

低分子肝素钙在妇科肿瘤腹腔镜术后预防深静脉血栓中的临床效果

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Clinical effects of low molecular weight heparin in laparoscopic gynecologic oncology surgery for prevention of deep vein thrombosis

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【Abstract】 Objective: To investigate clinical effects of low molecular weight heparin in laparoscopic gynecologic oncology surgery for prevention of deep vein thrombosis. **Methods:** From 2011 to 2014, 120 cases of laparoscopic surgery patients with gynecologic tumors were selected, they were divided into the control group and the observation group. 54 patients in the control group were implemented with no similar treatment, 66 patients in the observation group were implemented with subcutaneous low molecular weight heparin anticoagulation for 10d. Two groups of anti-Xa activity, activated partial thromboplastin time (APTT), prothrombin time (PT), lower limb circumference, blood flow index, incidence of complications were compared. **Results:** In observed postoperative 5d fibrinogen, D-dimer was (2.77 ± 0.73) g/L, (0.63 ± 0.18) μg/ml, were lower than the control group, the difference was statistically significant (P = 0.019, P = 0.029). PT were (13.85 ± 3.93) s, (13.95 ± 3.14) s, higher than control group, the difference was statistically significant (P = 0.042, P = 0.034). In observation group lower limb circumference, blood flow velocity were (20.33 ± 3.52) cm, (0.95 ± 0.18) m/s, better than the control group, the difference was statistically significant (P = 0.021, P = 0.019). Observation group complication rate 3.03% (2/66) and 9.26% (5/54) in the control group had statistically significant difference (P = 0.004). **Conclusion:** Low molecular weight heparin anticoagulation has good effect on blood flow for gynecologic cancer patients after laparoscopic surgery, for prevention of deep vein thrombosis.

【Key words】 low molecular weight heparin, anticoagulation, gynecologic oncology, deep vein thrombosis

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【摘要】 目的: 探讨低分子肝素钙抗凝方案应用于妇科肿瘤腹腔镜术后预防深静脉血栓的临床效果以及安全性。方法: 选择2011年1月-2014年12月120例实施妇科肿瘤腹腔镜术患者,按数字表法随机分为对照组与观察组,对照组54例患者不使用其他抗凝剂和影响凝血功能的药物;观察组66例患者实施低分子肝素钙皮下注射抗凝,持续10d,对比两组患者血清学指标、活化部分凝血活酶时间(APTT)、凝血酶原时间(PT)、下肢周径、血流指标、并发症发生率。结果: 观察组术后5d纤维蛋白原、D-二聚体分别为(2.77 ± 0.73) g/L、(0.63 ± 0.18) μg/ml,均低于对照组,对比差异有统计学意义(P = 0.019, P = 0.029);观察组术后3d、术后5d PT分别为(13.85 ± 3.93) s、(13.95 ± 3.14) s,优于对照组,对比差异有统计学意义(P = 0.042, P = 0.034);观察组下肢周径、血流速度分别为(20.33 ± 3.52) cm、(0.95 ± 0.18) m/s,优于对照组,对比差异有统计学意义(P = 0.021, P = 0.019);并发症发生率观察组3.03% (2/66) 与对照组9.26% (5/54) 对比差异有统计学意义(P = 0.004)。结论: 低分子肝素钙抗凝方案应用于妇科肿瘤腹腔镜术后可以有效改善患者血流状态,预防深静脉血栓形成。

【关键词】 低分子肝素; 抗凝; 妇科肿瘤; 深静脉血栓

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深静脉血栓是妇科肿瘤术后常见并发症,腹腔镜术中由

于采取膀胱截石体位同时气腹压力对盆腔血管压迫性较大,造成患者下肢静脉回流,增加下肢深静脉血栓形成风险,对患者预后及生活质量均有很大影响^[1-2]。因此抗凝治疗是腹腔镜妇科手术后的重要环节,本文旨在探讨低分子肝素钙抗凝方案应用于妇科肿瘤腹腔镜术后预防深静脉血栓的效果以及安全性,为临床选择抗凝方案提供参考,选择120例行妇科肿瘤腹腔镜术患者实施不同抗凝治疗做对比研究,现将

