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输尿管镜钬激光碎石术与开放手术对输尿管上段结石患者氧化应激和炎性因子的影响*

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摘要目的:探讨输尿管镜钬激光碎石术与开放手术对输尿管上段结石患者氧化应激和炎性因子的影响。**方法:**选取2015年8月~2018年9月期间安徽省中医药大学第一附属医院收治的输尿管上段结石患者117例为研究对象,根据手术方式的不同将患者分为对照组(n=58,开放手术)和观察组(n=59,输尿管镜钬激光碎石术),比较两组患者的治疗效果、氧化应激指标以及炎性因子指标变化情况,观察两组术后并发症发生情况。**结果:**两组患者结石清除率、结石复发率比较无差异($P>0.05$),观察组手术、术后下床、住院的时间均明显短于对照组,术中出血量少于对照组($P<0.05$)。两组患者术后3d、术后7d丙二醛(MDA)、皮质醇(Cor)水平均高于术前,且先升高后降低($P<0.05$),超氧化物歧化酶(SOD)水平低于术前,且先降低后升高($P<0.05$),术后3d、术后7d观察组MDA、Cor水平低于对照组,SOD水平高于对照组($P<0.05$)。两组患者术后3d、术后7d白介素-2(IL-2)、白介素-6(IL-6)、肿瘤坏死因子- α (TNF- α)水平均高于术前,且先升高后降低($P<0.05$),术后3d、术后7d观察组IL-2、IL-6、TNF- α 水平低于对照组($P<0.05$)。观察组术后并发症发生率低于对照组($P<0.05$)。**结论:**输尿管镜钬激光碎石术治疗输尿管上段结石安全有效,同时还可改善临床指标,减轻机体氧化应激与炎性应激反应。

关键词:输尿管镜钬激光碎石术;开放手术;输尿管上段结石;氧化应激;炎性因子

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Effects of Ureteroscopic Holmium Laser Lithotripsy and Open Surgery on Oxidative Stress and Inflammatory Factors in Patients with Upper Ureteral Calculi*

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ABSTRACT Objective: To investigate the effects of ureteroscopic holmium laser lithotripsy and open surgery on oxidative stress and inflammatory factors in patients with upper ureteral calculi. **Methods:** 117 patients with upper ureteral calculi who were admitted to the First Affiliated Hospital of Anhui University of Traditional Chinese Medicine from August 2015 to September 2018 were selected as the study subjects. According to the different surgical methods, the patients were divided into control group (n=58, open surgery) and observation group (n=59, ureteroscopic holmium laser lithotripsy). The therapeutic effect, oxidative stress index and inflammation factors index of the two groups were compared. The occurrence of complications after operation in the two groups was observed. **Results:** There was no significant difference in stone clearance rate and recurrence rate between the two groups ($P>0.05$). The operation time, the time of getting out of bed after operation and the time of hospitalization in the observation group were significantly shorter than those in the control group, and the intraoperative bleeding volume was less than that in the control group ($P<0.05$). The levels of malondialdehyde (MDA) and cortisol (Cor) in the two groups at 3d after operation and 7d after operation were higher than those before operation, and increased first and then decreased ($P<0.05$). The level of superoxide dismutase (SOD) was lower than that before operation, and decreased first and then increased ($P<0.05$). The levels of MDA and Cor of the observation group at 3d after operation and 7d after operation were lower than those of the control group, and the SOD was higher than that of the control group ($P<0.05$). The levels of interleukin-2 (IL-2), interleukin-6 (IL-6) and tumor necrosis factor- α (TNF- α) in the two groups at 3d after operation and 7d after operation were higher than those before operation, and increased first and then decreased ($P<0.05$). The levels of IL-2, IL-6 and TNF- α in the observation group at 3d after operation and 7d after operation were lower than those in the control group ($P<0.05$). The incidence of postoperative complications in the observation group was lower than that in the control group ($P<0.05$). **Conclusion:** Ureteroscopic holmium laser lithotripsy is safe and effective in the treatment of upper ureteral calculi. It can also improve clinical indicators and reduce oxidative stress and inflammatory stress.

