doi: 10.13241/j.cnki.pmb.2018.08.028

奥曲肽治疗急性弥漫性腹膜炎术后患者的临床疗效及对血清内毒素和 TNF-α、IL-6 水平的影响 *

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摘要 目的：探讨奥曲肽治疗急性弥漫性腹膜炎术后患者的临床疗效及对血清内毒素和肿瘤坏死因子 -α(TNF-α)、白细胞介素 -6(IL-6)水平的影响。**方法：**收集我院 2014 年 5 月 ~2016 年 5 月收治的 86 例急性弥漫性腹膜炎患者，按照不同治疗方式分作对照组与研究组，每组 43 例。两组均采用手术治疗，对照组术后予以常规治疗，研究组基于对照组加以奥曲肽治疗，两组均持续治疗 14 天。比较两组临床疗效，治疗前后血清内毒素和 TNF-α，IL-6 水平的变化及不良反应发生情况。**结果：**治疗后，研究组总有效率显著高于对照组(P<0.05)；两组血清内毒素和 TNF-α、IL-6 水平均较治疗前显著下降，且研究组上述指标明显低于对照组(P<0.05)。研究组不良反应发生率显著低于对照组(P<0.05)。**结论：**奥曲肽可显著提高急性弥漫性腹膜炎术后患者的临床疗效，有效降低血清内毒素和 IL-6、TNF-α 水平，且安全性较高。

关键词：急性弥漫性腹膜炎；奥曲肽；临床疗效；内毒素；肿瘤坏死因子 -α；白细胞介素 -6

中图分类号：R656.41 **文献标识码：**A **文章编号：**1673-6273(2018)08-1536-04

Clinical Efficacy of Octreotide in the Treatment of Patients with Acute Diffuse Peritonitis and Influence on the Serum Endotoxin and TNF-α and IL-6 Levels*

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ABSTRACT Objective: To research the clinical efficacy of octreotide in the treatment of patients with acute diffuse peritonitis and influence on the serum endotoxin and Tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6) levels. **Methods:** 86 cases o patients with acute diffuse peritonitis admitted from May 2014 to May 2016 were collected and divided into the control group and the research group with 43 cases in each group according to different treatment methods. Both groups were treated with surgical treatment, and the control group was treated with routine treatment after operation, while the research group was treated with octreotide based on the control group, both groups were continuously treated for 14 days. The clinical efficacy, changes of serum endotoxin and TNF-α, IL-6 level before and after treatment and incidence of adverse reactions were compared between two groups. **Results:** The total effective rate of research group was 93.02%, which was significantly higher than that of the control group (74.42%, P<0.05). After treatment, the serum endotoxin and TNF-α and IL-6 levels of both group were significantly decreased, which were obviously lower in the research group than those of the control group (P<0.05). The incidence of adverse reactions of research group was 6.97%, which was lower than that of the control group (37.21%, P<0.05). **Conclusion:** Octreotide can enhance the clinical efficacy of acute diffuse peritonitis patients with high safety, and reduce the levels of serum endotoxin and IL-6 and TNF-α.

Key words: Acute diffuse peritonitis; Octreotide; Curative effect; Endotoxin; Tumor necrosis factor-α; Interleukin-6

Chinese Library Classification(CLC): R656.41 Document code: A

Article ID: 1673-6273(2018)08-1536-04

前言

急性弥漫性腹膜炎是一种外科常见急腹症，多继发于腹腔内污染、脏器破裂及穿孔，导致细菌和内毒素发生移位，并启动机体细胞防御系统，刺激、IL-6 及 TNF-α 等炎性因子的生成，引起中毒性休克及多个脏器功能异常[1,2]。El-Toukhy N 等[3]研究显示炎性因子浓度异常所致的局部性炎症反应和急性弥漫性腹膜炎病情进展有着显著的相关性，建议通过多种方式调节炎症反应，抑制病情加重。手术是腹膜炎的重要治疗手段，能够有效控制病灶源，净化腹腔，但急性弥漫性腹膜炎由于分布较为广泛，难以有效控制炎症反应[4,5]。尽快控制腹膜炎引起的全身反应、避免重要脏器功能受损是其治疗的关键。Béchade C 等[6]研究显示急性弥漫性腹膜炎术后应用奥曲肽能够达到较好的疗效，但奥曲肽作为生长抑素的一种类似物能够使胰内分泌激

* 基金项目：广东省自然科学基金项目（S201201000916）

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（收稿日期：2017-07-10 接受日期：2017-07-31）

素、生长激素等病理性分泌受到抑制，但其是否能够影响急性弥漫性胰腺炎中细胞因子的表达仍有待临床考察[7,8]。本研究主要探讨了奥曲肽治疗急性弥漫性腹膜炎术后患者疗效及对血清内毒素和 TNF-α、IL-6 水平的影响。

