

· 老年人周围血管疾病诊治专栏 ·

## 脉络舒通丸联合利伐沙班治疗下肢深静脉血栓形成后综合征的临床效果

孙燕<sup>1</sup>, 于艺伟<sup>2</sup>, 刘宗芬<sup>2</sup>, 刘涛<sup>1</sup>, 孙震<sup>3</sup>, 张杰峰<sup>1</sup>, 孙波<sup>1\*</sup>

(潍坊市人民医院: <sup>1</sup> 血管外科, <sup>3</sup> 中医科, 山东 潍坊 261041; <sup>2</sup> 潍坊医学院临床医学院, 山东 潍坊 261000)

**【摘要】目的** 探讨脉络舒通丸联合利伐沙班治疗下肢深静脉血栓形成后综合征(PTS)的临床效果。**方法** 回顾性分析2019年6月至2020年9月潍坊市人民医院血管外科收治的60例下肢深静脉血栓形成后综合征患者的临床资料。根据治疗方法不同将患者分为对照组和观察组,各30例。对照组患者给予利伐沙班片、弹力袜等基础治疗措施,观察组患者在对照组治疗方法的基础上,给予口服脉络舒通丸。记录患者 Villalta 评分和血液中纤维蛋白原含量(FIB)、活化部分凝血活酶时间(APTT)、白细胞介素-6(IL-6)、超敏C反应蛋白(hs-CRP)等指标及不良反应发生情况。采用SPSS 22.0统计软件进行数据分析。根据数据类型,分别采用t检验、 $\chi^2$ 检验或Fisher精确检验进行组间比较。**结果** 治疗后观察组 Villalta 评分(包括肢体肿胀、疼痛、色素沉着等)明显优于对照组[(6.17±2.20)和(7.43±1.50)分];炎症指标(IL-6、hs-CRP)与FIB水平明显低于对照组[(32.35±4.68)和(48.75±5.21)pg/ml, (13.51±3.89)和(18.87±4.28)mg/L, (2.43±0.41)和(2.79±0.47)g/L],差异均有统计学意义( $P<0.05$ )。2组患者APTT及不良反应发生情况比较,差异均无统计学意义( $P>0.05$ )。**结论** 脉络舒通丸联用利伐沙班可显著提升PTS的治疗效果,改善患者凝血功能和炎症反应情况,且安全性较好。

**【关键词】** 静脉血栓形成;脉络舒通丸;利伐沙班;炎症反应

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## Clinical effect of Mailuo Shutong Pills combined with rivaroxaban in treatment of sequelae of lower extremity venous thrombosis

SUN Yan<sup>1</sup>, YU Yi-Wei<sup>2</sup>, LIU Zong-Fen<sup>2</sup>, LIU Tao<sup>1</sup>, SUN Zhen<sup>3</sup>, ZHANG Jie-Feng<sup>1</sup>, SUN Bo<sup>1\*</sup>

(<sup>1</sup>Department of Vascular Surgery, <sup>3</sup>Department of Chinese Medicine, Weifang People's Hospital, Weifang 261041, Shandong Province, China; <sup>2</sup>School of Clinical Medicine, Weifang Medical University, Weifang 261000, Shandong Province, China)

**【Abstract】 Objective** To explore the clinical effect of Mailuo Shutong Pills combined with rivaroxaban in the treatment of post-deep vein thrombosis syndrome of lower extremity. **Methods** A retrospective study was conducted of the clinical data of 60 patients with sequelae of lower extremity deep venous thrombosis treated in the Department of Vascular Surgery of Weifang People's Hospital from June 2019 to September 2020. According to the treatment regimen, they were divided into control group ( $n=30$ ) and study group ( $n=30$ ). The control group received basic treatment such as rivaroxaban tablets and elastic stockings, and the study group were treated with additional Mailuo Shutong Pills. The Villalta score, fibrinogen (FIB), activated partial thromboplastin time (APTT), interleukin-6 (IL-6) and high-sensitivity C-reactive protein (hs-CRP) were recorded. SPSS statistics 22.0 was used for data analysis. According to the data type,  $t$ -test,  $\chi^2$  test, or Fisher's exact test was used for comparison between groups. **Results** After treatment, the study group had significantly better Villalta score (including swelling, pain and pigmentation of the affected extremity), lower inflammatory indexes (IL-6 and hs-CRP) and FIB than the control group [(6.17±2.20) vs (7.43±1.50) points, (32.35±4.68) vs (48.75±5.21) pg/ml, (13.51±3.89) vs (18.87±4.28) mg/L, (2.43±0.41) vs (2.79±0.47) g/L,  $P<0.05$ ]. There were no significant differences in APTT and adverse reactions between the two groups ( $P>0.05$ ). **Conclusion** Mailuo Shutong Pills combined with rivaroxaban can significantly enhance the therapeutic efficacy in PTS, improving blood coagulation and inflammatory reaction with good safety.

