

doi: 10.13241/j.cnki.pmb.2014.15.026

乌司他丁与沐舒坦治疗严重烧伤伴吸入性损伤的疗效分析*

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摘要 目的: 探讨严重烧伤伴中重度吸入性损伤患者早期联合使用大剂量乌司他丁与沐舒坦的临床疗效。**方法:** 选择2003年5月~2013年5月在我院接受治疗的185例严重烧伤伴中重度吸入性损伤患者,随机分为两组,治疗组93例,对照组92例。两组患者在确诊为中重度吸入性损伤后,立即给予传统常规治疗:吸氧、视情尽早预防性气管切开、湿化气道及气道灌洗、翻身拍背吸痰、呼吸机辅助呼吸等。治疗组在常规治疗的基础上给予乌司他丁40万单位,每隔8h静脉滴注,沐舒坦450mg,每隔12h微泵静推;对照组给予乌司他丁10万单位,每隔8h静滴,沐舒坦30mg,每隔8h静滴,疗程为10天,比较两组患者急性肺损伤(ALI)的发生率、急性呼吸窘迫综合征(ARDS)的发生率、呼吸机使用时间、死亡率。**结果:** 治疗组93例患者,治愈92例,死亡1例,死亡率为1.08%(1/93),治疗过程中发生ALI34例,ARDS12例,呼吸机使用时间为 (4.2 ± 2.1) d。对照组92例患者治愈88例,死亡4例,死亡率为4.35%(4/92),治疗过程中发生ALI43例,ARDS17例,呼吸机使用时间为 (8.2 ± 2.7) d。两组患者ALI发生率、ARDS发生率、呼吸机使用时间、治愈率差异均有统计学意义($P < 0.05$)。**结论:** 对于严重烧伤伴中重度吸入性损伤的患者,在气管切开的前提下,给予常规传统治疗的同时,采用大剂量乌司他丁与沐舒坦早期联合使用给药,能够明显的提高治愈率,降低并发症,值得在临床上广泛推广应用。

关键词: 乌司他丁;沐舒坦;严重烧伤;疗效

中图分类号: R644 **文献标识码:** A **文章编号:** 1673-6273(2014)15-2906-03

Efficacy of High-dose Ulinastatin and Ambroxol Using for Early Combination of Severe Burns with Severe Inhalation Injury*

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ABSTRACT Objective: To investigate the clinical efficacy of large doses Ulinastatin with ambroxol using for severe burns with severe inhalation injury in patients with early joint. **Methods:** 185 cases of severe burns with severe inhalation injury from May 2003 to May 2013 treated in our hospital were selected and randomly divided into two groups, the treatment group with 93 cases, 92 cases of the control group. Both groups were diagnosed with moderate to severe inhalation injury, immediately given the traditional conventional treatment: oxygen, depending on the situation as soon as possible preventive tracheotomy airway humidification and airway lavage, stand back suction, ventilator-assisted breathing. Treatment group was given Ulinastatin 400,000 units every 8h intravenously Ambroxol 450mg, every 12h micropump bolus on the basis of the conventional treatment; control group were given ulinastatin 100,000 units every 8h infusion, ambroxol 30mg, every 8h intravenously, treatment for 10 days. Acute lung injury(ALI) the incidence of acute respiratory distress syndrome (ARDS) the incidence of ventilator use of time, death rate were compared between the two groups of patients with. **Results:** The treatment group, 93 patients were cured 92 cases, 1 patient died, the mortality rate was 1.08% (1/93), the course of treatment ALI34 cases, ARDS12 cases, mechanical ventilation time was (4.2 ± 2.1) d. Control group, 92 patients were cured 88 cases, 4 deaths, the mortality rate was 4.35% (4/92), the course of treatment ALI43 cases, ARDS17 cases, mechanical ventilation time was (8.2 ± 2.7) d. Two groups of patients the incidence of ALI, ARDS incidence of ventilator use of time, the cure rate differences were statistically significant ($P < 0.05$). **Conclusion:** For severe burns with severe inhalation injury patients, tracheotomy premise, given conventional treatment, giving high-dose ulinastatin conjunction with ambroxol early could significantly improve the cure rate, reduce complications, so it was worth widely used in clinical application.