1 资料与方法

1.1 一般资料

86 例急性弥漫性腹膜炎患者入选标准：符合急性弥漫性腹膜炎相关诊断标准[9](伴恶心、呕吐、急性腹痛表现，腹部可见反跳痛及压痛，腹肌紧张，实验室提示白细胞计数上升，并经腹腔穿刺明确诊断)；继发性腹膜炎；手术指征明确；入院时间在发病 24 h 以内；意识清晰；无本研究药物禁忌症。排除哺乳或者妊娠阶段；代谢性疾病；过敏性体质。对照组 23 例女，20 例男；年龄 20~57 岁，平均(40.76± 5.12)岁；继发原因：18 例阑尾穿孔，16 例十二指肠溃疡穿孔，6 例胃溃疡穿孔，3 例其他。研究组 21 例女，22 例男；年龄 19~58 岁，平均(40.11± 5.98)岁；继发原因：17 例阑尾穿孔，15 例十二指肠溃疡穿孔，7 例胃溃疡穿孔，4 例其他。两组一般临床特征比较差异均无统计学意义(P>0.05)，具有可比性。

1.2 治疗方法

对照组术后接受常规治疗，予以营养支持、静脉补液、解痉镇痛等治疗。研究组基于对照组加以奥曲肽治疗，将 0.3 mg 奥曲肽 (山西平顺日鑫制药有限公司，1 mL:0.1 mg，国药准字 H20040405)与 50 mL0.9%氯化钠注射液充分稀释，予以患者静脉滴注，速度维持在 0.025 mg/h，持续使用 14 天。于用药结束时对疗效予以评估，并观察患者的恢复，及不良反应发生情况。

1.3 观察指标

1.3.1 疗效观察 临床表现全部消失，血清指标无异常，未见腹腔残留脓肿及炎性梗阻，切口可见一期愈合即治愈；临床表现有一定缓解，血清指标基本恢复，未见腹腔残留脓肿及炎性梗阻即好转；临床表现未见明显改变，血清指标异常，或者可见炎性肠梗阻等并发症即无效[10]。

1.3.2 指标测定 于治疗前后抽取患者 2 mL 晨起静脉血，将其进行常规分离并于低温环境中保存待检。内毒素 IL-6、TNF-α 按酶联免疫法进行，试剂盒分别来自：三明博峰生物科技有限公司、广州伊德科技有限公司、长沙多边科技有限公司。

1.4 统计学分析

数据处理选用 SPPS18.0 进行，用($\bar{x}\pm s$)表示计量资料，组间比较选用 t 检验，用[例(%)]表示计数资料，比较用 x^2 检验，P<0.05 有统计学意义。

2 结果

2.1 两组临床疗效比较

治疗后，研究组总有效率为 93.02%，明显高于对照组(74.42%，P<0.05)，见表 1。

表 1 两组临床疗效比较[例(%)]

Table 1 Comparison of the clinical curative effect between two groups[n(%)]

Groups	n	Cured	Improved	Invalid	Effective rate
Control group	43	14(32.56)	18(41.86)	11(25.58)	32(74.42)
Research group	43	21(48.84)	19(44.19)	3(6.97)	40(93.02)#

Note: Compared with the control group, #P<0.05.

2.2 两组恢复效果比较

研究组每日胃肠减压量、排气时间、症状缓解时间均明显低于对照组(P<0.05)，见表 2。

表 2 两组恢复效果比较($\bar{x}\pm s$)

Table 2 Comparison of the recovery effect between two groups($\bar{x}\pm s$)

Groups	n	Gastrointestinal decompression(ml/d)	Anal exhaust time(h)	Symptom Relief Tim(d)
Control group	43	321.42± 40.11	39.62± 4.86	5.90± 0.73
Research group	43	235.09± 29.30#	27.65± 3.32#	3.21± 0.40#

Note: Compared with the control group, #P<0.05.

2.3 两组治疗前后血清内毒素和 TNF-α、IL-6 水平比较

治疗前，两组血清内毒素和 TNF-α、IL-6 水平比较差异无统计学意义(P>0.05)；治疗后，两组血清内毒素和 TNF-α、IL-6 水平均较治疗前显著降低，且研究组以上指标明显低于对照组(P<0.05)，见表 3。

2.4 两组不良反应发生情况的比较

两组均有残留脓肿、切口感染、炎性肠梗阻发生，研究组不良反应率(6.97%)较对照组显著降低(31.21%，P<0.05)，见表 4。

3 讨论

腹膜作为一种浆膜能够吸收腹腔内的毒素、空气、血液及积液，且可分泌液体，受胆汁、胰液、胃液等消化液及细菌刺激后发生充血，诱导肥大细胞释放多种刺激因子，增加血管通透性，导致系列病理改变[11,12]。腹膜炎可包含原发性及继发性，并可按累及范围分作局限性及弥漫性，其中继发性的急性弥漫性腹膜炎较为常见，能够出现程度不一的发热、呕吐、腹痛等表现，且可伴一定程度的中毒现象，其病情较为危急，未经及时治疗者容易发生休克或者死亡[13,14]。临床研究表明外科手术能够抑制急性弥漫性腹膜炎的进展，决定患者病情的转归，但术后因手术操作、麻醉等因素能够导致水电解质产生紊乱，引起胃