**【Key words】** venous thrombosis; Mailuo Shutong Pills; rivaroxaban; inflammatory response

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Corresponding author: SUN Bo, E-mail: ppboter2008@126.com

下肢深静脉血栓形成后综合征(post thrombosis syndrome, PTS),指急性下肢深静脉血栓形成(deep

venous thrombosis, DVT)6个月后出现的慢性下肢静脉功能不全的临床表现,包括患肢沉重、胀痛、静脉

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通信作者: 孙波, E-mail: ppboter2008@126.com

曲张、皮肤瘙痒、色素沉着、湿疹等,严重者出现下肢高度肿胀、脂性硬皮病、经久不愈的溃疡。在诊断为下肢DVT的最初2年内,即使经过规范的抗凝治疗,仍有20%~55%的患者发展为PTS,其中5%~10%的患者发展为严重的PTS,严重影响患者的生活质量<sup>[1]</sup>。对于此类患者,临床中以药物保守治疗和外科手术干预处理为主。其中,相当多的患者因没有手术指征或自身原因选择药物保守治疗,药物治疗以抗凝、消肿等对症治疗为主。近年来,中药因其疗效稳定、副作用小、患者依从性高等原因逐渐进入临床医师的视野。脉络舒通丸为纯中药制剂,具有清热解毒、化瘀通络、祛湿消肿的功效<sup>[2]</sup>。目前脉络舒通丸已在急性期深静脉血栓形成中应用,其在预防下肢深静脉血栓形成加重及复发方面得到临床肯定,对亚急性期静脉血栓导致的双下肢肿胀、疼痛、肤色暗红等也有改善。但其在下肢深静脉血栓形成后综合征患者中的应用缺乏系统的临床研究,尤其是对于已经有下肢远端溃疡形成的患者,长期应用的效果需进一步验证。本研究探讨脉络舒通丸联合利伐沙班治疗下肢深静脉血栓形成后综合征(PTS)的临床效果,为临床用药提供依据。

## 1 对象与方法

### 1.1 研究对象

回顾性分析2019年6月至2020年9月潍坊市人民医院血管外科收治的60例PTS患者的临床资料,根据治疗方法的不同将患者分为对照组和观察组,各30例。所有患者均使用超声或下肢静脉造影评估下肢静脉情况。对照组男18例,女12例;年龄49~80岁(60.4±8.5)岁;病程0.5~3(1.2±0.6)年。观察组男20例,女10例;年龄47~77(61.2±8.2)岁;病程0.3~2.5年(1.3±0.5)年。2组患者一般资料比较,差异无统计学意义( $P>0.05$ ),具有可比性。

纳入标准:(1)经下肢静脉彩超或造影证实PTS,或者符合《中医病证诊断疗效标准》<sup>[3]</sup>中“臌疮”的诊断标准;(2)年龄30~80岁;(3)语言表达能力正常,对自身症状及一般状况有判断能力,且能描述病情变化及生活质量等内容;(4)对研究内容知情同意。

排除标准:(1)严重凝血功能障碍;(2)严重心脑血管疾病;(3)严重肝、肾疾病;(4)严重传染病;(5)已行髂静脉支架植入。

### 1.2 治疗方法

对照组患者给予口服利伐沙班片[(拜尔制

药公司,国药准字H20140132)20mg/次,1次/d]抗凝治疗、穿弹力袜辅助治疗等基础治疗措施,不采用其他消肿、抗炎药物,治疗1个月后观察疗效。

观察组患者在对照组治疗方法的基础上,给予脉络舒通丸(鲁南厚普制药有限公司,国药准字Z20090636)口服治疗,1瓶/次,3次/d,7d为1个疗程。治疗1个月后观察疗效。