Key words: Ulinastatin; Mucosolvan; Severe burns; Efficacy

Chinese Library Classification: R644 **Document code:** A

Article ID: 1673-6273(2014)15-2906-03

* 基金项目: 卫生部科技计划项目(W2012ZT72)

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(收稿日期: 2013-10-11 接受日期: 2013-11-08)

前言

吸入性损伤指的是呼吸道、甚至肺部实质的损伤,主要是由热、化学损伤同时存在引起^[1]。严重烧伤的病人常存在吸入性损伤,如果深度烧伤创面清理不及时,极易发生全身感染,而吸入性损伤如果未得到及时治疗,常可引发窒息、急性肺损伤、肺部严重感染及急性呼吸窘迫综合症(ARDS)等病症^[2-6]。因此,吸入性损伤是烧伤病人治疗的重点及难点,有极高的病死率。本研究选择 185 例严重烧伤伴中重度吸入性损伤患者,探讨了大剂量乌司他丁(广东天普医药公司生产)与沐舒坦(盐酸氨溴索,勃林格殷格翰公司生产)早期联合使用在治疗严重烧伤伴中重度吸入性损伤的疗效,现报告如下。

1 资料与方法

1.1 临床资料

2003 年 5 月~2013 年 5 月在我院接受治疗的 185 例严重烧伤伴中重度吸入性损伤患者,其中男 142 例,女 42 例,年龄 14~65 岁,平均年龄(36.8±14.8)岁。烧伤面积 50%~97% TBSA,Ⅲ度烧伤面积 25%~94%,均为火焰烧伤。中度吸入性损伤 136 例,重度吸入性损伤 49 例。随机的分为两组,治疗组 93 例,对照组 92 例,两组患者在年龄、性别、烧伤程度及吸入性损伤程度等方面的差异无统计学意义,具有可比性。

1.2 治疗方法

185 例严重烧伤患者确诊有吸入性损伤后,按常规传统方法给予立即吸氧,尽早气管切开,冲洗气道,排除分泌物,解除

气道梗阻,保持气道畅通,湿化气道及气道灌洗,翻身拍背吸痰,必要时呼吸机辅助呼吸,全身应用抗生素,并采用雾化吸入 2 mL 0.45% 氯化钠溶液 +5 mg 地塞米松 +8U 庆大霉素 +15 mg 沐舒坦。治疗组在常规治疗的基础上给予乌司他丁 40 万单位,每隔 8h 静脉滴注,沐舒坦 450 mg,每隔 12 h 微泵静推,疗程为 10 天;对照组给予乌司他丁 10 万单位,每隔 8 h 静滴,沐舒坦 30 mg,每隔 8h 静滴,疗程为 10 天。患者治疗期间积极给予营养支持,抗感染,尽早修复深度烧伤创面,不定期的床边支气管镜检查和治疗,必要时应用呼吸机辅助呼吸治疗。加强护理,鼓励患者深呼吸和有效咳嗽,排痰困难者拍背吸痰,1 次/2~4h,利于气道分泌物排出。比较两组患者的临床疗效。

1.3 统计学分析

运用 SPSS19.0 软件对数据进行统计分析,两组病例治愈率的比较采用 χ^2 检验, $P<0.05$ 表示差异有统计学意义。

2 结果

2.1 两组患者的治疗效果

185 例严重烧伤伴中重度吸入性损伤患者,治愈 180 例,死亡 5 例。治疗组 93 例患者,治愈 92 例,死亡 1 例,病人死于急性肾功能衰竭,治疗组死亡率为 1.08%(1/93),对照组 92 例患者治愈 88 例,死亡 4 例,2 例死于急性肾功能衰竭,1 例死于烧伤脓毒症,1 例死于多器官功能障碍综合症(MODS),对照组死亡率为 4.35%(4/92),两组患者死亡率差异有统计学意义($P<0.05$)。见表 1。

表 1 两组患者临床疗效

Table 1 Comparison of clinical efficacy of two groups

Category	number of cases	Cure	Death	Cure rate(%)
Treatment group	93	92	1	1.08*
Control group	92	88	4	4.35

注:*表示与对照组相比, $P<0.05$ 。

Note: * indicates $P<0.05$ comparing with control group.

