

POSTER PRESENTATION

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# Protective effects of low dose stabilized haemoglobin solution in experimental global ischaemia-reperfusion injury

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## Introduction

We previously reported that low doses of the purified stabilized bovine haemoglobin (EXP1) improved survival in a severe haemorrhage reperfusion model with beneficial effects on oxidative stress (unpublished data). We here report additional findings on a similar formulation, EXP2, at different doses using the same model of shock resuscitation.

## Methods

Male Wistar rats (weight  $306 \pm 15$ g) underwent arterial and central venous cannulation, tracheostomy, bladder catheterization and placement of a liver tissue  $pO_2$  sensor (Oxford Optronix, Oxford, UK). Controlled haemorrhage (45% of estimated blood volume) was induced over 15 minutes and sustained shock (MAP target 40-45 mmHg) was maintained for an additional 75 minutes. After crystalloid resuscitation, animals were randomized to receive a bolus injection of either Ringer's lactate (control) or EXP2 at 200, 400 or 900 mg/kg (New A Innovation Limited, Hong Kong). 700 mg/kg is approximately equivalent to a one-unit blood transfusion. Continuous i.v. fluid administration (10 mg/kg/hr) was then infused for the following 4 hours. Echocardiography, blood gas analysis, blood pressure and liver tissue  $pO_2$  were measured pre- and post- insult, and then at hourly intervals. Two-way ANOVA with post-hoc t testing was used to detect statistically significant differences.

## Results

Four-hour survival was 50%, 87.5%, 66.7% and 62.5% for the control, 200, 400 and 900 mg/kg groups, respectively.

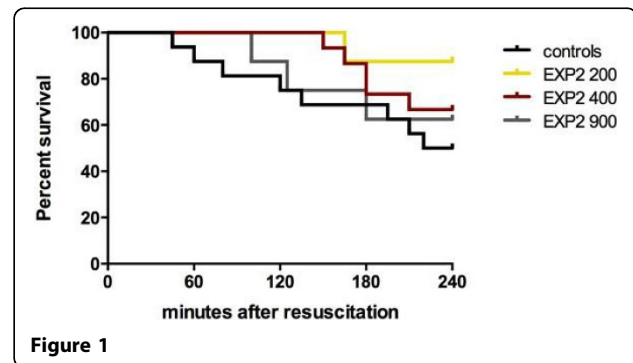


Figure 1

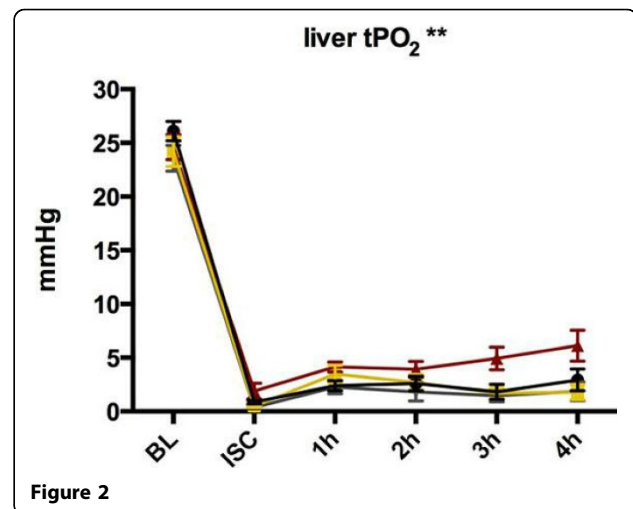
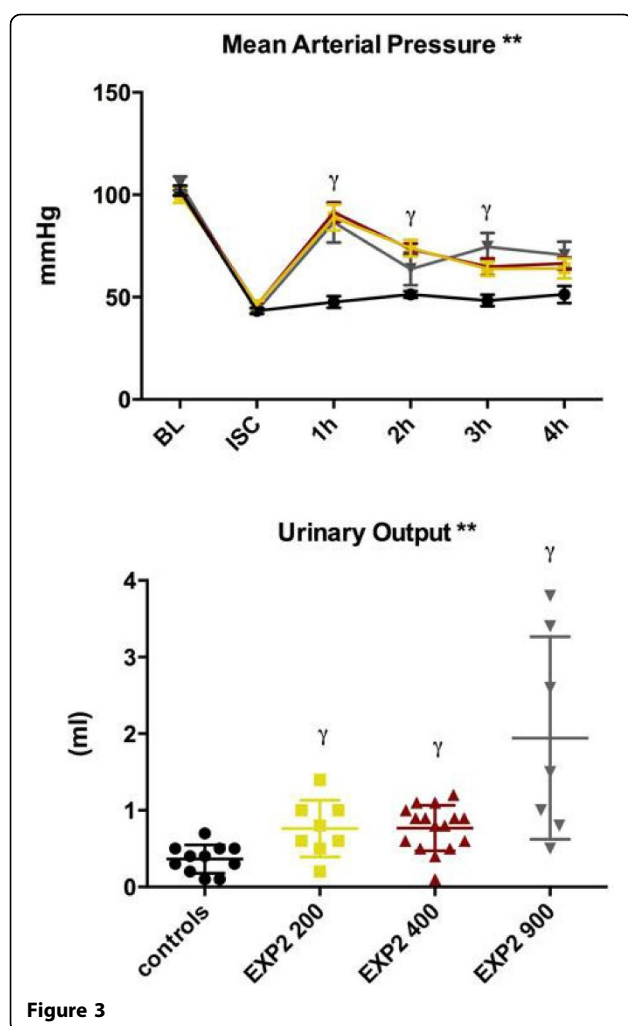


Figure 2

Small but significant changes were seen in plasma Hb levels, no changes were seen in lactate or oxygen delivery, while liver tissue  $pO_2$  increased only in the 400 mg/kg group. Notably, urine output improved at all EXP2 doses,

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particularly in the 900 mg/kg group, though the pressor effect was identical for all doses of EXP2.

### Conclusions

Low dose stabilized haemoglobin solution has potential utility in the treatment of global ischaemia-reperfusion injury though further work is needed to clarify optimal dose and mechanism(s) of action.

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