

- rates between hemiarthroplasty and total hip replacement for intracapsular hip fractures[J]. *Orthopedics*, 2013, 36(4):384-389
- 9 胡洪波,李玉民,张龙龙,等. 全髋和半髋关节置换术治疗老年股骨颈骨折疗效分析[J]. *中国骨与关节损伤杂志*,2012,27(12):1105-1107
 - 10 Leonardsson O, Rolfson O, Hommel A, *et al.* Patient - reported outcome after displaced female neck fracture; a national survey of 4467 patients [J]. *J Bone Joint Surg Am*, 2013, 95(18):1693-1699
 - 11 Avery PP, Baker RP, Walton MJ, *et al.* Total hip replacement and hemiarthroplasty in mobil, independent patiets with a displaced intracapsular fracture of the femoral neck; a seven - to ten - year follow - up report of a prospective randomized controlled trial[J]. *J Bone Joint Surg Br*, 2011, 93(8):1045-1048
 - 12 Hedbeck CJ, Enoscon A, Lapidus G, *et al.* Comparision of bipolar hemiarthroplasty with total hip arthroplasty for displaced femoral neck fractures; a concise four - year follow - up of a randomized trail[J]. *J Bone Joint Surg Am*, 2011, 93(5):445-450
 - 13 廖亮, 赵劲民, 苏伟, 等. 全髋与半髋关节置换治疗老年股骨颈骨折的 Meta 分析 [J]. *中国组织工程研究与临床康复*, 2010, 22(14):3391-3394
 - 14 Hopley C, Stengel D, Ekkernkamp A, *et al.* Primary total hip arthroplasty versus hemiarthroplasty for displaced intracapsular hip fractures in older patients: systematic review[J]. *BMJ*, 2010, 340:c2332
 - 15 Macaulay W, Nellans KW, Garvin KL, *et al.* Prospective randomized clinical trial comparing hemiarthroplasty to total hip arthroplasty in the treatment of displaced femoral neck fractures: winner of the Dorr Award [J]. *J Arthroplasty*, 2008, 23(6):2-8
 - 16 Ossendorf C, Scheyer MJ, Wanner GA, *et al.* Treatment of femoral neck fractures in elderly patients over 60 years of age - which is the ideal modality of primary joint replacement? [J]. *Patient Saf Surg*, 2010, 4(1):16-20
 - 17 Stoffel KK, Nivbrant B, Headford J, *et al.* Does a bipolar hemiprosthesi offer advantages for elderly patients with neck of femur fracture? A clinical trial with 261 patients[J]. *ANZ J Surg*, 2013, 83(4):249-254
 - 18 Van den Bekerom MP, Hilverdink EF, Sierevelt IN, *et al.* A comparison of hemiarthroplasty with total hip replacement for displaced intracapsular fracture of the femoral neck: a randomised controlled multicentre trial in patients aged 70 years and over [J]. *J Bone Joint Surg Bm*, 2012, 92(10):1422-1428
 - 19 Jameson SS, Kyle J, Baker PN, *et al.* Patient and implant survival following 4323 total hip replacements for acute neck fracture: a retrospective cohort Study using National Joint Registry data[J]. *J Bone Joint Surg Br*, 2012, 94(11):1557-1566

(收稿日期:2014-02-18)

(修回日期:2014-03-27)

乌司他丁联合参麦注射液治疗急性胰腺炎相关肺损伤的临床研究

郑 建 吕 望 郑忠盛

摘 要 **目的** 观察乌司他丁联合参麦注射液对急性胰腺炎相关急性肺损伤的临床治疗效果。**方法** 选取急性胰腺炎相关肺损伤患者 60 例,随机分为乌司他丁+参麦组(US 组)、乌司他丁组(U 组)和对照组(C 组),每组 20 例。C 组给予常规治疗,U 组在常规治疗基础上每日静脉滴注乌司他丁(6000U/kg),US 组在常规治疗基础上每日静脉滴注乌司他丁(6000U/kg)和参麦注射液(0.6ml/kg)。分别于治疗前、治疗后第 3、7 天行动脉血气分析,计算氧合指数,测定血清 TNF- α 、IL-1 β 和 IL-6 浓度。**结果** 与 C 组比较,U 组和 US 组治疗后 3 和 7 天血清 TNF- α 、IL-1 β 和 IL-6 浓度下降,治疗后 7 天氧合指数升高($P<0.05$);与 U 组比较,US 组治疗后 7 天血清 TNF- α 、IL-1 β 和 IL-6 浓度下降,氧合指数升高($P<0.05$)。**结论** 乌司他丁联合参麦注射液能进一步抑制炎性介质释放,减轻急性胰腺炎相关肺损伤。

