mRNA 表达水平分别与安慰剂组比较，均显著降低($P<0.01$)。三个治疗组之间的 Ang AT_1 受体 mRNA 表达水平及分别与假扎组比较，均无显著差异($P>0.05$)。**结论**：Cap 和 Los 均可逆转大鼠心肌梗死后 Ang AT_1 受体 mRNA 表达水平的增高。

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Effects of recombinant human endothelial-derived interleukin-8 on hemorrhagic shock in rats[1]

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KEY WORDS interleukin-8; endothelins; epoprostenol; 6-ketoprostaglandin F1 alpha; hemorrhagic shock

AIM: To study the effects of recombinant human endothelial-derived interleukin-8 (IL-8) on hemorrhagic shock. **METHODS**: A profound hemorrhagic shock in rats was produced by exsanguination from femoral artery with mean arterial blood pressure (MABP) maintained at 5.32 kPa for 90 min. After transfusion, IL-8 250 $\mu g \cdot kg^{-1}$ was iv injected. Plasma endothelin-1 (ET-1) and 6-ketoprostaglandin $F_{1\alpha}$ (6-KPGF$_{1\alpha}$) contents were determined with radioimmunoassay. **RESULTS**: After iv IL-8, the MABP in IL-8 group was elevated obviously ($P<0.01$), the rat survial 2 h after infusion was increased ($P<0.05$). During profound shock the plasma ET-1 levels were higher (21 ± 4 *vs* 8.2 ± 1.8 ng·L^{-1}, $P<0.01$) and the plasma 6-KPGF$_{1\alpha}$ contents lower than those in normal rats (107 ± 12 *vs* 157 ± 11 ng·L^{-1}, $P<0.01$). IL-8 remarkably reduced the plasma ET-1 levels (10 ± 4 ng·L^{-1}, $P<0.01$) and enhanced plasma 6-KPGF$_{1\alpha}$ contents (368 ± 16 ng·L^{-1}, $P<0.01$). **CONCLUSION**: IL-8 has beneficial antishock effects.

Interleukin-8 (IL-8), a cytokine produced by endothelial cells and monocytes, plays an important role in inflammatory response and immune regulation[1,2]. IL-8 is a potent inhibitor of neutrophil adhesion to cytokine-activated endothelial monolayers and protects these monolayers from neutrophil-mediated damage[3]. IL-8 leads to protective effects in myocardial ischemia and reperfusion[4] and preserves vasorelaxant responses by promoting release of endothelium-derived relaxing factor[5]. But the effect of IL-8 on hemorrhagic shock was not studied. The purpose of the present work was to study the effects of IL-8 on hemorrhagic shock.

MATERIALS AND METHODS

IL-8 (Department of Immunology, Beijing Medical University); murine endothelin-1 (ET-1) RIA kit (Peninsula Lab, USA); murine 6-ketoprostaglandin $F_{1\alpha}$(6-KPGF$_{1\alpha}$) RIA kit (Institute of Basic Medicine of PLA General Hospital, Beijing).

Profound hemorrhagic shock Adult Wistar rats (♂, $n=32$, weighing 200 - 250 g) bred by the Animal Center of Beijing Medical University were anesthetized with ip urethane 1 g·kg^{-1}. A catheter filled with 5 % sodium citrate solution was inserted into the left carotid artery and connected to a pressure transducer and a polygraph to record the mean arterial blood pressure (MABP). The femoral artery was exsanguinated and the MABP was maintained at 5.32 kPa by further bleeding or autotransfusion for 90 min.

Experimental protocol Rats were randomly divided into 4 groups. 1) IL-8 group: After MABP being kept constant at 5.32 kPa for 90 min, all of the autologous blood was reinfused, and normal saline (15 mL·kg^{-1}) was infused into femoral vein, IL-8 250 $\mu g \cdot kg^{-1}$ was added to normal saline. The changes of the MABP for 2 h and survival rate 2 h after transfusion were observed; 2) Control group: received the same amount of vehicle. 3) Sham operation group with IL-8: After

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90 min, IL-8 250 $\mu g \cdot kg^{-1}$ was iv injected. The changes of the MABP were observed after administration. 4) Sham operation group: except IL-8, the treatment was as same as sham operation group with IL-8.

Plasma ET-1, 6-KPGF$_{1\alpha}$ assay Blood samples were taken from the carotid artery of rats before, 90 min after shock, 2 h after transfusion. The contents were determined by RIA.

Statistical analysis Data were expressed as $\bar{x} \pm s$ and compared with t-test.

RESULTS

MABP The preshock MABP did not show noticeable difference between the IL-8 and control groups ($P > 0.05$). After transfusion and iv IL-8, the MABP of the shock rats rose obviously. Shock state was remarkably improved. Compared with the control group, the difference was quite significant ($P < 0.01$). In the sham operation rats, iv IL-8 250 $\mu g \cdot kg^{-1}$ alone caused hypotension (Fig 1).

