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复方菝葜颗粒联合 PT 新辅助化疗方案对晚期宫颈癌的疗效探讨 *

王小特[1] 谭宝利[2△] 赵雪静[1] 张方方[1] 邹雅芝[1]

（1 空军第 986 医院妇产科 陕西 西安 710054；2 陕西省宝鸡市解放军联勤保障部队第九八七医院综合内科 陕西 宝鸡 721004）

摘要 目的：研究复方菝葜颗粒联合 PT 新辅助化疗方案对晚期宫颈癌的疗效。**方法：**选择 2013 年 1 月～2016 年 12 月我院收治的 63 例晚期宫颈癌患者，随机分为两组。对照组使用 PT 新辅助化疗方案，其中顺铂的剂量为 75 mg /m^2，紫杉醇为的剂量为 175 mg/m^2；观察组联合口服复方菝葜颗粒，每次 3 次，每次服用 1 袋。两组均连续治疗 1 个月，然后进行广泛性手术治疗。治疗前后，比较两组的瘤体最大直径和免疫功能指标；并记录患者的远期生存情况。**结果：**治疗后，观察组的有效率为 80.64 %，明显高于对照组(56.25 %，*P*<0.05)；两组的瘤体最大直径均较治疗前明显降低 (*P*<0.05)，且观察组宫颈癌患者的瘤体最大直径明显低于对照组(*P*<0.05)；对照组的 CD_3^+、CD_4^+、IgM、IgA、IgG 较治疗前明显降低(*P*<0.05)，观察组的 CD_3^+、CD_4^+、IgM、IgA、IgG 较治疗前明显升高(*P*<0.05)，且观察组 CD_3^+、CD_4^+、IgM、IgA、IgG 明显高于对照组(*P*<0.05)；观察组 1 年生存率为 93.55 %(29/31)、2 年生存率为 83.87 %(26/31)、3 年生存率为 77.42 %(24/31)，均明显高于对照组(*P*<0.05)。**结论：**复方菝葜颗粒联合 PT 新辅助化疗方案能改善晚期宫颈癌患者的免疫功能，提高远期生存率。

关键词：复方菝葜颗粒；PT 新辅助化疗方案；晚期宫颈癌

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A Study on the Effect of Compound Smilax Granule Combined with Pt Neoadjuvant Chemotherapy on the Advanced Cervical Cancer*

WANG Xiao-te[1], TAN Bao-li[2△], ZHAO Xue-jing[1], ZHANG Fang-fang[1], ZOU Ya-zhi[1]

(1 Department of Obstetrics and Gynecology, No.986 Hospital of the Air Force, Xi'an, Shaanxi, 710054, China;

2 Department of General Internal Medicine, 987th Hospital of PLA Joint Services Crops, Baoji, Shaanxi, 721004, China)

ABSTRACT Objective: To investigate the effect of compound Smilax granule combined with Pt neoadjuvant chemotherapy on the advanced cervical cancer. **Methods:** 63 cases of patients with advanced cervical cancer who were treated in our hospital from January 2013 to December 2016, were selected and divided into two groups randomly. The control group was given Pt neoadjuvant chemotherapy, the dose of cisplatin was 75 mg/m^2, the dose of paclitaxel was 175 mg/m^2. The observation group was treated by compound Smilax granules three times a time, one bag a time. Both groups were treated continuously for 1 month. Then they were given extensive surgical treatment. Before and after treatment, the tumor diameter and immune function indexes of the two groups were compared, and the long-term survival of patients was recorded. **Results:** After treatment, he effective rate of observation group was 80.64 %, which was significantly higher than control group (56.25 %, *P*<0.05). After treatment, the maximum diameter of tumor in the two groups were significantly decreased (*P*<0.05), which was significantly lower in the observation groupthan that in the control group (*P*<0.05). After treatment, the CD_3^+, CD_4^+, IgM, IgA and IgG in the control group were significantly lower (*P*<0.05), and the CD_3^+, CD_4^+, IgM, IgA and IgG in the observation group were significantly higher (*P*<0.05), and the CD_3^+, CD_4^+, IgM, IgA and IgG in the observation group were significantly higher than those in the control group (*P*<0.05). The 1-year survival rate of the observation group was 93.55 % (29/31), the 2-year survival rate was 83.87 % (26/31), the 3-year survival rate was 77.42 % (24/31), which were all significantly higher than that of the control group (*P*<0.05). **Conclusion:** Compound Smilax granule combined with Pt neoadjuvant chemotherapy can improve the immune function and long-term survival rate of patients with advanced cervical cancer.