关键词 急性胰腺炎 肺损伤 乌司他丁 参麦注射液

[中图分类号] R [文献标识码] A

Clinical Study on Ulinastatin Combined with Shenmai Injection in Attenuating Lung Injury Associated with Acute Pancreatitis. Zheng Jian, Lü Wang, Zheng Zhongsheng. Department of Critical-care Medicine, Wenzhou Integrated Traditional Chinese and Western Medicine Hospital Affiliated to Zhejiang Chinese Medicine University, Zhejiang 325000, China

Abstract Objective To study the therapeutic effects of Ulinastatin combined with Shenmai injection on acute lung injury associat-

作者单位:325000 浙江中医药大学附属温州市中西医结合医院重症医学科(郑建);325000 温州市人民医院急诊科(吕望);325000 温州市瓯海区人民医院血透室(郑忠盛)

ed with acute pancreatitis. **Methods** Sixty patients diagnosed associated as acute pancreatitis complicated with lung injury were enrolled and randomized into Ulinastatin + Shenmai (US) Group, Ulinastatin (U) Group and Control (C) Group. The patients in C Group received conventional therapy, while extra intravenous administration of Ulinastatin (6000U/kg, 1 time per day) was given in U Group, and additional Shenmai injection (0.6ml/kg, 1 time per day) was given in US Group based on same therapy received in U Group. The concentrations of serum TNF- α , IL-1 β and IL-6 were measured, and blood gases were detected before therapy initiation, 3d and 7d after therapy. **Results** As compared to C Group, the levels of serum TNF- α , IL-1 β and IL-6 were decreased at 3d and 7d post-therapy, and oxygenation index at 7d post-therapy was enhanced ($P < 0.05$). serum TNF- α , IL-1 β and IL-6 levels at 7d post-therapy were lower and oxygenation index was higher in US Group than those in U Group, respectively ($P < 0.05$). **Conclusion** Treatments of Ulinastatin combined with Shenmai injection could further inhibit the release of inflammatory cytokines and attenuate lung injury in patients with acute pancreatitis.

Key words Acute pancreatitis; Lung injury; Ulinastatin; Shenmai injection

急性胰腺炎为临床上常见的危重病症,病死率高,其中急性肺损伤或急性呼吸窘迫综合征最为常见,主要的病理生理特点为全身炎症反应综合征和多器官功能障碍综合征。因此早期抗炎治疗可减轻肺损伤,提高急性胰腺炎的救治。乌司他丁是一种广谱丝氨酸蛋白酶抑制剂,可抑制多种蛋白酶和脂酶的活性,减少胰腺的自身消化,已经广泛用于急性胰腺炎的治疗。参麦注射液是临床常用的中成药剂,具备抗炎和抗脂质过氧化、改善微循环等药理作用。本研究拟观察乌司他丁联合参麦注射液改善急性胰腺炎患者炎症反应和相关肺损伤的效果,为临床治疗提供参考。

