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Evaluating the Effect of Antihistamine on Trauma-induced Endotheliopathy (EoT) in a Rat Model of Polytrauma-Hemorrhage

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Introduction

Trauma-induced endotheliopathy (EoT) is strongly correlated with post-trauma mortality and morbidity. Post-injury activation of mast cells and subsequent histamine release contributes to the disruption of the endothelial cell barrier and an increase in vascular permeability. This study evaluated the therapeutic effect of acute antihistamine administration on EoT in a rat model of polytrauma and hemorrhage (PTH).

Objective/Hypothesis

The objective of this study is to evaluate the outcome of acute administration of antihistamine in the rat model of polytrauma with hemorrhagic shock.

We hypothesize that acute administration of antihistamine mitigate the endotheliopathy of trauma (EoT).

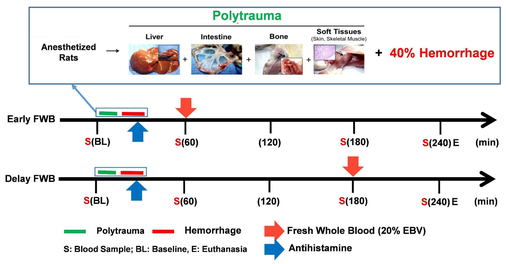
Methods

Isoflurane-anesthetized Sprague-Dawley rats were subjected to polytrauma, including multi-organ crush injuries and femur fracture, followed by a 40% hemorrhage.

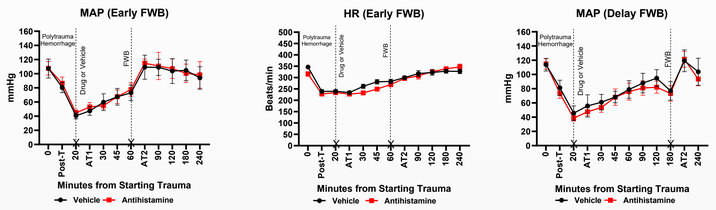
Twenty minutes after PTH, rats received either the vehicle (Veh) or 1 mg/kg diphenhydramine-HCL (DPH) intravenously. This was followed by fresh whole blood resuscitation (FWB) at 1 or 3 hr postinjury (early FWB or delay FWB, respectively).

Key EoT biomarkers, Syndecan-1 (SDC1) and thrombomodulin (TM), were measured by ELISA at baseline and 1, 3, or 4 hr after trauma. Primary outcomes also included lactate levels, hemodynamics, and lung wet/dry weight ratio (LWDR) to assess tissue edema.

