第41卷 第2期
2016年2月

贵 阳 医 学 院 学 报
JOURNAL OF GUIYANG MEDICAL COLLEGE

Vol. 41 No. 2
2016. 2

烧伤早期注射胰岛素对大鼠心、肾损害的影响*

袁新章**，王 伟，李伟人***
(贵州医科大学附院 烧伤整形科，贵州 贵阳 550004)

[摘 要] **目的**：探讨烧伤早期皮下注射精蛋白生物合成胰岛素对延迟复苏大鼠心、肾损害的影响。**方法**：32只SPF级SD大鼠随机均分为假伤组、即时复苏组、延迟复苏组与延迟复苏治疗组4组；即时复苏组、延迟复苏组与延迟复苏治疗组大鼠置于(95.0±0.5)℃热水中15 s，制作30%烧伤总面积(TBSA)的Ⅲ°烫伤动物模型，假伤组置37 ℃温水中15 s模拟烫伤；即时复苏组和延迟复苏组伤后立即腹腔注射生理盐水(40 mL/kg)，延迟复苏治疗组伤后立即在右后肢腹侧面皮下注射精蛋白生物合成胰岛素(2.0 U/kg)，延迟复苏组与延迟复苏治疗组伤后6 h时腹腔注射生理盐水(40 mL/kg)；各组均于伤后24 h时采集腹主动脉血，采用分光光度法测定血糖(BG)、乳酸脱氢酶(LDH)、肌酸激酶(CK)、尿素氮(BUN)及肌酐(Cr)。**结果**：即时复苏组、延迟复苏组与延迟复苏治疗组BG、LDH、CK、BUN、Cr均显著高于假伤组($P<0.05$)，延迟复苏组BG、LDH、CK、BUN、Cr显著高于即时复苏组($P<0.05$)，延迟复苏治疗组BG、LDH、CK、BUN、Cr显著低于延迟复苏组($P<0.05$)，延迟复苏治疗组LDH、CK显著高于即时复苏组($P<0.05$)，延迟复苏治疗组BG、Cr显著低于即时复苏组($P<0.05$)，延迟复苏治疗组BUN与即时复苏组比较无显著差异($P>0.05$)。**结论**：烧伤早期皮下注射精蛋白生物合成胰岛素可减轻延迟复苏大鼠的心脏及肾脏损害。

[关键词] 烧伤；复苏；胰岛素；心脏；肾
[中图分类号] R644 [文献标识码] A [文章编号] 1000-2707(2016)02-0179-03

Effect of Hypodemic Injection of Protamin Biosynthetic Insulin on the Damage of Heart and Kidney of Delayed Resuscitation Rats in the Early Stage of Burn Injury

YUAN Xinzhang, WANG Wei, LI Weiren
(*Department of Burn and Plastic Surgery, the Affiliated Hospital of Guizhou Medical University, Guiyang 550004, Guizhou, China*)

[**Abstract**] **Objective**: To investigate the effect of hypodemic injection of protamin biosynthetic insulin on the damage of hearts and kidneys of rats with delayed resuscitation in the early stage of burn injury. **Method**: Thirty-two specific-pathogen free Sprague-Dawley rats were randomly divided into 4 groups, namely, sham burn group, immediate resuscitation group, delayed resuscitation group and delayed resuscitation treatment group, with 8 rats in each group. The rats of immediate resuscitation group, delayed resuscitation group and delayed resuscitation treatment group were immersed in (95 ± 0.5)℃ hot water for 15 seconds to make empyrosis rat model of 30% total burn surface area, Ⅲ degree burn injury. The sham burn group was immersed in 37 ℃ warm water for 15 seconds to simulate burns. Immediate resuscitation group and delayed resuscitation group received an intraperitoneal injection of physiological saline (40 mL/kg) after burn injury immediately, while delayed resuscitation treatment group received subcutaneous injection of protamine biosynthetic insulin｛(2.0 U/kg) in the ventral side of the right hind limb after burn injury immediately. Delayed resuscitation group and de-

*[基金项目]贵州省卫生厅科学技术基金(gzwkj2011-1-022)
**贵州医科大学2013级外科学烧伤整形科硕士研究生
***通信作者 E-mail:gz_lwr@163.com
网络出版时间:2016-02-23 网络出版地址:http://www.cnki.net/kcms/detail/52.5012.R.20160223.2045.048.html