资料与方法

1. 一般资料:本研究经医院伦理委员会批准,并与患者或授权人签订知情同意书。选择2007年2月~2013年4月收住笔者医院科室住院保守治疗的确诊急性胰腺炎相关肺损伤患者60例,患者年龄45~60岁,男女不限,无肺结核、慢性支气管炎、哮喘及慢性阻塞性肺疾病等病史,无乌司他丁或参麦注射液过敏史。参照ARDS柏林新标准^[1],急性胰腺炎相关肺损伤指在急性胰腺炎基础上出现以下临床表现:①已知临床发病或呼吸症状新发或加重后1周内;②X线或CT扫描示双肺致密影,并且胸腔积液、肺叶/肺塌陷或结节不能完全解释;③无法用心力衰竭或体液超负荷完全解释的呼吸衰竭。如果不存在危险因素,则需要进行客观评估(如超声心动图)以排除流体静力型水肿;④氧合指数($\text{PaO}_2/\text{FiO}_2$, OI) $\leq 300\text{mmHg}$;轻度: $\text{OI} = 201 \sim 300\text{mmHg}$,且呼气末正压(PEEP)或持续气道正压(CPAP) $\leq 5\text{cmH}_2\text{O}$;中度: $\text{OI} = 101 \sim 200\text{mmHg}$,且 $\text{PEEP} \geq 5\text{cmH}_2\text{O}$;重度: $\text{OI} \leq 100\text{mmHg}$,且 $\text{PEEP} \geq 10\text{cmH}_2\text{O}$ 。入选患者采用信封法随机分为乌司他丁+参麦组(US组)、乌司他丁组(U组)和对照组(C组),每组20例。

2. 治疗方法:C组患者入科后即接受急性胰腺炎常规综合治疗,包括禁食和持续胃肠减压,控制感染,应用质子泵抑制剂和生长抑素减少胰腺外分泌,对症及营养支持治疗;U组

患者在常规综合治疗的基础上,每日单次静脉滴注乌司他丁 6000U/kg (100ml 生理盐水稀释),持续1周,其余治疗措施同C组。US组患者每日单次静脉滴注参麦注射液 0.6ml/kg (100ml 生理盐水稀释),持续1周,其余治疗同U组。由不知情分组的研究者进行指标测定。

3. 指标测定:在治疗前、治疗后3和7天分别抽取桡动脉血样 1.0ml 行血气分析,测定动脉氧分压(arterial oxygen partial pressure, PaO_2)、动脉二氧化碳分压(arterial carbon dioxide partial pressure, PaCO_2),计算氧合指数(oxygenation index, OI): $\text{OI} = \text{PaO}_2/\text{FiO}_2$ (FiO_2 为吸入氧浓度)。抽取外周静脉血 5ml ,分离血清,用ELISA法测定TNF- α 、IL-1 β 和IL-6浓度。

4. 统计学方法:采用SPSS 15.0进行统计学处理,以均数 $\pm$ 标准差($\bar{x} \pm s$)表示,组内比较采用重复测量数据方差分析,组间比较采用单因素方差分析,计数资料比较采用 χ^2 检验, $P < 0.05$ 为差异有统计学意义。

结 果

1. 一般情况比较:3组患者年龄、体重、性别构成比差异无统计学意义($P > 0.05$)。

2. 炎性指标比较:与治疗前比较,治疗后3和7天3组患者血清TNF- α 、IL-1 β 和IL-6浓度下降($P < 0.05$);与C组比较,U组和US组患者治疗后3和7天血清TNF- α 、IL-1 β 和IL-6浓度降低($P < 0.05$);与U组比较,US组患者治疗后7天血清TNF- α 、IL-1 β 和IL-6浓度降低($P < 0.05$),详见表1。

3. 血气分析指标比较:与治疗前比较,治疗3和7天后两组患者 OI 升高($P < 0.05$);与C组比较,U组和US组患者治疗后7天 OI 升高($P < 0.05$);与U组比较,US组患者治疗后7天 OI 升高($P < 0.05$)。组内及组间 PaCO_2 差异均无统计学意义($P > 0.05$),详见表2。