Key words: Ureteroscopic holmium laser lithotripsy; Open surgery; Upper ureteral calculi; Oxidative stress; Inflammatory factors

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前言

输尿管结石是临床常见的疾病,主要由于尿液排出过少致使尿液中溶解度较小的草酸钙、磷酸钙等形成微小结石^[1-3]。临床主要表现为血尿、绞痛,可伴发尿路梗阻及感染,较大或表面粗糙的结石会导致输尿管严重梗阻,进而损害肾功能^[4,5]。由于输尿管上段结石的治疗关键在于及时清除结石,对于药物治疗无法缓解的患者必须通过手术治疗以避免严重并发症的发生^[6,7]。以往临床手术治疗常采用开放手术治疗,结石清除率较高,但该类手术创伤较大、术后恢复慢,一定程度上影响患者预后^[8]。近年来输尿管镜钬激光碎石术逐渐应用于临床,主要是利用输尿管镜结合腔内碎石技术以进行治疗^[9-11],但其有效性尚需大样本量研究验证。鉴于此,本研究通过探讨输尿管镜钬激光碎石术与开放手术对输尿管上段结石患者的影响,以期为临床术式的选择提供参考。

1 资料与方法

1.1 一般资料

选取安徽省中医药大学第一附属医院于2015年8月~2018年9月接收的输尿管上段结石患者117例为研究对象,纳入标准:(1)经输尿管CT、逆行肾盂造影、泌尿系B超等检查确诊;(2)临床表现为上腹部持续性钝痛、绞痛、血尿;(3)结石部位位于第4腰椎下缘以上,停留时间>8周;(4)患者及其家属知情本次研究且已签署了同意书;(5)均具备手术指征者。排除标准:(1)合并严重肝肾功能障碍者;(2)合并严重脊柱畸形、结核者;(3)合并糖尿病、高血压等基础疾病者;(4)妊娠及哺乳期妇女;(5)合并凝血功能障碍者;(6)合并其他部位结石者。根据手术方式的不同将患者分为对照组(n=58,开放手术)和观察组(n=59,输尿管镜钬激光碎石术),其中对照组男36例,女22例,年龄34~65岁,平均(48.28±5.23)岁;结石最大直径9~16mm,平均(11.37±1.86)mm;患病部位:左侧35例,右侧23例。观察组男38例,女21例,年龄32~64岁,平均(48.39±4.91)岁;结石最大直径9~17mm,平均(11.05±1.97)mm;患病部位:左侧38例,右侧21例。两组患者一般资料对比无差异(P>0.05),本研究已获取我院伦理学委员会批准进行。

1.2 方法

对照组给予开放手术治疗,硬膜外麻醉,于患者腹部或腰部作一常规切口,游离输尿管周围组织,作一纵行切口取出结石。观察组给予输尿管镜钬激光碎石术治疗,操作如下:硬膜外麻醉,取截石位,行气管插管,低压下灌注生理盐水,将德国WOLF公司生产的F8~9.8硬质输尿管镜插入至输尿管,观察输尿管结石情况,同时检查患者是否并发输尿管狭窄等。待输尿管镜自尿道进入膀胱后,找到患侧输尿管开口,轻轻置入泥鳅导丝,沿导丝走向置入扩张器,并保留外鞘,确定结石位置后,引入钬激光光纤,确保其接触到结石,设置钬激光参数:能力0.5~1.5J,频率10~20Hz,将结石碎至2~3mm,待其自行排出。两组患者手术结束后置入双J管引流,术后4~6周即可拔出,术后给予常规抗感染处理。

1.3 观察指标

比较两组患者的治疗效果,包括结石清除率、结石复发率、手术时间、术后下床时间、术中出血量、住院时间。于术前、术后3d、术后7d采集患者清晨空腹静脉血6mL,3200r/min离心10min,离心半径8cm,采用酶联免疫吸附法检测氧化应激指标:丙二醛(Malondialdehyde,MDA)、皮质醇(Cortisol,Cor)、超氧化物歧化酶(Superoxide dismutase,SOD)以及炎症因子指标:白介素-6(Interleukin-6,IL-6)、肿瘤坏死因子- α (Tumornecrosis factor- α ,TNF- α)、白介素-2(Interleukin-2,IL-2),试剂盒购自武汉华美生物科技有限公司,严格遵守试剂盒说明书进行操作。观察两组患者术后并发症发生情况。

