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乌司他丁治疗急性胰腺炎的临床疗效及对患者血清炎性因子水平的影响

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摘要 目的：观察乌司他丁在急性胰腺炎临床治疗中的作用效果，分析其临床治疗价值。**方法**：选取我院治疗的急性胰腺炎患者178例，根据治疗方法不同分为观察组和对照组，每组89例。对照组患者采用奥曲肽治疗，观察组患者采用乌司他丁与奥曲肽联合治疗。观察并比较治疗前后患者APACHEⅡ评分和血清炎症因子变化及临床疗效。**结果**：入院时，两组血清CRP、IL-1、IL-6、TNF-α、APACHEⅡ评分无统计差异(P>0.05)，治疗后，组内CRP、IL-1、IL-6、TNF-α、APACHEⅡ评分明显下降(P＜0.05)；观察组CRP、IL-1、IL-6、TNF-α、APACHEⅡ评分显著低于参照组(P＜0.05)；观察组临床总有效率(86.52%)显著高于参照组(71.91%)，观察组并发症(12.36%)明显低于参照组(24.72%)，P<0.05，组间有统计差异。**结论**：乌司他丁能够显著提升急性胰腺炎的临床疗效，促进患者康复，其作用机制可能与抑制炎症因子表达有关。

关键词：乌司他丁；急性胰腺炎；IL-1；IL-6；CRP；TNF-α

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Effect of Ulinastatin on Acute Pancreatitis and Serum Levels of Inflammatory Factors in Patients

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ABSTRACT Objective: To observe the clinical effect of ulinastatin on acute pancreatitis and the serum levels of inflammatory factors in patients. **Methods:** 178 cases with acute pancreatitis who were treated in our hospital were selected and according to the different treatment methods, the patients were divided into the observation group and the control group, with 89 cases in each group. The patients in the observation group were treated with UTI and octreotide, while the patients in the control group were treated with octreotide. Then the changes of APACHEⅡ score and serum inflammatory factors of patients were observed and compared before and after treatment. **Results:** At admission, the levels of serum CRP, IL-1, IL-6, TNF-α and APACHEⅡ score were without statistical differences (P> 0.05). After treatment, the CRP, IL-1, IL-6, TNF-α and APACHEⅡ score in the two groups significantly decreased (P<0.05). The CRP, IL-1, IL-6, TNF-α and APACHEⅡ scores in the observation group were significantly lower than those of the control group (P <0.05). The total clinical efficiency rate of the observation group was 86.52%, which was significantly higher than 71.91 in the control group, and the complications in the observation group was 12.36%, which was significantly lower than 24.72% in the control group, and the differences were statistically significant (P<0.05). **Conclusion:** Ulinastatin can significantly improve the clinical efficacy of acute pancreatitis, and promote the rehabilitation of patients, and its mechanism may be related to inhibition of inflammatory cytokine expressions.

Key words: UTI; Acute pancreatitis; IL-1; IL-6; CRP; TNF-α

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前言

急性胰腺炎作为由于消化酶异常引发的一类急性炎症性疾病，如不及时治疗，能够引发腹腔继发性感染、多器官功能衰竭而死亡[1-3]。本临床研究通过客观总结乌司他丁在急性胰腺炎治疗中的效果，旨在为临床急性胰腺炎药物选择提供体方案，现报道如下：

1 资料与方法

1.1 一般资料

回顾选取我院2012年1月-2016年6月期间确诊为“急性胰腺炎”并接受药物姑息疗法的178例病患，病例选择标准[4]：①经血清学检测、超声、临床表现等综合分析后，确诊符合急性胰腺炎诊断标准[5]；②发病时间不足48 h；③符合姑息性治疗要求；④无药物使用禁忌；⑤知情同意，资料完整；⑥既往身体健康；⑦排除胰胆管造影术、胰胆外科手术史者；⑧排除合并肾功能不全、恶性肿瘤、心肺功能不全等基础疾病者；⑨排除妊娠、哺乳、精神异常等特殊群体。根据姑息性治疗方案分为2组，即观察组(乌司他丁＋奥曲肽治疗)和参照组(独用奥曲肽)各89例，观察组病患人口学资料：男:女=46:43，病患年龄区间29-51岁，平均(40.85± 4.87)岁；参照组病患人口学资料：男:女=45:44，病患年龄区间28-50岁，平均(40.97± 4.84)岁，两组间