表 1 3 组患者血清炎症指标比较($\bar{x} \pm s, n = 20, \text{ng/L}$)				
指标	组别	治疗前	治疗后 3 天	治疗后 7 天
TNF- α	C 组	12.6 $\pm$ 3.1	9.3 $\pm$ 2.7 [*]	7.6 $\pm$ 2.3 [*]
	U 组	13.7 $\pm$ 3.4	6.8 $\pm$ 1.9 ^{**}	5.3 $\pm$ 1.6 ^{**#}
	US 组	14.2 $\pm$ 2.8	6.2 $\pm$ 2.0 ^{**}	3.2 $\pm$ 1.0 ^{**#Δ}
IL-1 β	C 组	9.4 $\pm$ 2.6	7.2 $\pm$ 1.5 [*]	6.5 $\pm$ 2.0 [*]
	U 组	9.6 $\pm$ 3.0	5.3 $\pm$ 1.6 ^{**}	4.5 $\pm$ 1.3 ^{**#}
	US 组	10.2 $\pm$ 2.8	5.1 $\pm$ 1.4 ^{**}	3.2 $\pm$ 1.2 ^{**#Δ}
IL-6	C 组	168.0 $\pm$ 50.0	132.0 $\pm$ 46.0 [*]	109.0 $\pm$ 35.0 [*]
	U 组	162.0 $\pm$ 56.0	101.0 $\pm$ 40.0 ^{**}	89.0 $\pm$ 32.0 ^{**#}
	US 组	172.0 $\pm$ 61.0	89.0 $\pm$ 32.0 ^{**#}	63.0 $\pm$ 21.0 ^{**#Δ}

与治疗前比较, * $P < 0.05$; 与 C 组比较, [#] $P < 0.05$; 与 U 组比较, $\Delta P < 0.05$

表 2 3 组患者血气分析指标比较($\bar{x} \pm s, n = 20, \text{mmHg}$)				
指标	组别	治疗前	治疗后 3 天	治疗后 7 天
OI	C 组	211 $\pm$ 56	262 $\pm$ 48 [*]	284 $\pm$ 53 [*]
	U 组	213 $\pm$ 62	275 $\pm$ 52 [*]	329 $\pm$ 52 ^{**#}
	US 组	216 $\pm$ 58	282 $\pm$ 57 [*]	372 $\pm$ 56 ^{**#Δ}
PaCO ₂	C 组	30 $\pm$ 7	35 $\pm$ 8	34 $\pm$ 10
	U 组	32 $\pm$ 7	33 $\pm$ 6	37 $\pm$ 9
	US 组	30 $\pm$ 9	31 $\pm$ 8	35 $\pm$ 9

与治疗前比较, * $P < 0.05$; 与 C 组比较, [#] $P < 0.05$; 与 U 组比较, $\Delta P < 0.05$

讨 论

急性胰腺炎是胰腺因胰蛋白酶的自身消化作用而引起的疾病,病死率高,早期易并发急性肺损伤,甚至急性呼吸窘迫综合征等^[2]。目前认为,胰腺局部或全身的炎症反应是急性胰腺炎相关肺损伤的主要发生机制^[3]。胰腺血管壁及胰腺导管的破坏可激活胰腺组织单核-吞噬细胞,后者合成和释放多种细胞因子,细胞间黏附分子增加,与损伤的肺血管内皮细胞黏附增加使中性粒细胞等促炎性细胞在肺组织聚集,引发炎症反应的级联反应,导致全身炎症反应激活和肺损伤^[4]。另外,由于胰蛋白酶的超反应,激活了弹性硬蛋白酶及磷脂酶 A,对胰腺发生自身消化作用,破坏细胞脂肪膜和线粒体膜的甘油磷脂,能降解肺泡表面活性物质,最终导致急性肺损伤。本研究结果表明,急性胰腺炎相关肺损伤患者外周血 TNF- α 、IL-1 β 和 IL-6 浓度升高,与先前研究一致^[5]。因此,早期有效的抗炎治疗对于改善急性胰腺炎患者预后具有重要作用。

乌司他丁是从男性尿液中分离纯化的一种典型的 Kuniz 型的蛋白酶抑制剂,具有两个活性功能区。由于两个活性功能区均有其自身的抑酶谱且不完全重叠,这使得乌司他丁成为广谱蛋白水解酶抑制剂而

