

# EFFECTS OF HYDROXYETHYL STARCH 130/0.4 PRETREATMENT ON ENDOTOXIN-INDUCED ACUTE LUNG INJURY IN RATS

Cai Fang, M.D., Wei Zhang, M.D., Jun Ma, M.D.

Department of Anesthesiology, Affiliated Anhui Provincial Hospital of Anhui Medical University, Hefei, China

**Introduction:** Acute lung injury(ALI) has a high death rate reaching up to 30~40%,because of acute respiratory failure. Experimental evidence has documented the protective effect of hydroxyethyl starch(HES) 200/0.5 on ALI.HES130/0.4 is a novel preparation of colloid with the narrow molecular weight distribution.This study was designed to investigate the effect of HES130/0.4 on lipopolysaccharide(LPS)-induced ALI.

**Materials and methods:** Adult male Sprague-Dawley(SD) rats were randomly divided into six groups(12 rats/group): (a) Sham(saline 30ml/kg); (b) LPS alone(5mg/kg);(c,d and e) LPS(5mg/kg) plus HES (7.5ml/kg, 15ml/kg, 30ml/kg); and (f) HES alone (30ml/kg). HES130/0.4 was infused 1h before administration of LPS. Arterial blood gas,inflammation-related factors,pulmonary capillary permeability,pulmonary neutrophils infiltration and pathological examination were measured 4h after infusing LPS.

**Results:** We demonstrated that administration LPS could provoke severe injury in lung, characterized by  $\text{PaO}_2/\text{FiO}_2$  300mmHg. Pretreatment with HES at three different doses of 7.5ml/kg, 15ml/kg, 30ml/kg respectively increased  $\text{PaO}_2$ , while reduced pulmonary neutrophils infiltration, pulmonary capillary permeability and inflammatory factors. The changes of pathology were consistent with the results above, which attenuated lung injury,whereas,administration HES alone had no influence.

**Conclusions:** Pretreatment with 6%HES 130/0.4 at the dose of 15ml/kg most significantly mitigated LPS-induced ALI. The resultant effect might be that HES could downregulate expression of inflammatory factor,block aggregation of PMNs in lung ,reduce generation of oxygen free radicals and lower microvasclar permeability.

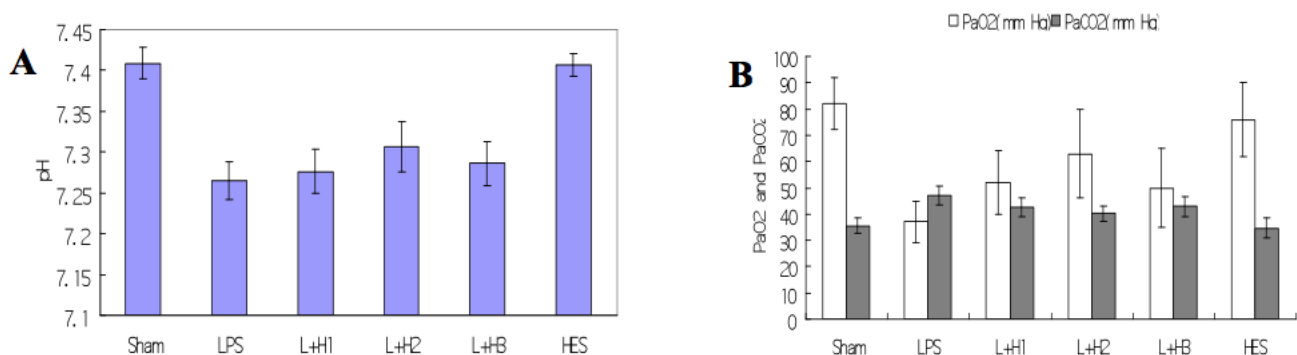
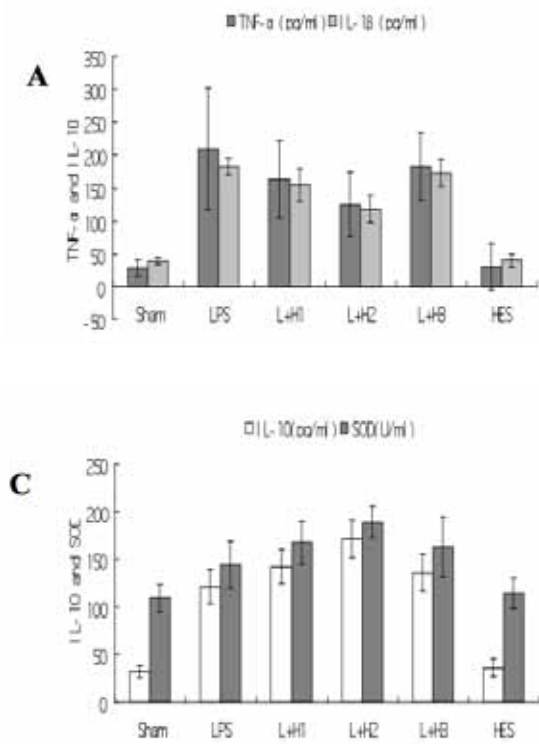
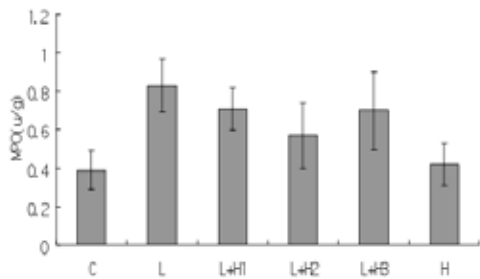