1.4 统计学方法

通过SPSS25.0软件处理统计数据,计数资料用率表示,行 χ^2 检验,计量资料用($\bar{x}\pm s$)表示,行t检验, $\alpha=0.05$ 设置为检验标准。

2 结果

2.1 两组患者治疗效果比较

两组患者结石清除率、结石复发率比较无差异(P>0.05),观察组术后下床、手术、住院的时间均明显短于对照组,术中出血量少于对照组(P<0.05),详见表1。

2.2 两组患者氧化应激指标比较

两组术前MDA、Cor、SOD水平比较无差异(P>0.05),两组患者术后3d、术后7dMDA、Cor水平均高于术前,且先升高后

表1 两组患者治疗效果比较

Table 1 Comparison of therapeutic effects of two groups

Groups	Stone clearance rate [n(%)]	Stone recurrence rate[n(%)]	Operative time (min)	Time of getting out of bed after operation(d)	Intraoperative bleeding volume (mL)	Time of hospitalization(d)
Control group (n=58)	57(98.28)	4(6.90)	81.58±18.32	1.08±0.16	73.16±10.74	7.24±1.57
Observation group (n=59)	55(93.22)	5(8.47)	45.15±10.48	0.57±0.11	12.19±2.59	4.92±0.93
χ^2/t	1.827	0.103	13.003	19.775	41.648	9.577
P	0.176	0.749	0.000	0.000	0.000	0.000

降低 ($P<0.05$), SOD 水平低于术前, 且先降低后升高 ($P<0.05$), 平高于对照组 ($P<0.05$), 详见表 2。
 术后 3d、术后 7d 观察组 MDA、Cor 水平低于对照组, SOD 水

表 2 两组患者氧化应激指标比较($\bar{x}\pm s$)

Table 2 Comparison of oxidative stress indexes between two groups($\bar{x}\pm s$)

Groups	MDA(nmol/mL)			Cor(ng/mL)			SOD(NU/mL)		
	Before operation	3d after operation	7d after operation	Before operation	3d after operation	7d after operation	Before operation	3d after operation	7d after operation
Control group(n=58)	4.41± 0.26	13.86± 0.36 ^a	9.36± 0.35 ^{ab}	203.25± 20.89	257.59± 24.21 ^a	233.25± 25.74 ^{ab}	85.94± 3.19	62.94± 4.89 ^a	71.72± 5.44 ^{ab}
Observation group(n=59)	4.33± 0.23	9.31± 0.57 ^a	5.39± 0.41 ^{ab}	202.23± 19.78	238.68± 16.10 ^a	219.47± 15.46 ^{ab}	86.03± 4.01	70.41± 4.73 ^a	79.76± 5.52 ^{ab}
t	1.950	50.631	55.315	0.267	4.897	3.457	0.132	8.254	7.797
P	0.054	0.000	0.000	0.790	0.000	0.001	0.895	0.000	0.000

Note: compared with before operation, ^a $P<0.05$; compared with 3d after operation, ^b $P<0.05$.

2.3 两组患者炎性因子指标比较

两组患者术前 IL-2、IL-6、TNF- α 水平比较差异无统计学意义 ($P>0.05$), 两组患者术后 3d、术后 7d IL-2、IL-6、TNF- α 水

平均高于术前, 且先升高后降低 ($P<0.05$), 术后 3d、术后 7d 观察组 IL-2、IL-6、TNF- α 水平低于对照组 ($P<0.05$), 详见表 3。

表 3 两组患者炎性因子指标比较($\bar{x}\pm s$)

Table 3 Comparison of inflammatory factors indexes between two groups($\bar{x}\pm s$)

Groups	IL-2(μ g/mL)			IL-6(pg/mL)			TNF- α (ng/mL)		
	Before operation	3d after operation	7d after operation	Before operation	3d after operation	7d after operation	Before operation	3d after operation	7d after operation
Control group(n=58)	6.53± 1.17	14.75± 1.68 ^a	10.86± 1.43 ^{ab}	7.24± 1.21	15.24± 1.85 ^a	11.13± 1.08 ^{ab}	1.31± 0.32	2.42± 0.57 ^a	1.97± 0.31 ^{ab}
Observation group(n=59)	6.58± 1.08	11.71± 1.26 ^a	7.82± 1.22 ^{ab}	7.28± 1.14	11.55± 1.71 ^a	8.64± 1.42 ^{ab}	1.35± 0.37	1.89± 0.63 ^a	1.52± 0.30 ^{ab}
t	0.236	10.895	12.165	0.181	11.013	10.478	0.614	4.687	7.842
P	0.814	0.000	0.000	0.857	0.000	0.000	0.540	0.000	0.000

Note: Compared with before operation, ^a $P<0.05$; compared with 3d after operation, ^b $P<0.05$.

