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乌司他丁辅助治疗急性重症胰腺炎的疗效及对 occludin、CRPI、IL-6 水平的影响 *

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摘要 目的: 研究乌司他丁辅助治疗急性重症胰腺炎的疗效及对咬合蛋白(Occludin)、C 反应蛋白(快速)(CRPI)、白细胞介素 6 (IL-6)水平的影响。**方法:** 选择 2014 年 12 月至 2016 年 11 月在我院进行治疗的 118 例急性重症胰腺炎患者, 随机将其均分为观察组(59 例)和对照组(59 例), 对照组给予常规治疗, 观察组患者则在对照组治疗方案的基础上增加乌司他丁辅助治疗, 两组患者的治疗疗程均为两周, 记录并比较两组患者治疗前后的血清 occludin、CRPI、IL-6 水平, 治疗后腹胀、腹痛、恶性呕吐及腹膜刺激征等体征消失时间及临床疗效。**结果:** 治疗后, 观察组和对照组患者的总有效率分别是 88.1%、69.5%, 观察组总有效率显著高于对照组($P < 0.05$); 观察组患者治疗后的血清 occludin 水平较对照组患者显著升高($P < 0.05$), 血清 IL-6 及 CRPI 水平显著低于对照组, 且腹胀、腹痛、恶性呕吐、腹膜刺激征等体征消失时间显著短于对照组($P < 0.05$)。**结论:** 乌司他丁辅助治疗重症急性胰腺炎的临床疗效显著优于常规治疗, 不仅能改善腹胀、腹痛、恶性呕吐及腹膜刺激征, 而且可有效降低患者血清 CRPI、IL-6 水平和提高 occludin 水平。

关键词: 乌司他丁; 急性重症胰腺炎; 咬合蛋白; C 反应蛋白(快速); 白细胞介素 6

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Effects of Magnesium Isobutyrate Supplementation on CAM-1, CRPI, IL-2 Levels and Organ Function in Patients with Acute Severe Pancreatitis*

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ABSTRACT Objective: To study the efficacy of ulinastatin in the treatment of acute severe pancreatitis and its effect on the serum occludin, C-reactive protein (rapid, CRPI) and Interleukin 6 (IL-6) levels. **Methods:** Eleven patients with acute severe pancreatitis from December 2014 to November 2016 were randomly divided into the observation group ($n=59$) and the control group ($n=59$). The control group was given routine treatment, while the patients in observation group were treated with ulinastatin on the basis of control group. Both groups were treated for two weeks. The serum occludin, CRPI and IL-6 levels were recorded and compared between the two groups before and after treatment. The disappearance time of abdominal distension, abdominal pain, malignant vomiting and peritoneal irritation signs and other signs and clinical efficacy were also compared. **Results:** After treatment, the total effective rate was 88.1% in the observation group and 69.5% in the control group ($P < 0.05$), the levels of serum occludin in the observation group were significantly higher than that in the control group ($P < 0.05$), the serum IL-6 and CRPI levels were significantly lower than those in the control group, the disappearance time of abdominal distension, abdominal pain, malignant vomiting and peritoneal irritation were significantly shorter in the observation group than those in the control group ($P < 0.05$). **Conclusion:** The clinical efficacy of ulinastatin in the treatment of severe acute pancreatitis is superior to conventional treatment, it can not only improved the bloating, abdominal pain, malignant vomiting and peritoneal irritation, but also effectively reduce the serum CRPI, IL-6 levels and increase the serum occludin level.

Key words: Ulinastatin; Acute severe pancreatitis; Bite protein; C-reactive protein (rapid); Interleukin 6

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前言

急性重症胰腺炎具有致死率高、预后差、病情严重等特征

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^[1],死亡率高达 76.2%,占消化内分泌系统疾病死亡率的 30%,生活中很多因素都会诱发急性重症胰腺炎的发生,包括过度酗酒、胆道性疾病及不良饮食习惯等^[2,3],该病症的临床表现主要有发热、腹痛、甚至是腹腔出现大量积水,以致于出现坏死性病灶,属于严重危险病症。相关研究表明^[4,5]各种细胞因子、炎症介质及补体等与急性重症胰腺炎的发生及发展密切相关。乌司他丁是一种提取于人尿中最精制的糖蛋白,具有蛋白酶抑制剂作用,对急性胰腺炎、慢性复发性胰腺炎及急性循环衰竭抢救治疗颇为有效。本研究重点研究了乌司他丁对急性重症胰腺炎的临床疗效及对患者血清 occludin、CRPI、IL-6 水平的影响。