layed resuscitation treatment group received intraperitoneal injection of physiological saline (40 mL/kg) 6 hours after burn injury. The abdominal aortic blood was collected 24 hours after burn injury in each group. The spectrophotometry was adopted for determination of blood glucose (BG), lactate dehydrogenase (LDH), creatine kinase (CK), blood urea nitrogen (BUN) and creatinine (Cr). **Results**: BG, LDH, CK, BUN and Cr in immediate resuscitation group, delayed resuscitation group and delayed resuscitation treatment group were significantly higher than their counterparts of sham burn group ($P<0.05$). BG, LDH, CK, BUN and Cr in delayed resuscitation group were totally higher than their counterparts of immediate resuscitation group ($P<0.05$). BG, LDH, CK, BUN and Cr in delayed resuscitation treatment group were significantly lower than their counterparts of delayed resuscitation group ($P<0.05$). LDH and CK in delayed resuscitation treatment group were significantly higher than their counterparts of immediate resuscitation group, while BG and Cr were significantly lower than their counterparts of immediate resuscitation group ($P<0.05$). There was no significant difference of BUN between delayed resuscitation treatment group and immediate resuscitation group ($P>0.05$). **Conclusion**: During the early stage of burn injury, hypodemic injection of protamine biosynthetic insulin can reduce the damage of heart and kidney of delayed resuscitation rats.

[**Key words**] burn; recovery; insulin; heart; kidney

胰岛素在严重烧伤休克复苏中具有潜在的应用价值,休克期应用普通胰岛素可降低大面积烧伤患者复苏所需胶－晶体溶液需要量,增加尿量,同时可减轻组织损伤程度和保护脏器功能[1]。胰岛素有多种类型,不同类型胰岛素的作用各有特点[2]。为探讨烧伤早期皮下注射胰岛素对延迟复苏大鼠器官损害的影响,参照甘精胰岛素治疗Ⅱ型糖尿病时发挥抗氧化效应的剂量[即<0.4 U/(kg·d)][3]以及人与大鼠用药剂量的换算关系[大鼠的剂量(mg/kg)＝6.25×人的剂量(mg/kg)][4],本实验观察了烧伤早期皮下注射精蛋白生物合成胰岛素(2.0 U/kg)对30%烧伤总面积(TBSA)延迟复苏大鼠心脏及肾脏损伤的保护作用。

1 材料与方法

1.1 实验动物

SPF级成年雄性SD大鼠32只,由第三军医大学大坪医院野战外科研究所医学实验动物中心提供(scxk 渝,2007－0005),体重200～250 g,清洁环境饲养、万级屏障系统,实验前适应性驯养1周。

1.2 主要仪器和试剂

721型分光光度仪购自山东高密彩虹分析仪器有限公司,TDL80－2B台式低速离心机上海沪誉仪器有限公司,微量可调加样器购自德国Eppendorf公司,长效精蛋白生物合成胰岛素购自丹麦诺和诺德公司,血糖(blood glucose,BG)、乳酸脱氢酶(lactate dehydrogenase,LDH)、肌酸激酶(creatinekinase,CK)、尿素氮(blood urea nitrogen,BUN)及肌酐(creatinine,Cr)测定试剂盒均购自中国南京建成生物工程研究所。

1.3 方法

32只SD大鼠按随机数字表法分为假伤组、即时复苏组、延迟复苏组与延迟复苏治疗组,每组8只。大鼠背部脱毛后,腹腔注射2.5％戊巴比妥钠(35 mg/kg)麻醉;参考文献[5]的方法,即时复苏组、延迟复苏组与延迟治疗组大鼠置于(95.0±0.5)℃热水中15 s,制作30% TBSA、Ⅲ°烫伤模型;假伤组仅置37 ℃温水中15 s模拟烫伤。假伤组和即时复苏组伤后立即腹腔注射生理盐水(40 mL/kg),延迟复苏治疗组伤后立即在右后肢腹侧面皮下注射精蛋白生物合成胰岛素(2.0 U/kg),延迟复苏组与延迟复苏治疗组伤后6 h时腹腔注射生理盐水(40 mL/kg)。各组大鼠分笼饲养,实验期间无死亡。各组大鼠伤后24 h开腹采集腹主动脉血,2 000 r/min离心10 min,取上清液,采用分光光度法测定血糖(BG)、乳酸脱氢酶(LDH)、肌酸激酶(CK)、尿素氮(BUN)及肌酐(Cr),按试剂盒说明书要求测定。

1.4 统计学方法

采用SPSS 17.0软件进行统计学分析。数据以均值±标准差($\bar{x}\pm s$)表示,组间比较采用单因素方差分析,$P<0.05$表示差异有统计学意义。

2 结果

即时复苏组、延迟复苏组与延迟复苏治疗组BG、LDH、CK、BUN及Cr显著高于假伤组,延迟复苏组BG、LDH、CK、BUN及Cr显著高于即时复苏组,延迟复苏治疗组BG、LDH、CK、BUN及Cr显著低于延迟复苏组,延迟复苏治疗组LDH、CK显著高于即时复苏组,延迟复苏治疗组BG、Cr显著低于即时复苏组,差异均有统计学意义($P<0.05$);延迟复苏治疗组BUN与即时复苏组比较差异无统计学意义($P>0.05$)。见表1。

表1　实验各组大鼠BG、LDH、CK、BUN、Cr结果($\bar{x}\pm s$)