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的人口学资料无明显的统计差异(P>0.05),病患间存在可比性。

1.2 治疗方法

在明确诊断急性胰腺炎之后,所有患者均接受禁食、胃肠检验、抗感染、早期肠内营养、制酸,解痉等基础疗效,参照组同时应用奥曲肽 (成都天台山制造有限公司 H20031207,0.1 mg)治疗:0.6 mg 奥曲肽 +500 mL0.9%氯化钠溶液, 微量静脉泵持续泵注,泵速 25 μg/h,每日 1 次。观察组在上述基础治疗、应用奥曲肽(与对照组相同)的同时,应用乌司他丁(广东天普生化医药股份有限公司 H19990134,10 万 u):20 万 U 乌司他丁 +250 mL5%葡萄糖溶液,静脉滴注,每日 1 次,滴速约为 45 滴 /min,连续 3d 减量至每次 10 万 U。连续治疗 7 d 为 1 疗程。

1.3 观察指标

在入院时、治疗 3 d、治疗 7 d、治疗 14 d 分别依据急性生理学和慢性健康状况评分量表 [6](acute physiology and chronic health evaluation,英文缩写 APACHEⅡ)进行评分,评价内容包括急性生理、年龄和慢性健康 3 大内容,分数越高,代表病情越重,预后越差。在以上时间点同时分别抽取外周血并制取血清,应用免疫组化法(ELISA)对血清学 C- 反应蛋白(CRP)、白细胞介素 -1(IL-1)、白细胞介素 -6(IL-6)和肿瘤坏死因子 -α(TNF-α)等炎症因子表达量, 所有试剂全部由上海船夫生物公司提供,检测过程依据说明书。同时统计治疗期间并发症情况。

1.4 疗效判定

在治疗 14 d 后,根据疗效判定标准[7]对治疗效果进行等级划分,评价等级包括痊愈(临床异常表现全部消失,血清学检测检测指标全部恢复正常)、有效(临床异常表现减减轻,血清学生化指标趋于正常) 、无效(临床异常表现未见改变、生化指标未见好转或病情恶化)。总有效率 = (痊愈 + 有效) ÷总病例数× 100%。

1.5 统计学分析

实验数据完成电子信息录入后, 通过 SPSS 统计分析程序(20.0 版)进行统计学处理软件,计量资料用 $\bar{x}\pm s$ 表示,计数资料为百分率表示,所有数据符合正态分布(方差齐),组内重复测量数据选择重复测量单因素分析,组间计量比较采取独立 t 检验比较,计数数据采取卡方检验,P< 0.05,有统计学差异。

2 结果

2.1 两组治疗前后炎症因子表达比较

入院时,两组病患血清 CRP、IL-1、IL-6、TNF-α 表达量均处于高水平,组间比较无统计差异(P>0.05),治疗后,两组的血清炎症因子水平均明显降低,组内治疗前后血清 CRP、IL-1、IL-6、TNF-α 表达量均有明显差异(P< 0.05);治疗后,观察组血清炎症因子表达水平显著低于参照组(P< 0.05)。见表 1。

表 1 两组治疗前后炎症因子表达比较

Table 1 Comparison of the expression levels of the inflammatory factors between two groups before and after treatment

Indicators	Time	Observation group	Control group	t	P
CRP(mg/L)	Before treatment	105.57± 12.36	104.82± 13.27	0.637	>0.05
	3 days after treatment	66.59± 6.08	75.69± 6.41	56.387	<0.05
	7 days after treatment	63.53± 5.62	70.62± 6.35	51.028	<0.05
	14 days after treatment	23.68± 4.15	35.39± 4.72	62.031	<0.05
	F	45.378	46.352		
	P	<0.05	<0.05		
IL-1(pg/ml)	Before treatment	70.18± 5.67	70.25± 6.73	1.572	>0.05
	3 days after treatment	44.15± 5.34	52.99± 5.97	52.684	<0.05
	7 days after treatment	30.53± 5.01	40.27± 5.36	52.672	<0.05
	14 days after treatment	13.62± 3.09	35.24± 3.98	66.175	<0.05
	F	51.267	58.063		
	P	<0.05	<0.05		
IL-6(pg/ml)	Before treatment	75.52± 5.39	75.61± 5.43	1.367	>0.05
	3 days after treatment	52.39± 5.12	63.38± 5.26	54.310	<0.05
	7 days after treatment	41.38± 4.57	56.35± 4.62	68.541	<0.05
	14 days after treatment	33.06± 2.95	42.85± 3.19	58.754	<0.05
	F	48.632	49.271		
	P	<0.05	<0.05		
TNF-α(pg/ml)	Before treatment	40.85± 4.87	40.85± 4.87	1.574	>0.05
	3 days after treatment	40.85± 4.87	40.85± 4.87	68.711	<0.05
	7 days after treatment	40.85± 4.87	40.85± 4.87	57.584	<0.05
	14 days after treatment	40.85± 4.87	40.85± 4.87	56.841	<0.05
	F	135.247	121.206		
	P	<0.05	<0.05		