1 资料与方法

1.1 一般资料

选择 2014 年 12 月至 2016 年 11 月在我院进行治疗的 118 例急性重症胰腺炎患者,入选标准^[6]:(1)经 CT 及其他检查,确诊急性重症胰腺炎者;(2)42~65 岁;(3)意识清醒;(4)心、肝、脾等重要脏器无严重病变;(5)治疗方案经患者及其家属知情同意。排除标准^[7]:(1)近两个月上消化道出现过大量出血者;(2)意识模糊不清者;(3)心、肝、脾等重要脏器严重病变者;(4)过敏性体质。观察组中,男 32 例,女 27 例,年龄 42~64 岁,平均年龄(52.71± 9.35)岁,平均发病时间(2.35± 0.94)h;对照组中,男 31 例,女 28 例,年龄 43~65 岁,平均年龄(53.04± 9.97)岁,平均发病时间(2.44± 0.91)h,两组一般资料比较差异无统计学意义(P>0.05),具有可比性,见表 1。

表 1 两组患者一般资料的比较

Table 1 Comparison of the general information between the two groups of patients

| Group | Sex | | Average age(a) | Mean onset time(h) |
|-------------------|------|--------|----------------|--------------------|
| | male | female | | |
| Observation group | 32 | 27 | 52.71± 9.35 | 2.35± 0.94 |
| Control group | 31 | 28 | 53.04± 9.97 | 2.44± 0.91 |

1.2 治疗方法

对照组采用肠胃减压、镇静止痛、灌洗腹腔膜、抑制酸和酶以及正常的营养支持和补液等一些列常规性治疗,另外采用法莫替丁(湖北荷普药业股份有限公司 国药准字 H20093273)对患者进行静脉滴注,80 mg/d,同时还静脉滴注 0.1%的普鲁卡因(上海旭东海普药业有限公司 国药准字 H31020817),20 mg/d,连续使用 14 d;观察组则在对照组治疗方案的基础上增加乌司他丁(广东天普生化医药股份有限公司 国药准字 H19990134)辅助治疗,将 40 万单位的乌司他丁溶于 500 mL 浓度为 5%的葡萄糖注射液或者 500 mL 浓度为 0.9%的氯化钠注射液中进行静脉滴注,2 次/d,持续应用 14 d。

1.3 观察指标

入院前后收集空腹静脉血 5 mL,常规离心后置于保温箱中备用,温度设置为 -80℃,采用免疫荧光法检测患者治疗前后血清 occludin 水平值,利用酶联免疫吸附法对治疗前后的 CRPI 及 IL-6 水平值进行检测,同时根据《急性胰腺炎诊治指南》

对两组患者治疗后的腹胀、腹痛、恶性呕吐、腹膜刺激征等体征消失时间进行比较评价^[8]。根据体征消失时间长短进行临床疗效评价:显效:以上症状体征 5 d 内完全消失且实验指标恢复正常;有效:上述指标在 5 d 内显著减轻;无效:上述指标在 10 d 内未见明显减轻。

1.4 统计学分析

数据处理采用 SPSS 19.0 统计软件进行,用均数± 标准差($\bar{x} \pm s$)表示计量资料,组间比较采用 t 检验,用[(n)%]表示计数资料,组间比较采用 χ^2 检验,以 P<0.05 为差异有统计学意义。

2 结果

2.1 两组治疗前后血清 occludin 水平的比较

治疗前,两组血清 occludin 水平比较差异无统计学意义(P>0.05);治疗后,观察组血清 occludin 水平明显高于对照组(P<0.05)。见表 2。

表 2 两组治疗前后血清 occludin 水平的比较($\bar{x} \pm s$)

Table 2 Comparison of the serum occludin levels between the two groups before and after treatment ($\bar{x} \pm s$)

| Group | Number of cases | Occludin(ng/L) | | t value | P value |
|-------------------|-----------------|------------------|-----------------|---------|---------|
| | | Before treatment | After treatment | | |
| Observation group | 59 | 111.12± 12.43 | 128.54± 18.35* | 6.037 | 0.000 |
| Control group | 59 | 109.42± 11.96 | 116.34± 12.83 | 3.030 | 0.003 |
| t value | | 0.757 | 4.185 | | |
| P value | | 0.451 | 0.000 | | |

Note: After treatment, compared with the control group, *P<0.05.

2.2 两组治疗前后血清 CRPI 及 IL-6 水平的比较

治疗前,两组血清 IL-6 及 CRPI 水平比较差异无统计学意义(P>0.05);治疗后,观察组血清 IL-6 及 CRPI 水平明显低于对

照组(P<0.05),见表 3。

2.3 两组症状体征消失时间比较

治疗后,观察组患者腹胀、腹痛、恶性呕吐、腹膜刺激征等

体征消失时间较对照组明显缩短(P<0.05),见表 4。

治疗后,观察组总有效率(88.1%)显著高于对照组(69.5%, P<0.05)。见表 5。

2.4 两组治疗后临床疗效比较

表 3 两组治疗前后血清 CRPI 及 IL-6 水平的比较($\bar{x} \pm s$)