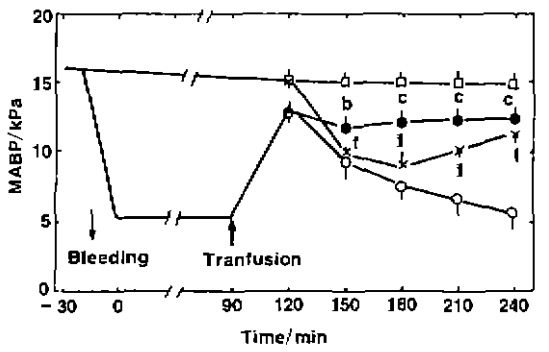

Fig 1. Time course of MABP during shock condition and different kinds of treatment. ○ **Control,** ● **IL-8 group,** × **Sham operation group with IL-8,** □ **Sham operation group,** $n = 8$, $\bar{x} \pm s$. $^bP < 0.05$, $^cP < 0.01$ *vs* **control group;** $^fP < 0.01$ *vs* **sham operation group.**

Plasma ET-1 and 6-KPGF$_{1\alpha}$ During profound hemorrhagic shock, the plasma ET-1 levels in rats were remarkably increased (*vs* preshock, $P < 0.01$) and the plasma 6-KPGF$_{1\alpha}$ contents were significantly decreased (*vs* preshock, $P < 0.01$). After transfusion and iv IL-8, the plasma ET-1 levels were significantly lowered (*vs* control and profound shock, $P < 0.01$) and the plasma 6-KPGF$_{1\alpha}$ contents were remarkably increased (*vs* control and profound shock, $P < 0.01$) (Tab 1).

Survival rate Compared with control group, the survival rate in treated group 2 h after transfusion and iv IL-8 was significantly increased ($P < 0.05$) (Tab 2).

Tab 1. Plasma endothelin-1 and 6-ketoprostaglandin F$_{1\alpha}$ contents in rats. $n = 8$, $\bar{x} \pm s$. $^cP < 0.01$ *vs* **control.**

Group	Contents/ng·L^{-1} Before shock	90 min after shock	2 h after transfusion
	Endothelin-1		
Control	8.4 ± 1.8	21 ± 4	18 ± 3
IL-8	8.2 ± 1.8	21 ± 4	10 ± 4^c
	6-Ketoprostaglandin F$_{1\alpha}$		
Control	164 ± 13	112 ± 13	132 ± 17
IL-8	157 ± 11	107 ± 12	368 ± 16^c

Tab 2. Effect of IL-8 on survival rate 2 h after transfusion. $n = 8$ **rats.** $^bP < 0.05$ *vs* **control group.**

Group	Alive	Dead	Survival rate
Control	3	5	37.5 %
IL-8	7	1	87.5 %^{b}

DISCUSSION

In the present study, the results showed that IL-8 elevated MABP, improved shock state, enhanced animal survival rate, and had beneficial antishock effect, suggesting that the effects of IL-8 on the endothelial function may be one of the mechanism of its antishock actions.

Hemorrhagic shock impairs endothelium-dependent relaxations[6-9]. The present results showed that the ET-1 increased obviously and the 6-KPGF$_{1\alpha}$ decreased remarkably 90 min after shock. ET-1, an endothelium-derived contracting factor (EDCF) produced by the endothelial cells, is an important shockgenic factor. Prostacyclin (PGI_2), an endothelium-derived relaxing factor (EDRF) produced by the endothelial cells, is a protective hormone of vasculature. PGI_2 is rapidly metabolized into inactive 6-KPGF$_{1\alpha}$ *in vivo*. The determination of 6-KPGF$_{1\alpha}$ content could directly reflect the change of PGI_2 level[10]. The increase of ET-1 and the decrease of PGI_2 contents are important causes leading to vascular contraction and shock.

IL-8 has important protective effects on

endothelium. IL-8 significantly reduced the ET-1 and increased PGI_2 plasma level, renewed the regulatory function of vascular endothelium, led to vascular endothelium-dependent relaxation, and improved the organ perfusion, which may be one of the mechanisms of its antishock effect. The angiectatic effect of IL-8 caused hypotension in the sham operation group. Therefore, IL-8 used to antishock must be on the basis of transfusion.

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重组人内皮细胞衍生的白细胞介素-8对大鼠失血性休克的作用[1]

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关键词 白细胞介素-8; 内皮素; 依前列醇; 6-酮前列腺素 $F_{1\alpha}$; 失血性休克

目的: 研究重组人内皮细胞衍生的白细胞介素-8 (IL-8)对失血性休克的作用. **方法**: 大鼠股动脉放血至 MABP 5.32 kPa, 维持 90 min, 复制晚期失血性休克模型. 输血后, 静脉注射 IL-8 250 $\mu g \cdot kg^{-1}$. 放免法测定血浆 ET-1 和 6-$KPGF_{1\alpha}$ 含量. **结果**: 给予 IL-8 后, MABP 显著提高, 休克状态改善, 2 h 存活率相应提高; 休克晚期血浆 ET-1 水平比正常明显升高 (21 ± 4 *vs* 8.2 ± 1.8 $ng \cdot L^{-1}$, $P < 0.01$), 血浆 6-$KPGF_{1\alpha}$ 含量明显降低 (107 ± 12 *vs* 157 ± 11 $ng \cdot L^{-1}$, $P < 0.01$). IL-8 显著降低血浆 ET-1 水平 (10 ± 4 $ng \cdot L^{-1}$, $P < 0.01$), 提高血浆 6-$KPGF_{1\alpha}$ 含量 (368 ± 16 $ng \cdot L^{-1}$, $P < 0.01$). **结论**: IL-8 具有较好的抗休克作用.

Corrigendum

This Acta 1997 May; **18** (3): 216. In the title, "side-chain of propranolol oxidation" should be "side-chain oxidation of propranolol."