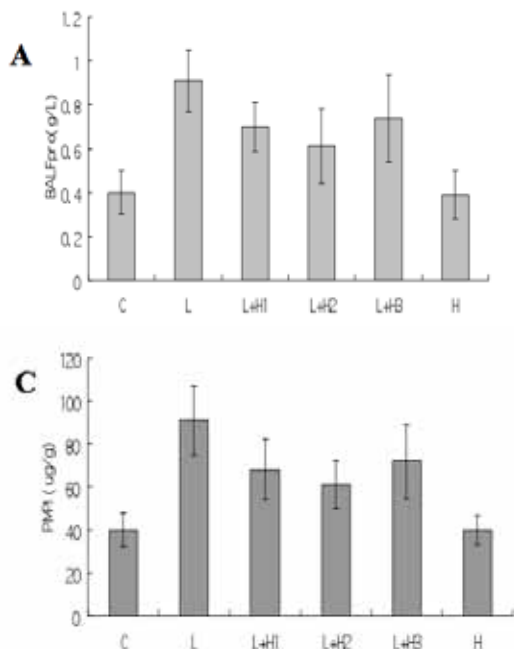
Figure 1. Effect of HES on Arterial blood gas(values of pH(A) and PaO<sub>2</sub>, PaCO<sub>2</sub> (B)in blood).HES at three doses(7.5ml kg<sup>-1</sup>,15ml kg<sup>-1</sup>,30ml kg<sup>-1</sup>)was given i.v. as an infusion 1h before administration of LPS(5mg kg<sup>-1</sup>). pH(A) and PaO<sub>2</sub>, PaCO<sub>2</sub> (B) were assessed 4h after LPS infusion.Data represent mean ± SD.\*P<0.05 versus Sham group, # P<0.05 L+H groups versus LPS group.



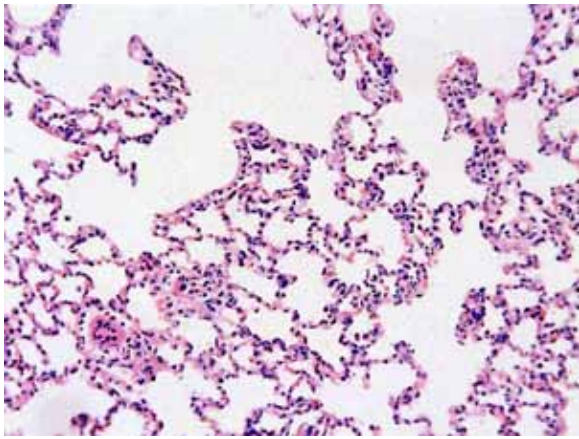
**Figure 2.** Effect of HES on LPS-induced systemic inflammation(values of TNF- $\alpha$ ,IL-1 $\beta$ ,MDA, IL-10 and SOD in serum).HES at three doses(7.5ml kg<sup>-1</sup>,15ml kg<sup>-1</sup>,30ml kg<sup>-1</sup>)was given i.v. as an infusion 1h before administration of LPS(5mg kg<sup>-1</sup>). Serum level of TNF- $\alpha$ ,IL-1 $\beta$ (A),MDA (B) and IL-10,SOD(C) were assessed 4h after LPS infusion.Data represent mean  $\pm$  SD.\*P<0.05 versus Sham group, # P<0.05 L+H groups versus LPS group.



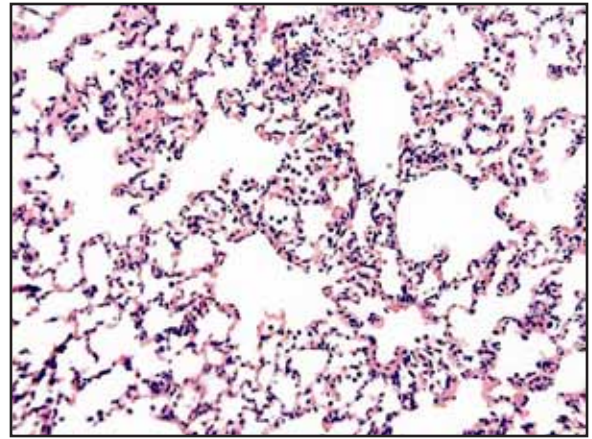
**Figure 3.** Effect of HES on LPS-induced neutrophils infiltration of the lung as assessed by MPO activity. HES at three doses(7.5ml kg<sup>-1</sup>,15ml kg<sup>-1</sup>,30ml kg<sup>-1</sup>)was given i.v. as an infusion 1h before administration of LPS(5mg kg<sup>-1</sup>). MPO activity in lung were assessed 4h after LPS infusion. Data represent mean  $\pm$  SD.\*P<0.05 versus Sham group, # P<0.05 L+H groups versus LPS group.