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研究结果报道如下。

1 资料与方法

1.1 一般资料

选择2011年1月-2014年12月120例实施腹腔镜妇科肿瘤手术患者,按数字表法随机分为对照组与观察组,对照组54例,观察组66例。对照组:年龄41~69岁,平均年龄(50.28±6.23)岁,子宫内膜癌40例,宫颈癌14例;观察组:年龄43~71岁,平均年龄(50.73±6.44)岁,子宫内膜癌48例,宫颈癌18例。对照组与观察组患者年龄、肿瘤类型等基线资料对比差异无统计学意义($P>0.05$) 均衡可比。

1.2 纳入标准

①术前经过影像学及病理学检查确诊;②患者无高凝体质^[3,4];③肝肾功能及心肺功能无明显异常;④对抗血小板聚集类药物、肝素药物等无过敏史^[5,6];⑤术前检查确认无血栓性疾病;⑥患者及家属对研究知情且同意,并且签署知情同意书;⑦本研究经过医院伦理委员会批准实施。

1.3 治疗方法

所有患者均在腹腔镜下实施肿瘤切除手术,包括双附件切除、广泛或者次广泛子宫切除以及盆腔淋巴结清扫术。对照组不使用其他抗凝剂和影响凝血功能的药物。观察组术

后次日开始使用低分子肝素钙抗凝 4 100U 低分子肝素钙皮下注射,每日一次,持续10d。两组患者术后均密切关注凝血指标,观察临床症状,发现相关症状后进行彩超检查,明确血栓。

1.4 观察指标

①血清学指标:纤维蛋白原、D-二聚体;②活化部分凝血活酶时间(APTT)、凝血酶原时间(PT);③下肢周径;④彩色多普勒超声行血流速度测定;⑤术后并发症。

1.5 统计学方法

本研究结果使用统计学软件 SPSS 21.0 分析,计量资料采用 t 检验,计数资料比较采用卡方检验,以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 观察组与对照组纤维蛋白原、D-二聚体比较

观察组术后5d纤维蛋白原、D-二聚体分别为(2.77±0.73)g/L、(0.63±0.18)μg/ml,均低于对照组,对比差异有统计学意义($t=4.667 P=0.019$; $t=3.967 P=0.029$);对照组纤维蛋白原、D-二聚体组内对比差异有统计学意义($F=4.024 P=0.024$; $F=3.553 P=0.032$),见表1。

表1 观察组与对照组纤维蛋白原、D-二聚体对比 ($\bar{x} \pm s$)

Tab.1 Fibrinogen, D-dimer comparison between observation group and control group ($\bar{x} \pm s$)

Group	n	Fibrinogen (g/L)			D-dimer (μg/ml)		
		Before surgery	3d after surgery	5d after surgery	Before surgery	3d after surgery	5d after surgery
Control group	54	2.57 ± 0.76	2.87 ± 0.84	3.94 ± 1.02	0.59 ± 0.14	0.60 ± 0.18	0.78 ± 0.21
Observation group	66	2.61 ± 0.72	2.76 ± 0.64	2.77 ± 0.73	0.60 ± 0.15	0.61 ± 0.17	0.63 ± 0.18
t	-	0.814	1.145	4.667	0.738	0.739	3.967
P	-	0.447	0.103	0.019	0.517	0.521	0.029

2.2 观察组与对照组活化部分凝血活酶时间比较

观察组术后3d、术后5d APTT 分别为(29.97±5.23) s、(30.68±4.64) s,优于对照组,对比差异有统计学意义($t=3.669 P=0.033$; $t=3.759 P=0.031$);对照组与观察组治疗前后组内不同时间节点 APTT 指标对比差异有统计学意义($F=4.876 P=0.021$; $F=5.971 P=0.010$),见表2。

2.3 观察组与对照组凝血酶原时间比较

观察组术后3d、术后5d PT 分别为(13.85±3.93) s、(13.95±3.14) s,优于对照组,对比差异有统计学意义($t=3.031 P=0.042$; $t=3.553 P=0.034$);对照组与观察组治疗前后组内不同时间节点 PT 指标对比差异有统计学意义($F=3.115 P=0.036$; $F=5.335 P=0.019$),见表3。

