Inflammatory cytokine profiles in a 24-hour brain stem death model

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Introduction

Organ transplantation still remains the mainstay treatment for end-stage organ failures. However, the availability of suitable organs for transplantation is insufficient for this demand. The majority of organs are donated by brain stem death (BSD) patients who have suffered an irreversible brain injury. Such patients experience organ damage, potentially through inflammatory responses, which significantly affect both the quantity and quality of organs availability for transplantation [1].

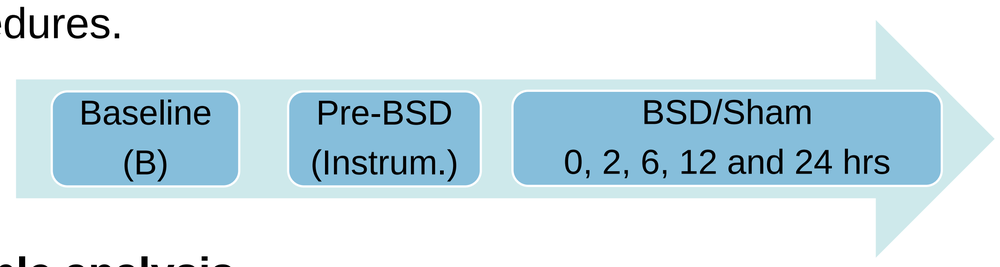
Aim

To determine profiles of inflammatory cytokine production and inflammatory cell infiltration in blood circulation and bronchoalveolar lavage (BAL) in a clinically relevant 24-hour ovine model of BSD.

Methods

Animals

- Six healthy female sheep (45–55 kg) underwent BSD induction by inflation of an extradural catheter [2], or Sham procedures.
- Sheep were monitored in an intensive care unit environment for 24 hours.
- Blood and BAL samples were collected during the procedures.



Sample analysis

- Neutrophil cells were counted in blood smear and BAL fluid using cytospin.
- Plasma and BAL cytokines (interleukin-6, 8, 10, 1β and TNFα) were assessed by ELISA.
- Data were expressed as mean ± SEM and noted as **P*<0.0 when compared to Sham unless otherwise stated.

Conclusions

This is the first report to demonstrate the inflammatory cytokine profiles in a 24 hour ovine model of BSD. BSD contributes to increased circulating neutrophils in the blood and neutrophil infiltration in the lung, which may contribute to systemic inflammation and lung dysfunction. Further development of this model will allow further investigation of novel therapies seeking to reduce the inflammatory response and organ injury induced by BSD.

References

1. Pratschke, J., et al., Brain death and its influence on donor organ quality and outcome after transplantation. Transplantation, 1999. 67(3): p. 343-8.
2. Watts, R.P., et al., Novel 24-h ovine model of brain death to study the profile of the endothelin axis during cardiopulmonary injury. Intensive Care Med Exp, 2015. 3(1): p. 31.