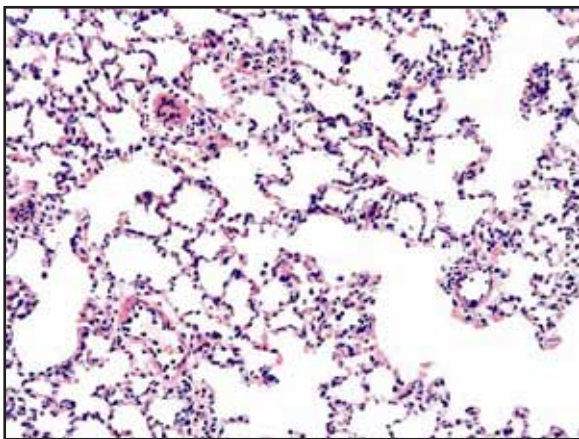
**Figure 4.** Effect of HES on LPS-induced high pulmonary capillary permeability(values of BALFpro,lung W/D ratio and PMPI) HES at three doses(7.5ml kg<sup>-1</sup>,15ml kg<sup>-1</sup>,30ml kg<sup>-1</sup>)was given i.v. as an infusion 1h before administration of LPS(5mg kg<sup>-1</sup>). BALFpro(A),lung W/D ratio(B)and PMPI(C) were assessed 4h after LPS infusion.Data represent mean  $\pm$  SD.\*P<0.05 versus Sham group, # P<0.05 L+H groups versus LPS group.



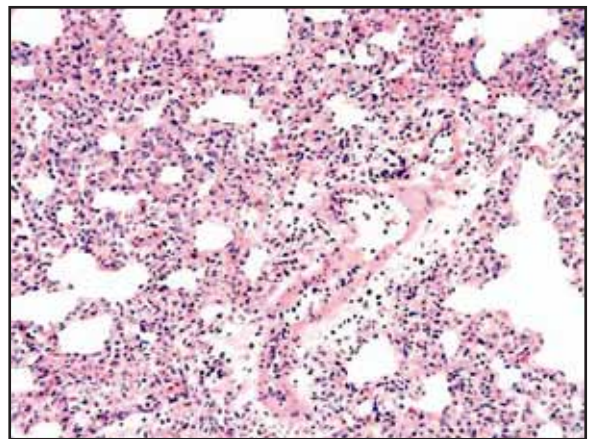
**SHA**



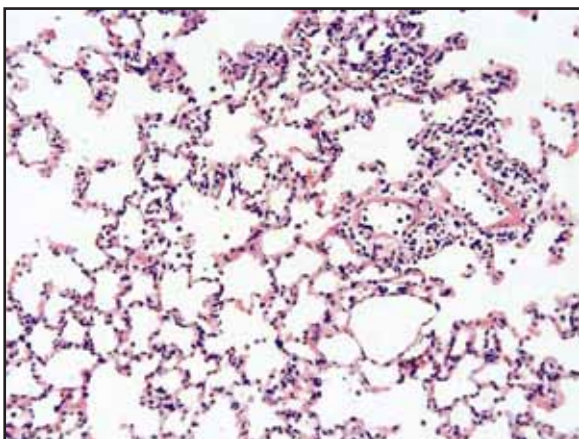
**L+H2**



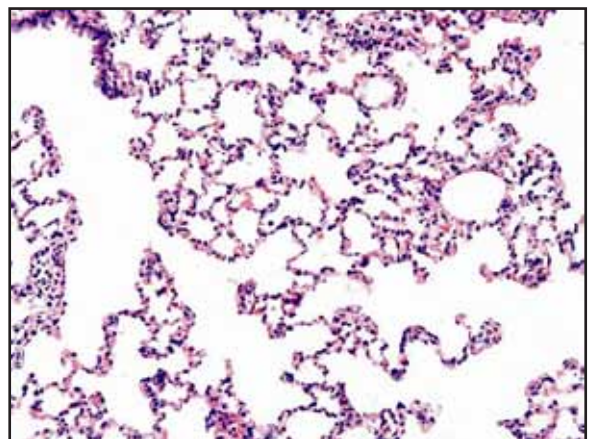
**L+H1**



**LPS**



**L+H3**



**HES**

*Figure 5. Effect of HES on LPS-induced lung injury. HES was given i.v. as an infusion 1h before administration of LPS (5mg kg<sup>-1</sup>). Pathological results of lung tissue in each group was assessed 4h after LPS infusion. The slices show a normal lung tissue from the Sham group and severe alveolar edema with inflammatory infiltration in the LPS group. Pretreatment with HES mitigated the pulmonary pathological changes in three L+H groups especially in group L+H2. (Hematoxylin and eosin stain, magnification 100)*