表2 观察组与对照组活化部分凝血活酶时间对比 ($\bar{x} \pm s$)

Tab.2 Partial thromboplastin time comparison between observation group and control group ($\bar{x} \pm s$)

Group	n	Before surgery	3d after surgery	5d after surgery	F	P
Control group	54	27.64 ± 3.24	24.34 ± 4.15	24.21 ± 4.07	4.876	0.021
Observation group	66	27.93 ± 3.86	29.97 ± 5.23	30.68 ± 4.64	5.971	0.010
t	-	0.927	3.669	3.759	-	-
P	-	0.197	0.033	0.031	-	-

表3 观察组与对照组凝血酶原时间对比 ($\bar{x} \pm s$)

Tab.3 Thromboplastin time comparison between observation group and control group ($\bar{x} \pm s$)

Group	n	Before surgery	3d after surgery	5d after surgery	F	P
Control group	54	12.59 ± 2.53	10.95 ± 3.14	10.75 ± 2.94	3.115	0.036
Observation group	66	12.77 ± 2.72	13.85 ± 3.93	13.95 ± 3.14	5.335	0.019
t	-	1.033	3.031	3.553	-	-
P	-	0.165	0.042	0.034	-	-

2.4 观察组与对照组下肢周径及血流速度比较

观察组下肢周径、血流速度分别为(20.33 ± 3.52) cm、(0.95 ± 0.18) m/s, 优于对照组, 对比差异有统计学意义($t = 4.412, P = 0.021; t = 4.724, P = 0.019$) ,见表4。

表4 观察组与对照组下肢周径及血流速度对比

Tab.4 Observation lower limb circumference and blood flow speed comparison between group and control group

Group	n	Lower limb circumference (cm)	Blood flow speed (m/s)
Observation group	66	20.33 ± 3.52	0.95 ± 0.18
Control group	54	25.83 ± 4.17	0.64 ± 0.11
t	-	4.412	4.724
P	-	0.021	0.019

2.5 并发症

观察组: 1例患者出现皮下瘀斑, 1例患者出现局部血肿, 超声检查显示为活动性出血; 对照组: 下肢深静脉血栓5例, 其中股静脉血栓1例, 髂静脉血栓1例, 小腿肌肉静脉丛血栓3例。观察组并发症发生率3.03% (2/66) 与对照组9.26% (5/54) 对比差异有统计学意义($\chi^2 = 6.148, P = 0.004$)。

3 讨论

妇科肿瘤术后患者静脉血管受损, 血液处于高凝同时血流速度慢, 容易造成深静脉腔内血液不正常的凝结, 引发静脉腔阻塞, 阻碍静脉血流, 对患者术后恢复影响很大, 严重影响患者生活质量。抗凝治疗对于血栓延伸及栓塞的预防至关重要^[7,8]。通过纤维蛋白将形成的血栓溶解, 有效预防血栓, 是妇科肿瘤术后的重要治疗环节。

低分子肝素抗凝后患者抗-Xa活性更强, 主要与抗凝机制有关, 低分子肝素, 是普通肝素的裂解片段^[9,10], 是蒸馏得到的部分, 在抗凝过程中具有选择性抗-Xa活性, 因此低分子肝素抗血栓以及出血作用是相互独立的, 因此从此角度分析低分子肝素抗凝安全性更高, 保证了抗血栓效果的同时控制了出血风险^[11,12]。同时低分子肝素使用后通过促进组织型纤维蛋白溶解酶激活物的释放而发挥纤溶作用, 经内皮细胞的介导作用使血管内皮和组织中的纤溶酶原激活^[13,14]转化为纤溶酶而促进纤溶作用, 并能保护血管内皮增加抗栓作用, 观察组患者纤维蛋白原、D-二聚体均低于对照组, 由于纤维蛋白原与全血黏度、血浆黏度、血沉及血小板聚集之间呈显著正相关, 观察组指标更低, 提示血液黏度、红细胞聚集、血小板聚集等过程控制较好, 避免血液处于高凝状态, 减少血栓形成; D-二聚体是纤维蛋白单体经活化因子XIII交联后, 再经纤溶酶水解所产生的一种特异性降解产物, 是一个特异性的纤溶过程标记物, 观察组纤维蛋白降解产物D水平较低, 表明患者体内纤维蛋白降解过程得到控制, 预防了血栓形成, 提升了血液动力学表现, 本文结果血流速度观察组更高也间接表明血栓预防效果更好。本文研究结果提示观察组APTT及PT相比术前有所改善, 表明低分子肝素钙阻碍了血小板凝聚形成血栓的速度, 改善了血栓向深静脉蔓延, 有效预防了深静脉血栓的发生, 而对照组未采用积极的抗凝治疗, 术后仍处于高凝状态, 本文结果也提示观察组深静脉血栓发生率明显更低。妇科肿瘤手术患者多数年龄偏