2.2 两组间治疗前后 APACHEⅡ评分比较

入院时, 两组病患 APACHEⅡ评分无统计差异(P>0.05),治疗后, 两组的 APACHEⅡ评分明显降低, 组内治疗前后 APACHEⅡ评分有明显差异(P< 0.05);治疗后,观察组 APACHE

Ⅱ评分显著低于参照组(P＜0.05)。见表2。

2.3 两组间临床疗效比较

观察组临床总有效率显著高于参照组,P＜0.05,组间有统计差异。见表3。

2.4 两组间并发症情况比较

两组均未见明显的药物副反应,且观察组并发症明显低于参照组,P<0.05,组间有统计差异。见表4。

表2 两组间治疗前后APACHEⅡ评分比较

Table 2 Comparison of the APACHEⅡ scores between two groups before and after treatment

Indicators	Time	Observation group	Control group	t	P
APACHEⅡ scores	Before treatment	16.18± 2.57	16.25± 2.79	0.635	>0.05
	3 days after treatment	12.82± 2.39	14.87± 3.06	23.057	＜0.05
	7 days after treatment	10.81± 2.14	12.93± 2.98	25.451	＜0.05
	14 days after treatment	5.46± 1.65	8.63± 1.92	35.742	＜0.05
	F	55.687	54.581		
	P	＜0.05	＜0.05		

表3 两组间临床疗效比较

Table 3 Comparison of clinical efficacy between the two groups

Groups	n	Cured	Effective	Ineffective	Total effective rate
Observation group	89	19	58	12	86.52%
Control group	89	14	50	35	71.91%
x^2					55.637
P					0.031

表4 两组间并发症情况比较

Table 4 Comparison of complications between the two groups

Groups	Shock	Acute renal failure	Acute respiratory distress syndrome	Pancreatic encephalopathy syndrome	Total
Observation group	89	19	4	1	12.36%
Control group	89	14	8	3	24.72%
x^2					63.597
P					0.023

3 讨论

急性胰腺炎作为炎症反应，在发病初期其体内TNF-α、IL-1、IL-6、CRP等炎症因子即可出现明显升高，而且在疾病发展过程中,上述因子作为炎症反应调节因素,能够通过诱发“瀑布效应”加重病理损伤、促进病情恶化,因此,在急性胰腺炎诊治过程中,积极监测炎症因子表达具有重要意义。本实验中选择监测血清CRP、TNF-α、IL-1、IL-6等代表性炎症因子表达水平,旨在客观评价病情变化和药物作用机制。药物姑息性治疗是目前治疗急性胰腺炎极为重要的手段,奥曲肽作为传统一线胰腺炎治疗药物,属于人工合成生长素,能够荣国抑制胰液、胰酶、胃酸、胰高血糖素等分泌对胰腺产生保护作用,同时奥曲肽的抗炎症因子作用也得到了临床的公认,因此,实验中将其作为对照药品,具有实践价值。近年来,乌司他丁在急性胰腺炎治疗中逐渐被推广,其作为酸性糖蛋白制剂,能够抑制水解酶、纤溶酶活性,研究证实[8]其对于胰腺炎具有积极治疗作用。但是目前关于乌司他丁治疗急性胰腺炎作用机制在临床极为少见。本实验显示，虽然单独用奥曲肽能够起到有效治疗急性胰腺炎、抑制炎症因子表达的效果,但是乌司他丁联合奥曲肽在临床疗效、炎症因子抑制效果、减少并发症方面均具有显著优势,由此可以认为，乌司他丁与奥曲肽能够协同增效治疗急性胰腺炎,其机制与抑制炎症介质产生密切相关，由于本实验样本小、未选取重症胰腺炎病例,因此仍有不足待临床补充。

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