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生长抑素联合消炎利胆片在急性结石性胆囊炎手术中的应用价值 *

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摘要 目的:研究生长抑素联合消炎利胆片在急性结石性胆囊炎手术中的应用价值。**方法:**选择 2016 年 8 月~2019 年 8 月我院进行胆囊切除术的 301 例急性结石性胆囊炎患者,随机分为两组。对照组围术期连续采用生长抑素治疗,术后连续用药 3 d,初始剂量为 250 μg 静脉注射,然后以 3 mg 的剂量静脉滴注,给药速度为 250 μg/h。观察组在生长抑素的基础上,术前 7 d 口服消炎利胆片,每天 3 次,每次 6 片,在饭前 30 min 服用,共计用药 7 d。**结果:**观察组术后发热、切口感染和疼痛剧烈的发生率明显低于对照组($P<0.05$)。两组术前的血清降钙素原(procalcitonin, PCT)、C 反应蛋白(C reactive protein, CRP)、促甲状腺激素(thyroid-stimulating hormone, TSH)、血清血清癌抗原(cancer antigen19-9, CA19-9)、血清胰岛素(Insulin, Ins)水平无明显差异($P>0.05$),术后 1 d,两组的血清 PCT、CRP 水平明显升高($P<0.05$),CA19-9、Ins 和 TSH 水平明显降低($P<0.05$),但两组相比无明显差异($P>0.05$),术后 7 d,两组的血清 PCT、CRP、CA19-9、Ins 和 TSH 水平均明显降低($P<0.05$),且观察组明显低于对照组($P<0.05$)。术后 7 d,两组的总胆红素(total bilirubin, TBil)、天冬氨酸转氨酶(Aspartate transaminase, AST)、碱性磷酸酶(alkaline phosphatase, AKP)、丙氨酸转氨酶(Alanine transaminase, ALT)水平明显降低($P<0.05$),白蛋白(albumin, PA)水平明显升高($P<0.05$),观察组的 ALT、AKP、AST、TBil 和 PA 水平明显优于对照组($P<0.05$)。**结论:**生长抑素联合消炎利胆片在急性结石性胆囊炎手术中有较高的应用价值,能减少术后并发症,改善机体的炎症反应和肝功能。

关键词:生长抑素;消炎利胆片;急性结石性胆囊炎;肝功能

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Application Value of Somatostatin Combined with Xiaoyanlidan Tablet in the Operation of Acute Calculous Cholecystitis*

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ABSTRACT Objective: To investigate the application value of somatostatin combined with Xiaoyanlidan tablet in the operation of acute calculous cholecystitis. **Methods:** From August 2016 to August 2019, 301 patients with acute calculous cholecystitis underwent cholecystectomy in our hospital were selected, divided into two groups randomly. The control group was treated with somatostatin for 3 days, the initial dose was 250 μg intravenously, then 3 mg intravenously, the speed of administration was 250 μg/h. On the basis of somatostatin, the observation group took Xiaoyan Lidan tablet 7 days before operation, 3 times a day, 6 tablets a time, 30 minutes before meals, a total of 7 days. **Results:** The incidence of postoperative fever, incision infection and severe pain in the observation group was significantly lower than that in the control group ($P<0.05$). There was no significant difference in the levels of PCT, CRP, CA19-9, ins and TSH between the two groups before operation ($P>0.05$). On the first day after operation, the levels of PCT, CRP, CA19-9, ins and TSH were significantly higher in the two groups ($P<0.05$), but there was no significant difference between the two groups ($P>0.05$). On the seventh day after operation, the levels of PCT, CRP, CA19-9, ins and TSH in the two groups were significantly lower than those in the observation group ($P<0.05$). Control group ($P<0.05$). 7 d after operation, the levels of alt, AKP, AST and TBIL in the two groups were significantly lower ($P<0.05$), and the levels of PA were significantly higher ($P<0.05$). The levels of alt, AKP, AST, TBIL and PA in the observation group were significantly higher than those in the control group ($P<0.05$). **Conclusion:** The combination of somatostatin and Xiaoyan Lidan tablet has high application value in the operation of acute calculous cholecystitis, which can reduce postoperative complications, improve the inflammatory response and liver function.