大, 血液表现为高凝状态, 同时由于全身麻醉以及淋巴结清扫过程中对下肢静脉压迫等原因, 术后血管血流速度减慢, 容易形成血栓, 同时腹腔镜手术中, CO₂形成的气腹压力一般是正常下肢静脉压力的3~5倍, 内压过大造成血管压力高, 血流缓慢, 本文研究结果提示观察组使用低分子肝素钙抗凝后下肢周径以及血流速度状态均优于对照组, 表明低分子肝素钙有效改善了血液高凝, 预防血栓形成。观察组并发症发生率明显低于对照组, 1例患者出现皮下瘀斑, 1例患者出现局部血肿, 均早期发现妥善处理后缓解, 但未发生下肢深静脉血栓。

综上所述, 低分子肝素钙抗凝方案应用于妇科肿瘤腹腔镜术后可以有效改善患者血流状态, 预防深静脉血栓形成, 值得临床推广应用。

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❖ 造血器·淋巴系肿瘤 ❖

培门冬酶治疗结外 NK/T 细胞淋巴瘤的临床疗效

胡媛媛, 高小见

Comparative study of pegaspargase treatment of extranodal NK/T-cell lymphoma

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【Abstract】 Objective: To analyze extranodal NK/T-cell lymphoma line pegaspargase clinical efficacy of L-asparaginase. **Methods:** Extranodal NK/T-cell lymphoma were patients selected, 171 patients were randomly divided into two groups, pegaspargase group and L-asparaginase enzyme group. Two groups were treated with radiation and chemotherapy both platinum-based. **Results:** Total of 171 extranodal NK/T-cell lymphoma patients, included pegaspargase group of 86 patients, L-asparaginase group 85 cases. Short-term effect $P < 0.05$, the difference was statistically significant. 3-month, 6-month, 1-year survival of the Logrank test $P = 0.000 < 0.05$. 3 months pegaspargase group 6-month, 1-year survival rate was significantly higher than that of L-asparaginase. Patients in both groups experienced hematological toxicity and nausea, vomiting and other reactions, nausea, vomiting, allergies, high blood sugar and other incidences $P < 0.05$, the difference was statistically significant. White blood cells, platelets decreased, the incidence of liver dysfunction comparison, $P > 0.05$, the difference was not statistically significant. **Conclusion:** Pegaspargase comparing L-asparaginase can significantly improve the short-term effect of extranodal NK/T-cell lymphoma.

【Key words】 extranodal NK/T-cell lymphoma, prognosis, risk factors, esophageal cancer, radiotherapy

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【摘要】 目的: 分析结外 NK/T 细胞淋巴瘤行培门冬酶与左旋门冬酰胺酶治疗的临床疗效。方法: 以 2009 年 6 月至 2014 年 12 月病理诊断为结外 NK/T 细胞淋巴瘤的患者为研究对象。将患者随机分为 2 组, 培门冬酶组和左旋门冬酰胺酶组, 两组均采用放疗以及以铂类为基础的两联方案化疗。在治疗结束后评价并对比患者的近期、远期疗效以及毒副反应。结果: 共搜集结外 NK/T 细胞淋巴瘤患者 171 例, 其中培门冬酶组 86 例,

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