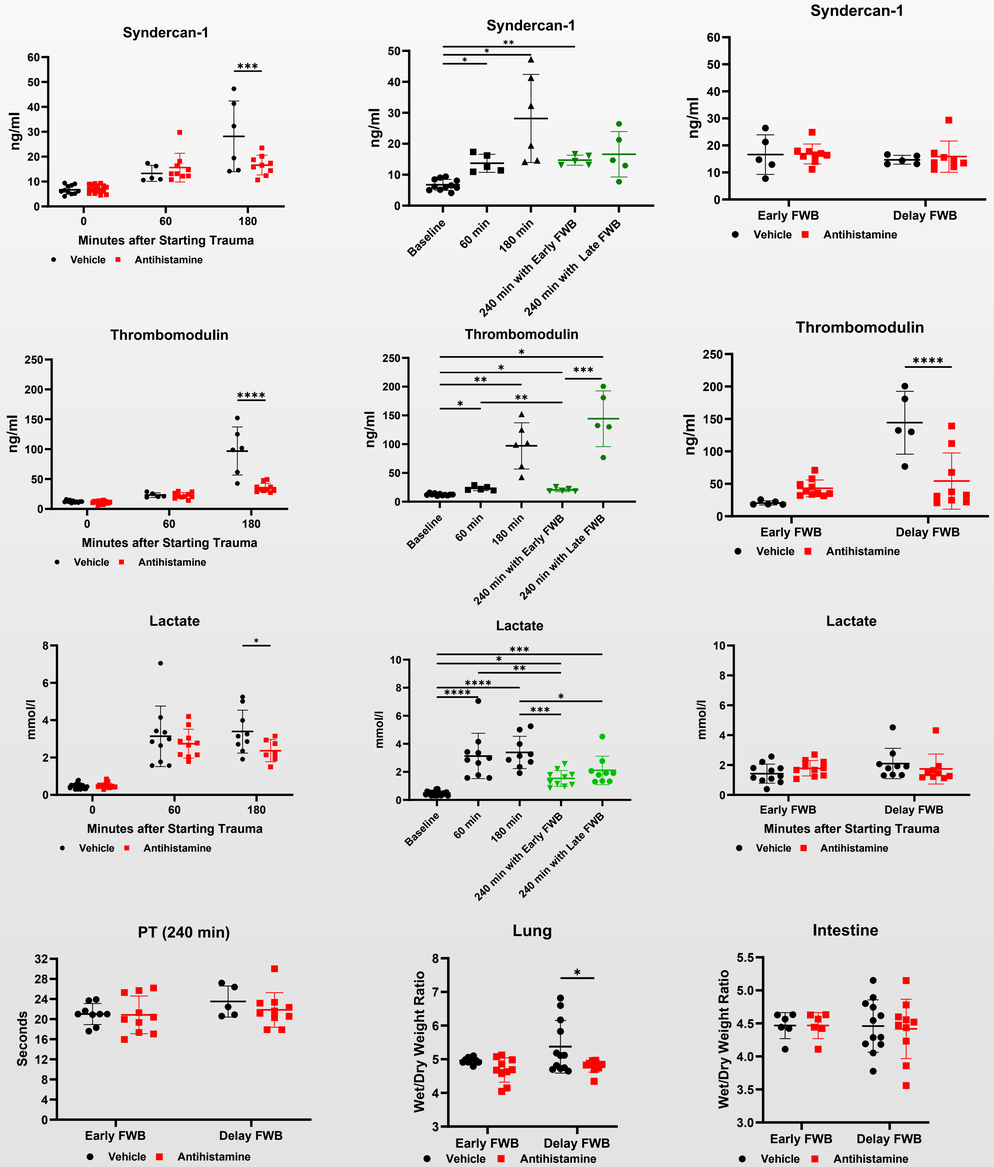
Study Scheme



Results



Post-T: post-trauma; AT1: after drug treatment; AT2: after FWB transfusion.



Summary

Prior to resuscitation, antihistamine treatment with DPH significantly attenuated the rise in the endotheliopathy (EoT) biomarkers SDC1 and TM at 3 hours post-injury compared to the Veh group.

Although limited-volume FWB resuscitation at either 1 or 3 hours post-injury stabilized SDC1 levels, TM levels continued to rise in the delayed FWB group.

Furthermore, antihistamine treatment with DPH significantly lowered TM levels at 4 hours in the delayed FWB group.

Additionally, DPH treatment significantly reduced lactate levels at 3 hours compared to the vehicle group, and significantly reduced LWDR following FWB resuscitation at both 1 and 3 hours post-injury.

Conclusion

Acute administration of an antihistamine mitigates EoT in this model as indicated by a reduction in the shedding of key glycocalyx components and improved vascular integrity, leading to decreased tissue edema.

These findings suggest that antihistamines may be a valuable adjunct therapy to improve outcomes following severe trauma and hemorrhage.

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Disclaimer: Research was conducted in compliance with Animal Welfare Act, the implementing Animal Welfare regulations, and the principles of the Guide for the Care and Use of Laboratory Animals. The Institutional Animal Care and Use Committee approved all research conducted in this study. The facility where this research was conducted is fully accredited by the AAALAC International.

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