2.2 两组患者并发症发生情况及呼吸机使用时间比较

治疗组治疗过程中发生 ALI34 例,发生率为 36.56%,ARDS12 例,发生率为 12.90%,呼吸机使用时间为(4.2±2.1)d;对照组治疗过程中发生 ALI43 例,发生率为 46.74%,

ARDS17 例,发生率为 18.48%,呼吸机使用时间为(8.2±3.7)d。两组患者 ALI 发生率、ARDS 发生率、呼吸机使用时间、治愈率差异均有统计学意义($P<0.05$)。见表 2。

表 2 两组患者并发症发生情况及呼吸机使用时间比较

Table 2 Comparison of incidence of complications and ventilator time in groups of patients

Category	例数	ALI	ARDS	呼吸机使用时间
Treatment group	93	34(36.56*)	12(12.90*)	(4.2±2.1)*d
Control group	92	43(46.74)	17(18.48)	(8.2±3.7)d

注:*表示与对照组相比, $P<0.05$ 。

Note: * indicates $P<0.05$ comparing with control group.

观察组用药过程中有 9 例发生不同程度的不良反应,其中 6 例出现恶心、呕吐、腹泻等症,3 例皮疹,不良反应发生率为 9.68%;对照组 8 例发生不同程度的不良反应,其中 5 例出现恶

心、呕吐、腹泻等症,3 例皮疹,不良反应发生率为 8.70%,两组不良反应发生率差异无统计学意义。出现不良反应的患者均经有效措施处理后好转,未终止用药。

3 讨论

严重烧伤伴吸入性损伤的患者常发生肺部并发症及全身性感染,是引发患者死亡的主要原因^[7-8]。相关研究报道,严重烧伤伴吸入性损伤的病死率可达 60%,而重度吸入性损伤的病死率能够达到 90%^[9-11]。因此,如何提高严重烧伤伴中重度吸入性损伤病人的治愈率,降低病死率,仍是烧伤工作者需不断研究的课题。

气管切开是治疗吸入性损伤的关键步骤,也是防止气道梗阻的有效措施,还有利于低氧血症的治疗^[12]。除了对明确有中重度吸入性损伤或高危呼吸困难的患者尽早气管切开,对于特重度烧伤还未准确判断损伤程度的患者,也应果断进行预防性气管切开^[13]。早期气管切开具有以下优点:①便于手术时呼吸道的管理;②便于清理黏膜脱落坏死组织及呼吸道分泌物;③便于机械通气^[14]。气管切开后应常规做心电图监测,观察氧分压(PaO₂)及血氧饱和度(SaO₂)的变化,如果 PaO₂降低到 85%以下,最好采用人工呼吸机辅助呼吸,便于二氧化碳排出及组织供氧^[15-17]。

乌司他丁可以抑制中性粒细胞分泌蛋白酶,抑制多种炎症反应,降低超氧化物歧化酶,减少氧自由基的释放,可以减轻炎症反应对机体器官的损害。沐舒坦具有促进粘液排除,溶解分泌物的特点,因此,可以促进烧伤患者排痰,改善其呼吸状态,保护呼吸道黏膜,保证呼吸道黏膜的表面活性物质发挥正常的作用^[18-20]。本研究对严重烧伤伴中重度吸入性损伤患者尽早气管切开,在常规治疗的基础上治疗组采用大剂量乌司他丁与沐舒坦联合用药,结果显示,治疗组 93 例患者,治愈 92 例,死亡 1 例,死亡率为 1.08%(1/93),对照组 92 例患者治愈 88 例,死亡 4 例,死亡率为 4.35%(4/92),两组患者死亡率差异有统计学意义(P<0.05)。治疗组 1 例死于急性肾功能衰竭,对照组 2 例死于急性肾功能衰竭,1 例死于烧伤脓毒症,1 例死于多器官功能障碍综合征(MODS)。说明了两组患者均取得了良好的治疗效果,患者的治愈率较目前研究报道高,而大剂量的乌司他丁与沐舒坦联合用药的效果优于小剂量的效果。另外,两组患者 ALI 发生率、ARDS 发生率差异均有统计学意义(P<0.05)。总之,采用大剂量乌司他丁与沐舒坦早期联合使用治疗严重烧伤伴中重度吸入性损伤的患者,能够明显的提高治愈率,降低并发症,值得在临床上广泛推广应用。