Key words: Somatostatin; Xiaoyan Lidan tablet; Acute calculous cholecystitis; Liver function

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前言

急性结石性胆囊炎是外科最常见的一种疾病,指的是由于结石堵塞在患者的胆囊管内,造成大量的胆汁淤积在胆囊中,加上受到细菌的侵袭,从而导致胆囊的急性炎症发作^[1,2]。患者的症状主要是右上腹发生阵发性的绞痛,而且伴有明显的腹肌强直以及触痛等表现^[3,4]。发病时由于局部充血、水肿和黏连,特别是当黏连发生在 Calot 三角部位时,会引起局部组织增厚,造成解剖关系不清^[5]。目前临床多采取手术方案切除胆囊来治疗急性结石性胆囊炎,效果较好。有研究发现,炎症反应是导致胆囊切除手术效果不佳的重要独立危险因素,单纯采用抗炎药物并不能有效地对抗胆囊组织的炎症反应^[6]。生长抑素作为一种多肽类的激素,有较强的抗炎效果,可以对机体的炎症反应进行抑制。消炎利胆片是临床治疗胆囊疾病的一种中药复方制剂,能产生较好的抗炎效果。但是临床尚未见关于生长抑素与消炎利胆片联用的研究。因此,本研究创新性地将生长抑素与消炎利胆片联用于急性结石性胆囊炎手术中,以分析其效果。

1 资料与方法

1.1 一般资料

选择 2016 年 8 月~2019 年 8 月我院进行胆囊切除术的 301 例急性结石性胆囊炎患者,纳入标准:(1)均符合《腹部外科实践》^[7]中的标准;(2)48 h 内有强烈的右上腹部疼痛,而且伴有腹膜刺激征,明显反跳痛、肌紧张以及压痛;(3)近期没有应用糖皮质激素治疗,没有免疫系统疾病史;(4)均知情同意;(5)对消炎利胆片以及生长抑素等相关药物没有药物过敏史。排除标准:(1)患有胆总管下端狭窄、重症胆管炎或者胆管肿瘤的患者;(2)CT 检查的结果显示胰腺的形态学出现改变,胰腺增大、胰管扩张或者胰腺密度不均的患者;(3)妊娠和哺乳期的女性;(4)出现意识障碍无法配合的患者;(5)上腹部有手术史或者有手术禁忌症的患者。用抽签法随机分为两组。观察组 150 例,

男 82 例,女 68 例;年龄 26~71 岁,平均 (52.41 ± 19.32) 岁;发病时间 2~15 h,平均 (6.93 ± 2.24) h;体温平均 (37.93 ± 1.42) ℃;身体质量指数平均 (26.38 ± 3.14) kg/m²。对照组 151 例,男 84 例,女 67 例;年龄 26~71 岁,平均 (51.93 ± 18.75) 岁;发病时间 2~15 h,平均 (6.84 ± 2.19) h;体温平均 (37.85 ± 1.36) ℃;身体质量指数平均 (26.44 ± 3.09) kg/m²。两组的基线资料具有可比性($P > 0.05$)。

1.2 治疗方法

对照组:围术期连续采用生长抑素(成都圣诺生物制药公司,国药准字 H20093270)治疗,术后连续用药 3 d,初始剂量为 250 μg 静脉注射,然后以 3 mg 的剂量静脉滴注,给药速度为 250 μg/h。观察组:在生长抑素的基础上,术前 7 d 口服消炎利胆片(广东康奇力药业公司国药准字 Z44023298),每天 3 次,每次 6 片,在饭前 30 min 服用,共计用药 7 d。

1.3 观察指标

观察两组术后发热、切口感染和疼痛剧烈等并发症情况。

在术前和术后 1 d、7 d,空腹抽取 4 mL 的静脉血,采取固相免疫色谱法测量两组的血清 PCT 水平,采取免疫比浊法测量两组的血清 CRP 水平,采取 ELISA 法测量两组的血清 TSH 水平、血清 CA19-9 以及血清胰岛素水平,试剂盒均购自上海哈灵生物公司。比较两组术前和术后 1 d、7 d 的血清 PCT、CRP、CA19-9、Ins 和 TSH 水平的改变。采取全自动生化分析仪测量术前和术后 7 d 的 TBil、PA、AST、AKP、ALT 水平。

1.4 统计学分析

采用 SPSS 21.0,计量资料用 $(\bar{x} \pm s)$ 表示,行 t 检验,计数资料用%表示,行 χ^2 检验, $P < 0.05$ 差异有统计学意义。

2 结果

2.1 术后发热、切口感染和疼痛剧烈的发生率比较

观察组术后发热、切口感染和疼痛剧烈的发生率明显低于对照组,两组对比差异有统计学意义($P < 0.05$),见表 1。

表 1 术后发热、切口感染和疼痛剧烈的发生率比较[例(%)]