Results

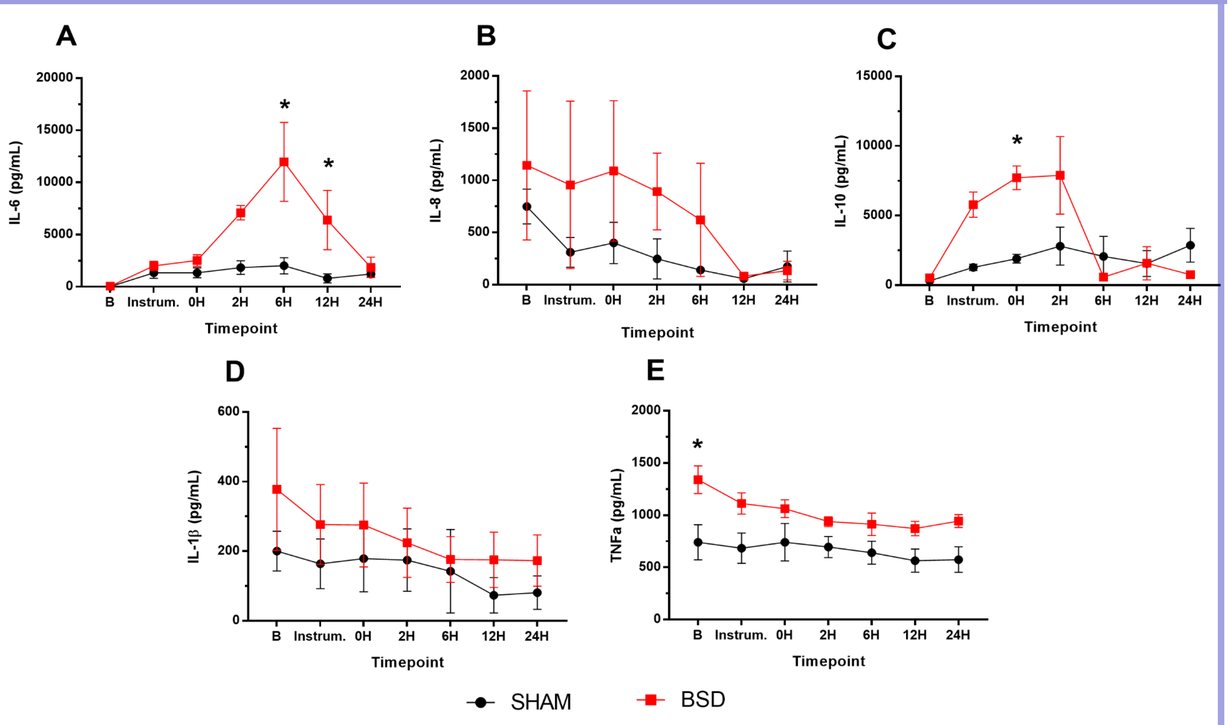


Figure 1. Whole blood plasma IL-6 (A), IL-8 (B), IL-10 (C), IL-1β (D) and TNFα (E) concentrations in Sham vs. BSD sheep (n = 3/group) at time baseline (B), pre-BSD (Instrum.), 0, 2, 6, 12 and 24 hours. **P*<0.05, versus Sham.