参考文献(References)

- [1] 胡晓骅,张会英,葛艳玲,等. 乌司他丁对严重烧伤后多脏器功能的保护作用[J]. 中华医学杂志, 2005, 85(41): 2889-2894
Hu Xiao-hua, Zhang Hui-ying, Ge Yan-ling, et al. Protective effect of ulinastatin for multiple organ after severe burns[J]. National Medical Journal of China, 2005, 85(41): 2889-2894
- [2] 谢康,黄跃生,安瑞等. 乌司他丁对严重烧伤患者伤后早期心肌损害的防治作用[J]. 中华烧伤杂志, 2006, 22(3): 180-183
Xie Kang, Huang Yue-sheng, An Rui, et al. The effect of ulinastatin in early injury myocardial damage in rats after severe burn patients[J]. Chinese Journal of Burns, 2006, 22(3): 180-183
- [3] 袁运长,尹邦良,周文杰,等. 大剂量沐舒坦对体外循环术后急性呼吸窘迫综合征患者的疗效观察[J]. 中国老年学杂志, 2010, 30(9):

1297-1298

- Yuan Yun-chang, Yin Bang-liang, Zhou Wen-jie, et al. Dose ambroxol on patients with acute respiratory distress syndrome after CPB[J]. Chinese Journal of Gerontology, 2010, 30(9): 1297-1298
- [4] 孙勇,孙曙光,王静,等. 谷氨酰胺联合乌司他丁对严重烧伤患者营养状况及免疫功能的影响[J]. 广东医学, 2010, 31(23): 3126-3128
Sun Yong, Sun Shu-guang, Wang Jing, et al. Glutamine Joint Ulinastatin on nutritional status and immune function of patients with severe burns[J]. Guangdong Medicine, 2010, 31(23): 3126-3128
- [5] 胡晓骅,葛艳玲,辛动,等. 乌司他丁对严重烧伤小型猪肠黏膜损伤的影响[J]. 中华烧伤杂志, 2003, 19(z1): 18-21
Hu Xiao-hua, Ge Yan-ling, Xin Dong, et al. Effect of Ulinastatin on small intestines mucosa severe burn injury[J]. Chinese Journal of Burns, 2003, 19(z1): 18-21
- [6] 徐鹏,方勇,俞为荣,等. 乌司他丁对严重烧伤早期患者肺组织的保护作用[J]. 上海交通大学学报(医学版), 2010, 30(12): 1474-1476.
Xu Peng, Fang Yong, Yu Wei-rong, et al. Lung protective effect of Ulinastatin in early severe burn patients[J]. Journal of Shanghai Jiao-tong University (Medical Sciences), 2010, 30(12): 1474-1476
- [7] 谢康,黄跃生. 乌司他丁对严重烧伤大鼠血清中致炎因子的影响及意义[J]. 第三军医大学学报, 2004, 26(18): 1643-1645
Xie Kang, Huang Yue-sheng. Influence and significance of Ulinastatin on severe burn serum proinflammatory cytokines[J]. Acta Academiae Medicinae Militaris Tertiae, 2004, 26(18): 1643-1645
- [8] 张庆洋. 乌司他丁联合血必净对严重烧伤患者的早期治疗效果[J]. 中华烧伤杂志, 2011, 27(3): 191-192
Zhang qing-yang. Early treatment effect of Ulinastatin joint Xuebijing in severely burned patients[J]. Chinese Journal of Burns, 2011, 27(3): 191-192
- [9] 谢才德,秦蓁,邹华兰,等. 急性呼吸窘迫综合征临床治疗观察及预后影响因素分析[J]. 现代生物医学进展, 2012, 12(25): 4921-4923
Xie Cai-de, Qin Zhen, Zou Hua-lan, et al. Analysis of acute respiratory distress syndrome clinical observation and prognostic factors[J]. Progress in Modern Biomedicine, 2012, 12(25): 4921-4923
- [10] 李卫,许涛,陆平言,等. 乌司他丁治疗严重烧伤的疗效分析[J]. 中华急诊医学杂志, 2008, 17(11): 1203-1205
Li Wei, Xu Tao, Lu Ping-yan, et al. Efficacy of Ulinastatin in the treatment of severe burns[J]. Journal of Emergency Medicine, 2008, 17(11): 1203-1205
- [11] 张庆洋,孙建平,张水良,等. 严重烧伤患者早期应用乌司他丁疗效观察[J]. 中华烧伤杂志, 2008, 24(6): 458-459
Zhang Qing-yang, Sun Jian-ping, Zhang Shui-liang, et al. Efficacy of early application of Ulinastatin in severely burned patients[J]. Chinese Journal of Burns, 2008, 24(6): 458-459
- [12] 李勇,吴峰,林挺岩,等. 大剂量沐舒坦治疗慢性阻塞性肺病急性加重期的临床研究[J]. 中华老年医学杂志, 2013, 32(2): 162-164
Li Yong, Wu Feng, Lin Ting-yan, et al. Dose ambroxol in the treatment of chronic obstructive pulmonary disease with acute exacerbation of clinical[J]. Chinese Journal of Geriatrics, 2013, 32(2): 162-164
- [13] 刘康峰,黄文娟,马劲光,等. 沐舒坦联合肺灌洗对重型颅脑损伤气管切开后患者肺部感染的疗效[J]. 中华神经医学杂志, 2011, 10(11): 1156-1159