Key words: Compound Smilax Granule; Pt Neoadjuvant Chemotherapy; Advanced Cervical Cancer

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前言

宫颈癌是全球女性生殖道中最常见的癌症之一，其发病率仅次于乳腺癌，我国新发宫颈癌患者占全球总数的 1/3[1-3]。该病

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作者简介：王小特(1972-)，女，本科，副主任医师，主要研究方向：妇科肿瘤微创治疗，电话：13891892279，E-mail：wxt1501059476@163.com

△ 通讯作者：谭宝利(1971-)，男，本科，副主任医师，主要研究方向：肿瘤内科，E-mail：15229957143@163.com

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在早期无显著的症状，发现时多属晚期，患者出现阴道排液量增多，尿急、尿频和肛门坠胀等[4,5]。宫颈癌治疗目前主要采取放疗和手术，虽可以促进疾病的恢复，但尚无法对亚临床病灶进行有效地控制，治疗后复发率较高[6,7]。因而探索一种高效和安全的治疗手段具有重大的临床意义。

近年来的研究认为在手术前期实施新辅助治疗能缩小宫颈癌患者的肿瘤病灶、提高手术的切尽率、降低术后的转移率和复发率、降低病理危险因素[8]。中医对于宫颈癌的发生发展有独特的认识，认为其发病原因在于房劳多产、饮食不节、情志不畅所致的正虚邪实。临床治疗多采用扶正与驱邪相结合，抑制癌细胞的浸润发展。复方菝葜颗粒具有软坚散结、清热解毒和滋阴益气的功效。本研究主要探讨了复方菝葜颗粒联合 PT 新辅助化疗方案对晚期宫颈癌的疗效。

1 资料与方法

1.1 一般资料

选择我院 2013 年 1 月～2016 年 12 月收治的 63 例晚期宫颈癌患者，用抽签法将其随机分为两组。观察组 31 例，年龄 29～72 岁，平均(46.14± 2.33)岁；体重 53～75 kg，平均(68.59± 12.11) kg；Karnofsky 评分平均为(73.65± 13.29)分；生长类型：内生型 10 例(占 32.26 %)，外生型 21 例(占 67.74 %)；病理分型：鳞癌 20 例(占 64.52 %)，腺癌 8 例(占 25.81 %)，鳞腺癌 3 例(占 9.68 %)。对照组 32 例，年龄 29～72 岁，平均(46.07± 2.48)岁；体重 53~75 kg，平均(68.44± 12.07) kg；Karnofsky 评分平均为(73.92± 12.24)分；生长类型：内生型 11 例(占 34.37 %)，外生型 21 例(占 65.62 %)；病理分型：鳞癌 18 例(占 56.25 %)，腺癌 10 例(占 31.25 %)，鳞腺癌 4 例(占 12.50 %)。两组的基线资料比较差异均无统计学意义，具有可比性(P>0.05)。

纳入标准：(1)年龄 29~72 岁；(2)根据症状、病史、宫颈组织活检以及阴道镜检查被确诊宫颈癌；(3)近半个月内没有使用过化疗药物或者可能会影响本研究疗效观察的药物；(4)肝肾功能没有受到明显的损害；(5)没有精神异常，神志比较清醒；(6)没有严重的内科疾病；(7)骨髓造血功能正常；(8)知情同意。排除标准：(1)近半个月内采取过其他药物治疗的患者；(2)不符合上面 8 项纳入标准的患者；(3)合并有急性感染或比较严重未得到有效控制的内科疾患的患者；(4)合并患有第二原发性恶性肿瘤的患者；(5)对紫杉醇、顺铂和复方菝葜颗粒等药物过敏的患者；(6)有严重的精神疾病、神志异常和抑郁症的患者；(7)妊娠或哺乳期的宫颈癌患者；(8)依从性差，无法严格地遵医嘱进行治疗的患者。