### 1.3 观察指标

(1)记录患者治疗前和治疗后1个月Villalta评分<sup>[4]</sup>;(2)测定空腹纤维蛋白原含量(fibrinogen, FIB)、活化部分凝血活酶时间(activated partial thromboplastin time, APTT)、白细胞介素-6(interleukin-6, IL-6)、超敏C反应蛋白(high-sensitivity C-reactive protein, hs-CRP)等指标;(3)超声检查血栓面积有无减少及血流情况;(4)记录患者不良反应发生情况。

### 1.4 疗效标准

根据静脉功能障碍评分制定相关评价标准<sup>[5]</sup>。显效:疼痛感和肿胀感完全消失,患肢与健肢周径相差 $<1$  cm,无明显色素沉着,超声检查未见下肢血栓。有效:疼痛感和肿胀感明显减轻,患肢与健肢周径相差1~2 cm,色素沉着明显减轻,超声检查提示下肢血栓面积比治疗前明显减少。无效:患者疼痛感和肿胀感的临床症状无明显变化,患肢与健肢周径相差 $>2$  cm,肤色差明显,超声检查下肢血栓面积无明显减少。总有效率=(显效+有效)/总例数 $\times 100\%$ 。

### 1.5 统计学处理

采用SPSS 22.0统计软件进行数据分析。计量资料以均数 $\pm$ 标准差( $\bar{x}\pm s$ )表示,组间比较采用 $t$ 检验。计数资料以例数(百分率)表示,组间比较采用 $\chi^2$ 检验。不良反应发生情况比较使用Fisher精确检验。 $P<0.05$ 为差异有统计学意义。

## 2 结果

### 2.1 2组患者Villalta评分比较

2组患者治疗前与治疗1个月后Villalta评分组内比较,差异均有统计学意义( $P$ 均 $<0.05$ );治疗后2组患者Villalta评分比较,观察组优于对照组( $P<0.05$ ;表1)。

表1 2组患者治疗前后Villalta评分比较

Table 1 Comparison of Villalta score between two groups before and after treatment ( $n=30$ , points,  $\bar{x}\pm s$ )

Group	Before treatment	After treatment	$t$	$P$ value
Control	19.63±2.36	7.43±1.50	29.050	<0.001
Study	18.60±3.56	6.17±2.20*	31.957	<0.001

Compared with control group, \* $P<0.05$ .

## 2.2 2组患者治疗后临床疗效比较

对照组患者总体有效率为73.33%,观察组为93.33%,观察组明显优于对照组( $P<0.05$ ;表2)。

表2 2组患者治疗后临床效果比较

Table 2 Comparison of clinical effects between two groups after treatment [n=30, n(%)]

Group	Marked effect	Valid	Invalid	Total effective rate
Control	13(43.33)	9(30.00)	8(26.67)	22(73.33)
Study	19(63.33)	9(30.00)	2(6.67)	28(93.33)*

Compared with control group, \* $P<0.05$ .

## 2.3 2组患者不良反应发生情况比较

治疗后对照组不良反应发生率为10.00%(3/30),观察组为6.67%(2/30),2组比较差异无统计学意义( $P>0.05$ ;表3)。

表3 2组患者不良反应发生情况比较

Table 3 Comparison of adverse reaction between two groups [n=30, n(%)]

Group	Bleeding	Sick	Liver injury	Adverse reaction ratio
Control	1(3.33)	1(3.33)	1(3.33)	3(10.00)
Study	0(0.00)	1(3.33)	1(3.33)	2(6.67)

## 2.4 2组患者血液流变学及相关炎症指标比较

观察组患者治疗前后FIB、APTT、IL-6、hs-CRP水平比较,差异均有统计学意义( $P$ 均 $<0.05$ );对照组治疗前后APTT、IL-6水平比较,差异均有统计学意义( $P$ 均 $<0.05$ )。治疗后组间FIB、IL-6、hs-CRP水平比较,观察组优于对照组( $P<0.05$ );APTT水平比较,差异无统计学意义( $P>0.05$ ;表4)。

