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Beta-blockade in experimental fluid-resuscitated sepsis: acute haemodynamic effects of esmolol differ in predicted survivors and non-survivors

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Introduction

Beta-blockade therapy during sepsis has a sound rationale in view of its cardiac, metabolic, inflammatory and other effects [1]. Whether it is safe and efficacious in both good prognosis and poor prognosis patients is yet to be ascertained. We have developed a 72-h fluid-resuscitated rat model of faecal peritonitis, where prognosis can be accurately predicted as early as 6 h post-insult based on the degree of myocardial depression (low stroke volume, high heart rate)[2]. This model offers a useful means of testing safety and efficacy.

Objectives

To compare dose-related haemodynamic effects of esmolol at 6 hours in predicted survivors and non-survivors from faecal peritonitis.

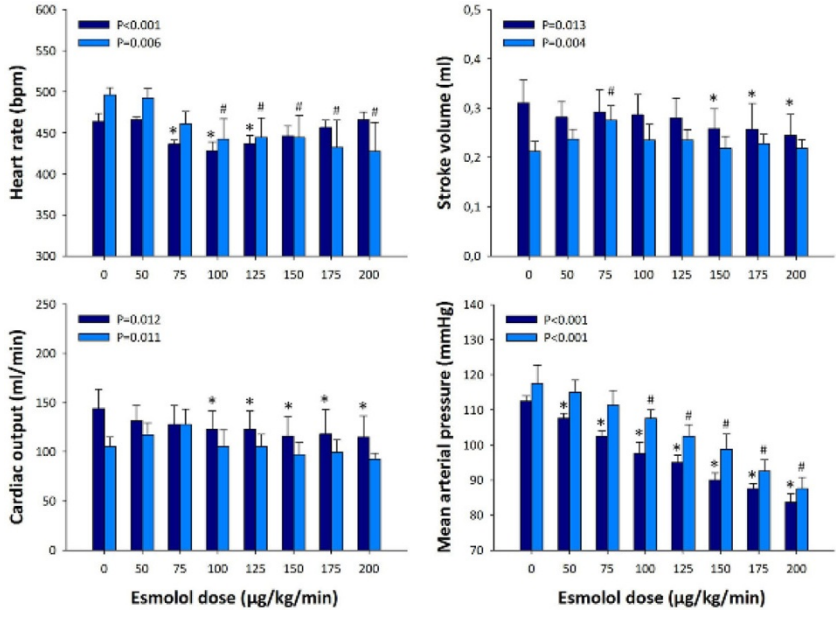

Figure 1 *p < 0.05 *vs.* baseline (good prognosis group, dark blue bars, N = 4). #p < 0.05 *vs.* baseline (poor prognosis group, light blue bars, N = 4).

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Methods

Instrumented male Wistar rats (350 ± 16 g) had sepsis induced with intraperitoneal injection of faecal slurry. Fluid resuscitation (10 ml/kg/h) was begun 2 h later. At 6 h, animals were divided into predicted survivors or non-survivors depending on a stroke volume cut-off of 0.20 ml. After an additional 10-ml/kg fluid bolus, esmolol was administered as a 500- μg/kg loading dose followed by an increasing stepwise infusion (50 to 200 μg/kg/min in 25- μg/kg/min increments 5 minutes apart). Heart rate, stroke volume and mean arterial pressure were recorded just prior to each dose increase. Repeated measures ANOVA and post-hoc Holm-Sidak test were used to seek statistically significant differences.

Results

Baseline stroke volume at 6h was significantly lower in poor prognosis animals (0.27 ± 0.07 vs. 0.18 ± 0.02 ml, $p < 0.05$). Stroke volume increased with low dose esmolol in predicted non-survivors, and this offset the reduction in heart rate (Figure 1). Cardiac output was thus maintained in predicted non-survivors but fell significantly in predicted survivors. Mean BP fell in parallel in both groups, though significant changes were seen earlier in predicted survivors.

Conclusions

Depending on their prognosis, septic rats show different haemodynamic responses to a short-term esmolol infusion at 6 h post-septic insult. Whether longer-term infusion is beneficial or harmful to these subgroups will be the subject of future study.

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