- [10] 张素芹, 郭安梅, 郭素香, 等. 两种诊断方法对术后认知功能障碍评估分析[J]. 现代生物医学进展, 2009, 9(20): 3929-3931
Zhang Su-qin, Guo An-mei, Guo Su-xiang, et al. Evaluation and analysis of two diagnostic methods of postoperative cognitive dysfunction [J]. Progress in Modern Biomedicine, 2009, 9(20): 3929-3931
- [11] 肖春红, 郭安梅, 郭素香, 等. 异氟醚对认知功能的影响机制[J]. 现代生物医学进展, 2010, 10(17): 3382-3383, 3346
Xiao Chun-hong, Guo An-mei, Guo Su-xiang, et al. Influence of isoflurane on cognitive function[J]. Progress in Modern Biomedicine, 2010, 10(17): 3382-3383, 3346
- [12] Dr. Hemanshu Prabhakar. Early cognitive Functions in Patients after Embolization in Neuroradiological Suite-A Comparison of Two Anesthetic Techniques[J]. Journal of Anesthesia & Clinical Research, 2011, 2(3): 1-3
- [13] Shih J, May LDV, Gonzalez HE, et al. Delayed environmental enrichment reverses sevoflurane-induced memory impairment in rats [J]. Anesthesiology, 2012, 116(3): 586-602
- [14] Dumas A, Dupuis GH, Searle N, et al. Early versus late extubation after coronary artery bypass grafting: effects on cognitive function[J]. Journal of cardiothoracic and vascular anesthesia, 1999, 13 (2): 130-135
- [15] Evered LA, Silbert BS, Scott DA, et al. Plasma amyloid beta42 and amyloid beta40 levels are associated with early cognitive dysfunction after cardiac surgery[J]. The Annals of Thoracic Surgery, 2009, 88(5): 1426-1432
- [16] Padmanabhan U, Leslie K, Eer AS, et al. Early cognitive impairment after sedation for colonoscopy: the effect of adding midazolam and/or fentanyl to propofol[J]. Anesthesia and Analgesia, 2009, 109(5): 1448-1455
- [17] Elsinga RM, Roze E, VanBraeckel K.N.J.A, et al. Motor and cognitive outcome at school age of children with surgically treated intestinal obstructions in the neonatal period[J]. Early human development, 2013, 89(3): 181-185
- [18] Evered LA, Silbert BS, Scott DA, et al. Plasma amyloid beta42 and amyloid beta40 levels are associated with early cognitive dysfunction after cardiac surgery[J]. The Annals of Thoracic Surgery, 2009, 88(5): 1426-1432
- [19] Mazul Sunko B, Hromatko I, Tadinac M, et al. Subclinical neurocognitive dysfunction after carotid endarterectomy-the impact of shunting [J]. Journal of neurosurgical anesthesiology, 2010, 22(3): 195-201