Table 3 Comparison of the serum CRPI and IL - 6 levels between the two groups before and after treatment($\bar{x} \pm s$)

| Group | Number of cases | CRPI(mg/L) | | T value | P value | IL-6(ng/mL) | | T value | P value |
|-------------------|-----------------|------------------|-----------------|---------|---------|------------------|-----------------|---------|---------|
| | | Before treatment | After treatment | | | Before treatment | After treatment | | |
| Observation group | 59 | 179.51± 50.34 | 73.56± 23.47*# | 14.652 | 0.000 | 71.53± 8.34 | 29.98± 5.46*# | 32.017 | 0.000 |
| Control group | 59 | 255.18± 68.34 | 131.52± 41.32* | 11.894 | 0.000 | 78.72± 8.24 | 43.86± 6.47* | 25.558 | 0.000 |
| T value | | 6.848 | 9.369 | | | 4.711 | 12.593 | | |
| P value | | 0.000 | 0.000 | | | 0.000 | 0.000 | | |

Note: Compared with this group before treatment, * P<0.05, compared with the control group after treatment, #P<0.05.

表 4 两组症状体征消失时间的比较($\bar{x} \pm s$)

Table 4 Comparison of the disappearance of symptoms and signs between two groups($\bar{x} \pm s$)

| Group | Number of cases | Bloating | stomach ache | Malignant vomiting | Peritoneal irritation |
|-------------------|-----------------|------------|--------------|--------------------|-----------------------|
| Observation group | 59 | 2.92± 0.41 | 1.77± 0.26 | 2.34± 0.31 | 1.86± 0.26 |
| Control group | 59 | 4.63± 0.86 | 3.81± 0.52 | 3.72± 0.36 | 4.25± 0.91 |
| T value | | 13.786 | 26.952 | 22.312 | 19.397 |
| P value | | 0.000 | 0.000 | 0.000 | 0.000 |

表 5 两组治疗后临床疗效的比较[例(%)]

Table 5 Comparison of the efficacy of the two groups [n(%)]

| Group | Number of cases | Very effective | Effective | Invalid | Total efficiency |
|-------------------|-----------------|----------------|-----------|----------|------------------|
| Observation group | 59 | 38(64.4) | 14(23.7) | 7(11.9) | 52(88.1) |
| Control group | 59 | 28(47.5) | 13(22.0) | 18(30.5) | 41(69.5) |
| χ^2 value | | | | | 6.141 |
| P value | | | | | 0.013 |

3 讨论

急性重症胰腺炎是临床常见的急腹症,也是急性胰腺炎中特殊的一种^[9],其诱导因素众多,包括过度酗酒、胆道性疾病及不良饮食习惯等。多种因素能够激活胰腺内胰酶,促进胰腺组织发生水肿,甚至是出现血肿和坏死等炎症反应,一旦胰腺坏死,随之伴随而来的并发症包含腹膜炎、感染及休克等^[10,11],这些症状被临床称为急性重症胰腺炎,具有致死率高、病情发展迅速及预后差的特征^[12]。

急性重症胰腺炎与炎症因子的产生及其级联瀑布效应密切相关,由中性粒细胞产生的炎症因子 IL-6 及 CRPI 在急性重症胰腺炎的发病过程中有着重要的作用,国外研究表明^[13,14]血清炎性细胞因子水平是预测严重程度的重要指标,对其进行动态观察水平变化情况可以充分反映药物治疗的有效性。IL-6 是众多炎性介质中重要的急性反应期炎症介质,主要变现产生于激活血管内皮细胞和炎性细胞,进而促进炎症反应发生,导致组织细胞的严重损伤。相关研究表明^[15,16]乌司他丁作为一种蛋白酶,可抑制多种酶活性,促进自由基的清除,减轻炎症反应,利于微循环衰竭状态的改善。研究表明^[17,18]经乌司他丁治疗一

个疗程后,急性重症胰腺炎患者血清 occludin 水平逐渐趋于正常值。本研究中,乌司他丁治疗后的患者血清 occludin 水平显著高于常规治疗组,且血清 IL-6 水平值下降更明显,提示乌司他丁可以显著提高血清 occludin 水平值和降低血清 IL-6 水平值。炎症因子致使机体胰腺的局部损害是急性重症胰腺炎的发病机制,相关研究表明^[19,20]CRPI 是一种非特异性免疫机制,可以激活补体及单核吞噬细胞系统,且能侵入真菌、细菌及寄生虫等,进而将其清除。本研究结果显示乌司他丁辅助治疗组治疗后的 CRPI 水平显著低于常规治疗组,总有效率(88.1%)显著高于常规治疗组,且前者的腹胀、腹痛、恶性呕吐、腹膜刺激征等体征消失时间更短。

综上所述,乌司他丁辅助治疗重症急性胰腺炎的临床疗效显著优于常规治疗,不仅能改善腹胀、腹痛、恶性呕吐及腹膜刺激征,可能与其有效降低患者血清 CRPI、IL-6 水平和提高 occludin 水平有关。

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(上接第 3462 页)

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