Table 1 Comparison of the incidence of postoperative fever, incision infection and severe pain [n(%)]

Groups	n	Postoperative fever	Incision infection	Severe pain	The total rate
Control group	151	24(15.89)	16(10.60)	13(8.61)	53(35.10)
Observation group	150	11(12.67)	5(3.33)	3(0.02)	19(12.67)*

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

2.2 血清 PCT、CRP、CA19-9、Ins 和 TSH 水平比较

两组术前的血清 PCT、CRP、CA19-9、Ins 和 TSH 水平无明显差异($P > 0.05$),术后 1 d,两组的血清 PCT、CRP 水平明显升高($P < 0.05$),CA19-9、Ins 和 TSH 水平明显降低($P < 0.05$),但两组相比无明显差异($P > 0.05$),术后 7 d,两组的血清 PCT、CRP、CA19-9、Ins 和 TSH 水平均明显降低($P < 0.05$),且观察组明显低于对照组($P < 0.05$),见表 2。

2.3 ALT、AKP、AST、TBil 和 PA 水平比较

术后 7 d,两组的 ALT、AKP、AST、TBil 水平明显降低($P < 0.05$),PA 水平明显升高($P < 0.05$),观察组的 ALT、AKP、AST、TBil 和 PA 水平明显优于对照组($P < 0.05$),见表 3。

3 讨论

急性结石性胆囊炎容易由于急性大量失血以及胆囊肿大而导致休克,不利于患者的生命安全^[8,9]。近年来,微创技术得到了迅猛的发展,已成为当前急性结石性胆囊炎的首选治疗方式^[10,11]。但是急性胆囊炎存在局部黏连以及局部炎症,而且渗出比较多,在腹腔镜手术时,部分患者会发生胆囊管损伤以及血管损伤等,不得不中转为开腹手术^[12-14]。有研究发现,炎症反应和胆囊周围渗液都是影响腹腔镜胆囊切除手术过程中转为开腹手术的重要危险因素^[15]。因而,对其局部的炎症反应进行抑制极为重要。但是单纯依靠抗炎药物和解痉药物不能有效抑制胆囊组织内的急性炎症反应^[16]。

表 2 血清 PCT、CRP、CA19-9、Ins 和 TSH 水平比较($\bar{x} \pm s$)
Table 2 Comparison of serum PCT, CRP, CA19-9, ins and TSH levels ($\bar{x} \pm s$)

Groups	n		PCT (ng/L)	CRP (mg/L)	CA19-9 (kU/L)	TSH (U/L)	Ins
Control group	151	Before surgery	11.24± 0.79	19.34± 1.27	183.67± 42.51	4.98± 1.03	30.27± 10.45
		Post operative 1 d	29.75± 3.46 [#]	47.36± 10.24 [#]	127.31± 24.35 [#]	4.71± 0.57 [#]	21.73± 3.45 [#]
		Post operative 7 d	9.13± 0.82 [#]	20.39± 3.57 [#]	103.24± 19.76 [#]	3.29± 0.46 [#]	18.36± 2.41 [#]
Observation group	150	Before surgery	11.36± 0.54	20.36± 1.15	182.54± 43.69	4.97± 1.02	31.86± 10.23
		Post operative 1 d	30.67± 4.28 [#]	46.31± 11.26 [#]	127.46± 25.39 [#]	4.70± 0.46 [#]	22.63± 4.29 [#]
		Post operative 7 d	5.49± 0.37 ^{*#}	11.64± 1.25 ^{*#}	53.89± 12.71 ^{*#}	2.17± 0.34 ^{*#}	10.47± 1.36 ^{*#}

Note: Compared with the control group, * $P<0.05$; compared with before surgery, [#] $P<0.05$; compared with post operative 1 d, ^{*} $P<0.05$.