表 3 两组治疗前后血清内毒素、TNF-α 及 IL-6 水平比较($\bar{x}\pm s$)

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

Groups	n	Time	Endotoxin (EU/ml)	TNF-α (ng/L)	IL-6 (ng/L)
Control group	43	Before treatment	24.98± 3.11	178.56± 22.24	154.30± 19.25
		After treatment	12.51± 1.50'	132.65± 16.62'	86.11± 10.79'
Research group	43	Before treatment	24.69± 3.50	177.65± 22.90	153.98± 20.86
		After treatment	9.33± 1..15#'	106.24± 12.80#'	38.76± 4.63#'

Note: Compared with the control group, #P<0.05; Compared with before treatment, ' P<0.05.

表 4 两组不良反应发生情况的比较[例(%)]

Table 4 Comparison of the incidence of adverse reactions between two groups[n(%)]

Groups	n	Residual abscess	Incision infection	Inflammatory bowel	Obstruction Incidence rate
Control group	43	5(11.62)	5(11.62)	6(13.95)	16(37.21)
Research group	43	1(2.32)	1(2.32)	1(2.32)	3(6.97)#

Note: Compared with the control group, #P<0.05.

肠功能出现一定程度的抑制，导致腹胀、腹痛等不适，甚者可出现肠梗阻及肠粘连，对患者康复与预后形成影响[15,16]。Mitrović M 等[17]研究发现急性弥漫性腹膜炎术后辅助奥曲肽治疗不仅能够纠正胃肠功能，且对腹腔脓肿、炎性肠梗阻等并发症的防治有重要作用。

奥曲肽临床多应用于胃肠道瘘管、重型胰腺炎、消化道出血、应激性溃疡等疾病，为环状化合物，其作用较为持久，能够起到和生长抑素相似的药理作用，且效果加较为持久，可使多种消化液释放及分泌受到抑制，缓解肠腔内淤血，使肠管内压力下降，促进胃肠功能的良好修复[18,19]。Kanno A 等[20]研究显示奥曲肽能够使门静脉压力下降，使内脏血流量减少，促进肠壁水肿吸收，消除肠腔内液体，确保水、电解质维持平衡，利于患者修复。本研究结果显示奥曲肽治疗的急性弥漫性腹膜炎术后患者的总有效率为 95.43%，显著高于常规治疗的患者，提示其能促进患者的恢复，进一步证实其临床效果。

机体胃肠道中肠杆菌、变形杆菌等革兰氏阴性细菌是急性弥漫性腹膜炎的常见病原菌，内毒素为其成分之一，在细菌凋亡后释放，可对宿主产生一定的毒性，导致微循环障碍等[21,22]。机体胃肠道粘膜受损后能够刺激内毒素过度生成，且急性弥漫性腹膜炎由于应激程度较大，能够影响肠道对内毒素的吸收能力，增加其水平[23]。有研究显示大量内毒素及细菌吸收入血后能够启动机体的防御机体，刺激系列炎症因子的生成，导致全身炎症反应[24]。TNF-α 是一种多效细胞因子，是参与免疫调节的主要因子，主要由活化的巨噬细胞及中性粒细胞合成，其生物功能比较广泛。机体正常状态下，血清水平比较低，能够调节应答反应刺激细胞生长、分化，其水平上升时能够参与炎症反应等生理病理过程，造成局部器官受损、免疫反应，严重者可损害机体系统，TNF-α 是机体神经、内分泌与免疫调节系统中极为主要的介质，机体感染后生成早于其他炎性细胞因子，能够促进致炎因子的合成与释放，修复毛细血管的内皮细胞损伤，进而使毛细血管的通透性能够增加，对机体造成危害[25,26]。IL-6 可刺激 B 细胞生成抗体，引起 T 细胞出现活化、增殖，从而调节机体的免疫应答，且可刺激炎性因子的释放，导致全身炎症反应，是机体组织损伤及炎症反应程度的特异性指标[27,28]。其次 IL-6 可引起血小板聚集，增加血液黏稠度，利于血栓形成，导致微循环异常。Cook AD 等[29]研究显示急性弥漫性腹膜炎患者血清内毒素和 IL-6、TNF-α 水平显著高于健康者。本研究中，两组治疗后上述指标均有一定下降，但经奥曲肽组下降更为明显，提示奥曲肽能够有效纠正机体的炎症反应，抑制其对组织产生的损伤，考虑与其可减轻免疫细胞所致的损伤，抑制病原菌的大量繁殖及生长，使肠道对内毒素的吸收能力增强，影响腹腔炎症因子的渗出，减轻炎症反应[30]。此外，奥曲肽治疗的急性弥漫性腹膜炎术后患者不良反应发生率明显较低，提示其对术后并发症可起到良好的预防作用，减轻患者痛苦。

综上所述，奥曲肽可显著提高急性弥漫性腹膜炎术后患者的临床疗效，有效降低血清内毒素和 IL-6、TNF-α 水平，且安全性较高。

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