2.4 两组患者并发症发生情况比较

对照组术后发生大出血 1 例、脓毒血症 2 例、切口感染 4 例、尿瘘 3 例, 并发症发生率为 17.24%(10/58); 观察组术后发生大出血 1 例、脓毒血症 1 例, 并发症发生率为 3.39%(2/59); 观察组术后并发症发生率低于对照组 ($\chi^2=6.097, P=0.014$)。

输尿管中下段结石的疗效已得到证实, 而关于其在输尿管上段结石的疗效尚存在一定争议, 就此展开探讨。

3 讨论

作为临床常见的泌尿系结石, 输尿管结石大多继发于肾结石, 较少见原发于输尿管结石, 输尿管结石若未能得到及时有效的治疗, 常继发输尿管黏膜损伤、感染以及输尿管穿孔等并发症^[12-14]。以往临床多采用针刺疗法、服排石汤、超声碎石等中西医结合治疗, 多数患者可治愈, 但仍有一部分患者经上述治疗无效, 为阻止病情的进一步发展, 此时可选择手术治疗。开放手术治疗输尿管上段结石疗效确切, 可有效清除结石, 但该术式对人体损伤较大, 术后并发症多, 因此寻找一种可有效促进患者康复的手术方式具有重要的临床意义^[15-17]。伴随着钬激光技术在临床的发展, 输尿管镜钬激光碎石术有望成为治疗输尿管上段结石的又一有效手段, 该术式采用高能脉冲式固体激光, 将结石气化为细小颗粒以排出体外^[18, 19]。现临床有关其治

本次研究结果表明, 两组结石清除效果相当, 但观察组术后下床、手术、住院的时间明显短于对照组, 术中出血量少于对照组, 可见输尿管镜钬激光碎石术治疗输尿管上段结石, 优势显著。钬激光波长为 2100 nm, 具有凝固止血、精准切割组织、粉碎结石等功能, 可通过低水密度的石英纤维传导, 并通过水分子的微爆破进行碎石, 有效清除结石, 利于患者术后恢复。此外, 输尿管镜下进行手术操作, 视野清晰, 可使钬激光直接对准结石进行碎石, 操作简单, 大大缩短手术时间^[20-22]。尽管输尿管镜钬激光碎石术属于微创术式, 但仍为有创手术类型, 可使机体产生不同程度的应激反应, 当机体受到创伤时神经分泌代谢产生变化, 引起血液中 MDA、Cor、IL-2、IL-6、TNF- α 升高、SOD 降低, 而血液中的应激指标变化可在一定程度上反应机体应激程度^[23-25]。既往研究表明^[26], 手术创伤引起的组织损伤, 其应激程度升幅与患者预后息息相关。本研究结果中术后 3d、术后 7d 观察组 MDA、Cor、IL-2、IL-6、TNF- α 低于对照组, SOD 高于对照组, 可见输尿管镜钬激光碎石术后引起的机体氧化、炎性应激反应程度更轻, 这可能是由于钬激光可通过人体自身结构

通道到达治疗靶位置,组织穿透浅,可准确将组织切割、消融,对周围组织损伤较轻,有效降低机体应激性反应程度^[27-29]。另外,观察组术后并发症发生率低于对照组,可见输尿管镜钬激光碎石术可有效减少术后并发症发生率,这与成俊等人^[30]研究结果基本一致。可能是由于该手术方式术后创伤小,可明显减少感染几率,加之术中应激程度较轻,利于患者术后恢复。

综上所述,输尿管镜钬激光碎石术治疗输尿管上段结石,可获得与开放手术相当的结石清除效果,且该术式对人体损伤较小,术后可促进患者恢复,同时可有效减轻机体氧化应激与炎性应激,减少并发症发生率。

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