被广泛应用。多项研究表明,乌司他丁可减轻急性胰腺炎局部及全身炎症,其机制可能为结合胰蛋白酶、 α -糜蛋白酶等丝氨酸蛋白酶和粒细胞弹性蛋白酶等多种酶类,与酶结合后抑制酶的活性,并促进酶的降解,缓解胰腺的自身消化^[6,7]。另外,乌司他丁抑制巨噬细胞内蛋白激酶 C 和核转录因子- κ B 信号转导通路,能剂量依赖性地减少 TNF- α 、IL-1、IL-6 和 IL-8 等炎性介质的释放^[8,9]。乌司他丁还可稳定溶酶体膜,清除自由基和减轻脂质过氧化损伤。参麦注射液是临床常用中药制剂,其有效成分为人参皂苷、麦冬皂苷及麦冬黄酮等。参麦注射液能够调节胰腺微循环、抗内毒素、促进胰腺损伤修复^[10,11]。参麦注射液可调节 Toll 样受体的表达,并抑制核转录因子- κ B 信号转导,下调其下游细胞间黏附分子-1 和 TNF- α 而减轻炎症反应^[12]。动物研究表明,参麦注射液可降低急性胰腺炎大鼠肺组织脂质过氧化损伤,抑制炎性介质 TNF- α 和 IL-1 β 合成,从而减轻肺组织炎性细胞浸润和肺泡破坏^[13]。本研究结果表明,乌司他丁和参麦注射液均能减轻急性胰腺炎患者炎性介质释放,改善肺功能,尤其是两者联用时治疗效果更为明显。综上所述,乌司他丁联合参麦注射液可进一步减少炎性介质释放,减轻急性胰腺炎患者相关肺损伤。

参考文献

- 1 ARDS Definition Task Force, Ranieri VM, Rubenfeld GD, *et al.* Acute respiratory distress syndrome: the Berlin definition[J]. JAMA, 2012, 307(23): 2526-2533
- 2 项立,胡卫东,龙子义,等. 不同年龄组重症急性胰腺炎临床特点及预后的研究[J]. 医学研究杂志, 2012, 41(6): 120-122
- 3 Cuzzocrea S, Mazzone E, Dugo L, *et al.* Absence of endogenous interleukin-6 enhances the inflammatory response during acute pancreatitis induced by cerulein in mice[J]. Cytokine, 2002, 18(5): 274-285
- 4 Ding JL, Zhou ZG, Zhou XY, *et al.* Attenuation of acute pancreatitis by peroxisome proliferator-activated receptor- α in rats: the effect on Toll-like receptor signaling pathways[J]. Pancreas, 2013, 42(1): 114-122
- 5 石金河,张建新,陈希妍,等. 银杏叶提取物注射液对重症急性胰腺炎患者炎症介质的影响[J]. 新乡医学院学报, 2013, 30(1): 921-923
- 6 Abraham P, Rodrigues J, Moulick N, *et al.* Efficacy and safety of intravenous ulinastatin versus placebo along with standard supportive care in subjects with mild or severe acute pancreatitis[J]. J Assoc Physicians India, 2013, 61(8): 535-538
- 7 Wang G, Wen J, Wilbur RR, *et al.* The effect of somatostatin, ulinastatin and Salvia miltiorrhiza on severe acute pancreatitis treatment[J]. Am J Med Sci, 2013, 346(5): 371-376

- 8 Rui M, Duan YY, Zhang XH, *et al.* Urinary trypsin inhibitor attenuates seawater - induced acute lung injury by influencing the activities of nuclear factor - κ B and its related inflammatory mediators[J]. *Respiration*, 2012, 83(4): 335 - 343
- 9 Babu BI, Genovese T, Mazzon E, *et al.* Recombinant human activated protein C (Xigris) attenuates murine cerulein - induced acute pancreatitis via regulation of nuclear factor κ B and apoptotic pathways[J]. *Pancreas*, 2012, 41(4): 619 - 628
- 10 罗灵和, 陈军贤, 钟燕敏, 等. 参麦注射液辅治急性胰腺炎疗效观察[J]. *浙江中西医结合杂志*, 2013, 23(1): 49 - 50
- 11 卢进军, 钟锋. 参麦注射液辅治急性胰腺炎效果观察[J]. *当代医学*, 2014, 20(5): 41 - 42
- 12 阮丽君, 赵明, 黄青松. 参麦对大鼠肾缺血再灌注损伤中 TLR4/NF - κ B 信号通路的影响[J]. *中国现代医学杂志*, 2013, 23(7): 11 - 14
- 13 于齐宏, 杜奕奇, 李兆申, 等. 参麦注射液减轻大鼠重症急性胰腺炎相关性肺损伤[J]. *第二军医大学学报*, 2013, 34(11): 1183 - 1186
- (收稿日期: 2014 - 07 - 17)
- (修回日期: 2014 - 09 - 02)

