impacting positively on survival.



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**Disclosure:** There are no unlabeled/unapproved uses of drugs or products.

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