(上接第 2808 页)

- Liu Kang-feng, Huang Wen-juan, Ma Jin-guang, et al. Efficacy of mucosolvan joint lavage for severe traumatic brain injury patients with pulmonary infection after tracheotomy[J]. Chinese Journal of Medicine, 2011, 10(11): 1156-1159
- [14] 贾东岩, 王志刚, 李亚光, 等. 沐舒坦雾化吸入联合静脉注射治疗脑卒中伴坠积性肺炎的疗效[J]. 中国老年学杂志, 2012, 32(17): 3804-3805
Jia Dong-yan, Wang Zhi-gang, Li Ya-guang, et al. Effect of mucosolvan inhalation combined with intravenous therapy for stroke efficacy hypostatic pneumonia[J]. Chinese Journal of Gerontology, 2012, 32(17): 3804-3805
- [15] 刘健, 施燕, 窦懿, 等. 早期应用乌司他丁对严重烧伤患者脏器功能的保护[J]. 上海交通大学学报(医学版), 2008, 28(5): 578-581
Liu Jian, Shi Yan, Dou Yi, et al. Early application of Ulinastatin in organ function protection in patients with severe burn[J]. Journal of Shanghai Jiaotong University (Medical Sciences), 2008, 28 (5): 578-581
- [16] 马培华, 时洪星. 沐舒坦治疗新生儿胎粪吸入综合征的临床研究[J]. 中国妇幼保健, 2008, 23(9): 1238-1239
Ma Pei-hua, Shi Hong-xing. Ambroxol in the treatment of neonatal meconium aspiration syndrome[J]. Chinese Maternal and Child Health, 2008, 23(9): 1238-1239
- [17] 李清平, 董文斌, 翟雪松, 等. 固尔舒与沐舒坦预防早产儿呼吸窘迫综合征的临床研究[J]. 中国妇幼保健, 2007, 22(21): 2944-2945
Li Qing-ping, Dong Wen-bin, Zhai Xue-song, et al. Guershu jointed with ambroxol in preventing preterm children with respiratory distress syndrome[J]. Chinese Maternal and Child Health, 2007, 22 (21): 2944-2945
- [18] 顾金萍, 于健, 王俊松, 等. 乌司他丁在急性呼吸窘迫综合征的临床应用研究[J]. 现代生物医学进展, 2012, 12(14): 2695-2697, 2705
Gu Jin-ping, Yu Jian, Wang Jun-song, et al. Clinical application of Ulinastatin in acute respiratory distress syndrome in[J]. Progress in Modern Biomedicine, 2012, 12(14): 2695-2697, 2705
- [19] 潘珍, 陈春泉. 乌司他丁对严重烧伤患者重要脏器保护作用的 Meta 分析[J]. 中国药师, 2012, 15(5): 700-704
Pan Zhen, Chen Chun-quan. Meta-analysis of protection effect of Ulinastatin in important organs in patients with severe burn[J]. Chinese pharmacist, 2012, 15(5): 700-704
- [20] 信文启, 李新宇, 周新, 等. 乌司他丁对大鼠毛细血管渗漏综合征肺毛细血管通透性的影响 [J]. 现代生物医学进展, 2010, 10(24): 4672-4674
Xin Wen-qi, Li Xin-yu, Zhou xin, et al. Influence of Ulinastatin for rat capillary leak syndrome, pulmonary capillary permeability[J]. Progress in Modern Biomedicine, 2010, 10(24): 4672-4674