## 3 讨论

PTS属中医学“赤脉”“青蛇毒”“臃疮”“脉痹”等范畴,其基本病机为湿气下注、气血瘀滞所致的脉络阻塞<sup>[2,6]</sup>,主要治疗原则为祛湿消肿、化瘀通络。现代医学认为,PTS相关临床表现主要由静脉高压导致,其由多种因素如瓣膜反流、持续静脉阻塞等造成<sup>[7]</sup>。

表4 2组患者治疗前后FIB、APTT、IL-6、hs-CRP水平比较

Table 4 Comparison of FIB, APTT, IL-6 and hs-CRP levels between two groups before and after treatment

(n=30,  $\bar{x}\pm s$ )

Group	Before treatment				After treatment			
	FIB(g/L)	APTT(s)	IL-6(pg/mL)	hs-CRP(mg/L)	FIB(g/L)	APTT(s)	IL-6(pg/mL)	hs-CRP(mg/L)
Control	2.93±0.39	31.53±2.76	77.85±5.37	26.37±3.96	2.79±0.47	38.87±4.89*	48.75±5.21*	18.87±4.28
Study	2.97±0.45	31.39±2.95	77.94±5.61	26.78±4.19	2.43±0.41**	38.34±5.47*	32.35±4.68**	13.51±3.89**

FIB: fibrinogen; APTT: activated partial thromboplastin time; IL-6: interleukin-6; hs-CRP: high-sensitivity C-reactive protein. Compared with before treatment, \* $P<0.05$ ; compared with control group after treatment, \*\* $P<0.05$ .

本研究结果显示,脉络舒通丸联用利伐沙班可显著提升PTS的治疗效果,与白斗等<sup>[8]</sup>研究结果一致。利伐沙班是一种新型口服抗凝药物,其为Xa因子直接抑制剂,治疗窗宽,不易受食物、药物及其他因素影响,服用后立即起效,且使用前不需要桥接抗凝<sup>[9-11]</sup>。脉络舒通丸主要成分为黄芪、金银花、水蛭、白芍等,黄芪补中益气、利水消肿;金银花清热解毒;水蛭化瘀散结、破血通络;白芍缓急止痛,诸药共用,可达益气活血、化瘀通络之功效。脉络舒通丸与利伐沙班联合应用时具有一定的协同作用,可提高临床疗效。

此外,观察组患者患肢周径、疼痛级别、色素沉着的改善程度明显优于对照组。下肢静脉曲张和活动后下肢肿胀、疲乏是本病的临床症状,但据回访结果来看,观察组症状更轻。究其原因可能在于,水蛭有抗血栓素、肝素、多肽类等有效成分,可发挥抗凝血酶作用;金银花有多种抗菌成分,可在一定程度上抑制炎性因子合成、分泌,这些已被现代药理学证实,从而有助于减轻机体的炎性反应。另有研究表明<sup>[12]</sup>,静脉血栓形成与炎症反应密切相关,静脉内血栓可刺激管壁产生炎症反应,而血清中IL-6和hs-CRP可介导血小板聚集并激活凝血因子从而形成血栓,因此,对于PTS患者的治疗应兼顾抗凝与抑制炎症因子水平2个方面。本研究结果显示,观察组FIB及IL-6、hs-CRP水平的改善程度明显优于对照组,这与张刚等<sup>[13]</sup>研究结果一致,脉络舒通丸可降低急性期DVT患者CPR、IL-6和FIB水平,从而缓解临床症状,证实了脉络舒通丸具有改善凝血功能及抑制机体炎症反应的作用,这可能是脉络舒通丸的重要机制之一。

综上所述,脉络舒通丸联用利伐沙班可显著提高PTS的治疗效果,其在西医抗凝治疗的基础上增加了中医活血散瘀、通络镇痛的功效,改善患者的凝血功能和炎症反应,对临床治疗具有一定的启发作用。

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