表 3 ALT、AKP、AST、TBil 和 PA 水平比较($\bar{x} \pm s$)
Table 3 Comparison of ALT, AKP, AST, TBIL and PA levels ($\bar{x} \pm s$)

Groups	n		ALT (U/L)	AST (U/L)	AKP (U/L)	TBil (μmol/L)	PA (mg/L)
Control group	151	Before surgery	103.72± 22.45	79.31± 11.54	148.36± 27.15	57.32± 12.48	173.68± 32.41
		Post operative 7 d	57.34± 12.85 [#]	71.53± 10.26 [#]	122.36± 19.47 [#]	36.48± 11.42 [#]	195.24± 36.71 [#]
Observation group	150	Before surgery	102.96± 23.41	78.36± 12.36	147.53± 28.31	58.14± 13.89	174.25± 30.76
		Post operative 7 d	28.97± 3.42 ^{*#}	33.59± 4.27 ^{*#}	79.34± 12.53 ^{*#}	25.19± 4.37 ^{*#}	273.48± 41.36 ^{*#}

Note: Compared with the control group, * $P<0.05$; compared with before surgery, [#] $P<0.05$.

生长抑素主要定位于胰腺 D 细胞和胃肠道自主神经系统,可以抑制胰岛素、胰蛋白酶以及胃肠道激素的合成与分泌,被大量地应用于急性胰腺炎的治疗^[17-20]。中西医结合治疗急性结石性胆囊炎在我国有满意的效果。认为中药能调节胆汁成分的水平,增强胆囊的收缩功能,改善胆道的动力功能,增加肠蠕动,进而改善内环境,有效预防或者降低胆囊结石的复发^[21]。消炎利胆片由溪黄草、苦木以及穿心莲等中药组成,具有利胆和解毒清热的药理效果,通过理气和补气等功能,能促进胆汁的排泄和加强胆囊的收缩,进而产生排石和利胆溶石的效果,主要用于胆道炎症、肝胆结石并发感染以及急性胆囊炎的治疗^[22]。本研究发现,观察组术后发热、切口感染和疼痛剧烈的发生率明显低于对照组。表明在急性结石性胆囊炎手术中联用消炎利胆片能减少术后的并发症。邓超^[23]等人利用消炎利胆片联合腹腔镜手术治疗急性胆囊炎发现,消炎利胆片用于急性胆囊炎患者并发症也显著低于对照组,与本研究类似,但是并发症主要有肝脓肿和门静脉炎,与本研究有所不同,主要可能与手术方法不同有关。说明消炎利胆片有抗炎的效果,有效的减少患者的疼痛感觉,降低术后并发症的发生情况。

PCT 和 CRP 是机体重要的炎性标志物^[24]。因为消炎利胆片具有较强的抗菌和解毒作用,因此能明显降低血清 PCT 和 CRP 水平。TSH 由人体的腺垂体分泌,其一旦升高会造成甲状腺功能的减退,并且会抑制括约肌的松弛功能,使胆总管结石的复发速度加快^[25,26],机体中发生胆结石后,肝脏功能会受损,导致 Ins 水平明显升高^[27]。CA19-9 是一种主要分布于胰腺和胆管上皮的糖类抗原^[28,29]。而消炎利胆片可以降低胆汁中钙离子含量和 TBIL 水平,减少胆汁内形成结石的可能。急性结石性胆囊炎的发病过程中大多会合并有肝功能受损,术中操作对肝脏造成的牵拉也会造成肝脏受损,而且,胆囊组织的急性炎症反

应也会明显抑制肝脏的合成功能^[30]。本研究显示,观察组术后 7 d 的 Ins 和 TSH 水平明显低于对照组,观察组的 ALT、AKP、AST、TBIL 和 PA 水平明显优于对照组。表明消炎利胆片能更好的改善术后的肝功能,与沈彬^[31]等人的研究一致,现代药理学研究发现,主要是消炎利胆片有利胆疏肝,能够改善肝脏的毒性及转氨酶的水平,降低术后 ALT、AKP、AST 等水平,消炎利胆片还可以明显促进胆汁的排泄,进而大大降低血清 TBIL 水平;通过改善肝脏功能,进而降低血清 ALT、AKP、AST 水平。对于急性结石性胆囊炎手术,手术创伤性大,不利于患者的预后,因此,在治疗中寻找可以改善术后炎性反应、疼痛的有效手段十分重要。目前国内的临床尚未见关于生长抑素与消炎利胆片在急性结石性胆囊炎手术联用,本研究创新性的将二者联合应用,取得了一定的效果,为急性结石性胆囊炎手术治疗提供了基础,但是本研究也存在一定的不足之处,没有对患者血清的炎性因子进行检测,没有进行术后远期的随访,观察患者的不良情况,因此在后续的研究还需扩大样本量深入研究,使此方法成熟,能够应用于临床。

综上所述,生长抑素联合消炎利胆片在急性结石性胆囊炎手术中有较高的应用价值,能减少术后并发症,改善机体的炎症反应和肝功能。

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