远隔缺血预处理对心脏瓣膜置换术患者肺功能、血流动力学和炎性因子的影响

李日著 陈宏明 罗世官 唐习强 易金远

摘 要 **目的** 探讨远隔缺血预处理对心脏瓣膜置换术患者肺功能、血流动力学和炎性因子的影响。**方法** 选取笔者医院行择期心脏瓣膜置换术的患者 60 例为受试对象, 随机分为远隔缺血预处理组(观察组)和对照组, 每组各 30 例。观察组的患者在麻醉诱导后给予加压远隔缺血预处理, 对照组则仅给予止血带。观察两组患者不同时间点肺功能、血流动力学和炎性因子的变化。**结果** 与麻醉诱导前(T_0)相比, 两组患者的肺泡 - 动脉氧分压差[alveolar - arterial oxygen tension gradient, $D(A - a)O_2$]、呼吸指数(respiratory index, RI)、肿瘤坏死因子 - α (tumor necrosis factor - α , TNF - α)、白细胞介素 - 6 (interleukin - 6, IL - 6) 和 8 (interleukin - 8, IL - 8) 和中心静脉压 (central venous pressure, CVP) 的水平均呈现显著升高 ($P < 0.05$), 而和氧合指数 (oxygenation index, OI)、心率 (heart rate, HR)、平均动脉压 (mean arterial pressure, MAP)、心脏指数 (cardiac index, CI) 和肺毛细血管嵌压 (pulmonary capillary wedge pressure, PCWP) 均出现不同程度的降低 ($P < 0.05$); 与对照组相比, 观察组患者肺功能和血流动力学指标的改善程度显著优于对照组 ($P < 0.05$), 但是两组患者炎性因子的比较则无明显差别 ($P > 0.05$)。**结论** 远隔缺血预处理可改善心脏瓣膜置换术患者肺功能和血流动力学指标, 但对炎性反应的抑制则无明显作用。

关键词 心脏瓣膜置换术 肺功能 血流动力学 炎性因子

[中图分类号] R654 [文献标识码] A

Effects of Remote Ischemic Preconditioning on Lung Function, Hemodynamic and Inflammatory Factors in Patients with Heart Valve Replacement Surgery. Li Rizhu, Chen Hongming, Luo Shiguan, *et al.* Department of Cardiac Surgery, Affiliated Hospital of Youjiang Medical College for Nationalities, Guangxi 533000, China

Abstract **Objective** To investigate the effects of remote ischemic preconditioning on lung function, hemodynamic and inflammatory factors in patients with heart valve replacement surgery. **Methods** Sixty patients with heart valve replacement surgery in our hospital were selected as subjects, and were divided into remote ischemic preconditioning group (observed group) and the control group according to the random number. Each group had 30 cases. Patients in the observed group were given pressure remote ischemic preconditioning after the induction of anesthesia, whereas the control group only received a tourniquet. Lung function, hemodynamics and inflammatory factors were observed in different time points. **Results** Compared to induction of anesthesia time point (T_0), alveolar - arterial oxygen tension gradient [$D(A - a)O_2$], respiratory index (RI) values, tumor necrosis factor - α (TNF - α), IL - 6, IL - 8 and CVP showed an increase in both two groups ($P < 0.05$), while OI values, HR, MAP and CI were in different degrees of reduction ($P < 0.05$). Moreover, compared with the control group, the degree of improvement in lung function and hemodynamic indices of patients in the observed group were significantly better than the control group ($P < 0.05$), but there was no significant difference in inflammatory factors ($P > 0.05$). **Conclusion** Remote ischemic preconditioning can improve lung function and heart valve replacement surgery in patients with hemody-