Tab.1　Results of BG, LDH, CK, BUN and Cr of rats in the 4 groups

组别	n	BG(mmol/L)	LDH(U/L)	CK(U/mL)	BUN(mmol/L)	Cr(μmol/L)
假伤组	8	6.48 ± 0.26	$1\,580.81\pm101.77$	0.54 ± 0.08	5.17 ± 0.65	40.13 ± 7.27
即时复苏组	8	$7.72\pm0.30^{(1)}$	$2\,525.25\pm90.35^{(1)}$	$0.78\pm0.10^{(1)}$	$7.49\pm0.51^{(1)}$	$89.25\pm8.09^{(1)}$
延迟复苏组	8	$8.80\pm0.44^{(1)(2)}$	$3\,721.38\pm136.14^{(1)(2)}$	$1.45\pm0.19^{(1)(2)}$	$8.38\pm0.74^{(1)(2)}$	$100.17\pm8.62^{(1)(2)}$
延迟复苏治疗组	8	$7.11\pm0.25^{(1)(2)(3)}$	$2\,845.12\pm79.71^{(1)(2)(3)}$	$1.05\pm0.21^{(1)(2)(3)}$	$7.10\pm0.58^{(1)(3)}$	$68.36\pm8.64^{(1)(2)(3)}$

(1)与假伤组比较$P<0.05$;(2)与即时复苏组比较$P<0.05$;(3)与延迟复苏组比较$P<0.05$

3 讨论

患者于烧伤6 h后或更晚开始复苏治疗,属于延迟复苏之列[6]。烧伤延迟复苏将导致多脏器并发症发生和病死率增加[7]。本实验结果显示,延迟复苏组烧伤后24 h时BG、LDH、CK和BUN、Cr均显著高于即时复苏组,提示延迟复苏可加重烧伤大鼠心脏及肾脏的损害,使血糖升高。在烧伤休克期,高血糖很常见[8]。动物实验结果也显示,TBSA30%、Ⅲ°烫伤大鼠的血糖伤后3 h时即显著升高,一直持续到伤后24 h时[9]。胰岛素作为体内重要的激素,调节糖、蛋白与脂肪的代谢,并具有器官保护、抗炎、抗凋亡效应[10]。本实验结果显示,延迟复苏治疗组心肌酶活力、肾功能均显著低于延迟复苏组,并且Cr显著低于即时复苏组,BUN与即时复苏组比较无显著差异,提示烧伤早期皮下注射精蛋白生物合成胰岛素可减轻延迟复苏大鼠的心脏及肾脏损害。但延迟复苏治疗组心肌酶活力仍显著高于即时复苏组,表明烧伤后即时复苏对保护脏器组织尤为重要。本实验结果同时显示,延迟复苏治疗组血糖水平较延迟复苏组显著降低但仍高于假伤组,这有助于减少低血糖发生风险。

综上,烧伤早期皮下注射精蛋白生物合成胰岛素可减轻延迟复苏大鼠的心脏及肾脏损害。在后续研究中,将进一步探讨胰岛素发挥器官保护效应的类型差异及其可能机制。

4 参考文献

[1] 施燕,张勤,郑捷新,等.胰岛素治疗在烧伤休克复苏中的应用初探[J].中华损伤与修复杂志, 2012(1):62-66.

[2] Asamoah E. Variability of insulin action and clinical effects[J]. The Endocrinologist, 2007(17):282-290.

[3] Monnier L, Colette C, Michel F, et al. Insulin therapy has a complex relationship with measure of oxidative stress in type 2 diabetes: a case for further study[J]. Diabetes Metab Res Rev, 2011(4):348-353.

[4] 施新酋.医用实验动物学[M].西安:陕西科学技术出版社, 1989:421.

[5] 冯世杰,花兰女,金曙雯,等.大鼠烫伤模型的制作[J].上海第二医科大学学报, 1995(2):195-197.

[6] 黎鳌,杨宗城.黎鳌烧伤学[M].上海:上海科学技术出版社, 2001:56-57.

[7] 邱啸臣,金以超,孙瑜,等.富氢盐水对延迟复苏烫伤大鼠血压及肺组织抗氧化能力的影响[J].中华烧伤杂志, 2010(6):435-438.

[8] Holm C, Hörbrand F, Mayr M, et al. Acute hyperglycaemia following thermal injury: friend or foe[J]. Resuscitation, 2004(1):71-77.

[9] 王伟,李伟人,孔豫苏,等.胰岛素对严重烫伤后早期大鼠血乳酸浓度及乳酸脱氢酶活力的影响[J].中国急救医学, 2013(8):746-748.

[10] Wang X, Tao L, Hai CX. Redox-regulating role of insulin: the essence of insulin effect[J]. Mol Cell Endocrinol, 2012(2):111-127.

(2015-08-30收稿,2015-12-20修回)

中文编辑:戚　璐;英文编辑:刘　华