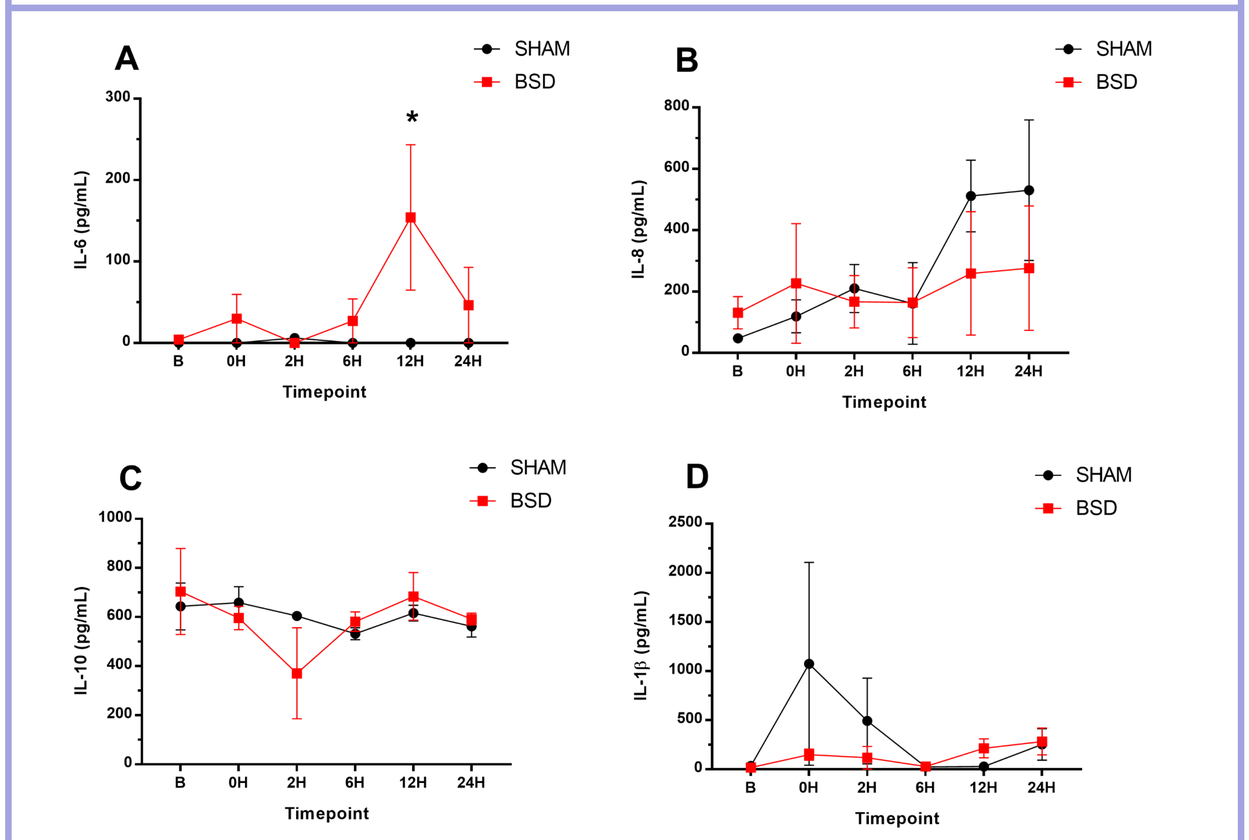


Figure 2. Bronchoalveolar lavage (BAL) IL-6 (A), IL-8 (B), IL-10 (C), and IL-1β (D) concentrations in Sham vs. BSD sheep (n = 3/group) at time baseline (B), 0, 2, 6, 12 and 24 hours. **P*<0.05, versus Sham.

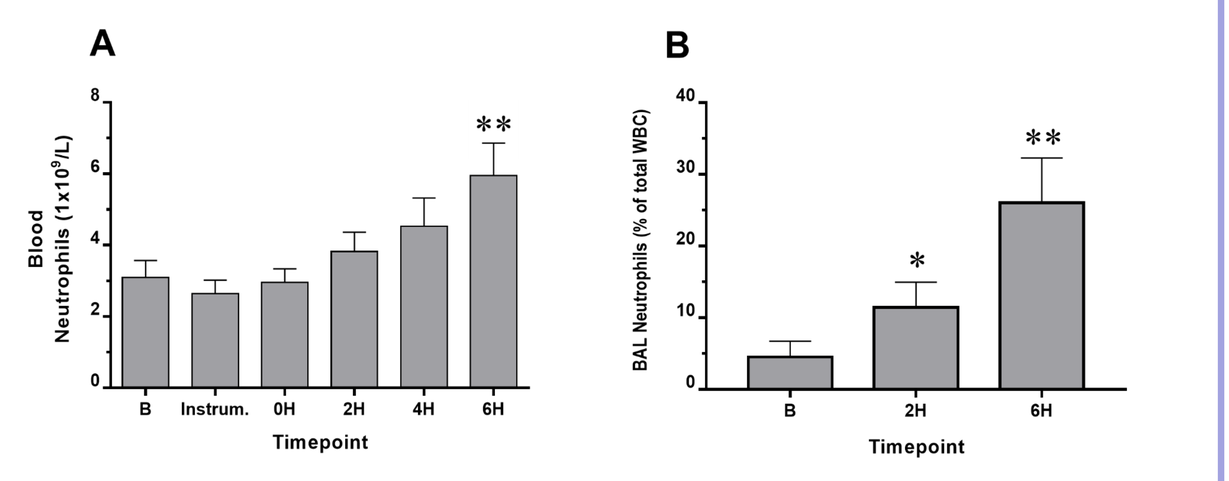


Figure 3. Whole blood (A) and bronchoalveolar lavage (B) neutrophil counts in BSD sheep (n = 3) at time baseline (B), 0, 2, 4, and 6 hours. **P*<0.05, versus Baseline.

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