1.2 治疗方法

对照组使用 PT 新辅助化疗方案，其中顺铂的剂量为 75 mg/m^2，紫杉醇为的剂量为 175 mg/m^2，采取 Seldinger 置管技术从晚期宫颈癌患者一侧股动脉进行插管至对侧的髂内动脉部位，而且通过造影检查显示晚期宫颈癌患者的盆腔血供情况，然后插进患者对侧的子宫动脉，在 30 min 内缓慢注射顺铂和紫杉醇，而且采用明胶海绵进行栓塞处理，把导管退回至髂内动脉的分支部位，注射剩余的药物剂量。观察组：联合口服复方菝葜颗粒，每次 3 次，每次服用 1 袋。两组均连续治疗 1 个月。然后进行广泛性手术治疗。

1.3 观察指标

疗效[9]：(1)完全缓解：肿瘤标志物水平恢复正常，全部病灶均消失；(2)部分缓解：基线病灶最长直径缩小》30 %；(3)稳定：基线病灶长径总比出现一定程度的缩小，但未达到部分缓解；(4)进展：出现新病灶。

比较两组治疗前后的瘤体最大直径。在治疗前后，空腹采集患者 3 mL 上肢静脉血，常规检测两组的 CD_3^+、CD_4^+、IgM、IgA、IgG。记录两组的 1 年、2 年和 3 年生存情况。

1.4 统计学分析

应用 SPSS 21.0 软件进行数据分析，计量资料以 ($\bar{x}$± s)表示，组间对比用 t 检验，计数资料用%表示，组间比较对比采用 x^2 检验，以 P<0.05 为差异有统计学意义。

2 结果

2.1 两组疗效对比

治疗后，观察组的有效率为 80.64 %(25/31)，明显高于对照组的 56.25 %(18/32)，组间对比有差异(x^2=4.325，P=0.038)，见表1。

表 1 两组疗效的比较[例(%)]

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

Groups	n	Complete remission	Partial remission	Stable	Progress	The total effect rate
Control group	32	10(31.25)	8(25.00)	12(37.50)	2(6.25)	18(56.25)
Observation group	31	11(35.48)	14(45.16)	5(16.13)	1(3.22)	25(80.64)*

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

2.2 两组治疗前后瘤体最大直径对比

治疗后，两组的瘤体最大直径均较治疗前明显降低(P<0.05)，且观察组明显低于对照组(t=4.105，P=0.000)，见表 2。

2.3 两组治疗前后的 CD_3^+、CD_4^+、IgM、IgA、IgG 对比

治疗后，对照组的 CD_3^+、CD_4^+、IgM、IgA、IgG 明显降低(P<0.05)，观察组的 CD_3^+、CD_4^+、IgM、IgA、IgG 明显升高(P<0.05)，且观察组的 CD_3^+、CD_4^+、IgM、IgA、IgG 明显高于对照组(P<0.05)，见表 3。

2.4 两组的 1 年、2 年和 3 年生存情况对比

观察组 1 年生存率为 93.55 %(29/31)、2 年生存率为 83.87 %(26/31)、3 年生存率为 77.42 %(24/31)，均明显高于对照组(P<0.05)，见表 4。

3 讨论

宫颈癌患者的发病年龄不断呈年轻化的趋势，常规的根治性放疗会对卵巢的生理功能产生严重的损伤[10-12]。大多数宫颈

表 2 两组治疗前后瘤体最大直径对比($\bar{x}\pm s$,cm)

Table 2 Comparison of the maximum diameter of tumor between the two groups before and after treatment($\bar{x}\pm s$, cm)

Groups	n	Before treatment	After treatment
Control group	32	4.09± 0.53	3.62± 0.41#
Observation group	31	4.11± 0.56	3.27± 0.25*#

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

表 3 两组治疗前后的 CD_3^+、CD_4^+、IgM、IgA、IgG 对比($\bar{x}\pm s$)

Table 3 Comparison of CD_3^+, CD_4^+, IgM, IgA and IgG between the two groups before and after treatment ($\bar{x}\pm s$)

Groups	n		CD_3^+(%)	CD_4^+(%)	IgM(g/L)	IgA(g/L)	IgG(g/L)
Control group	32	Before treatment	41.36± 12.25	32.27± 4.59	1.35± 0.17	1.24± 0.29	7.65± 0.89
		After treatment	32.27± 10.48#	24.59± 3.47#	1.03± 0.11#	1.02± 0.27#	5.48± 1.13#
Observation group	31	Before treatment	40.78± 11.49	33.65± 3.74	1.34± 0.15	1.25± 0.27	7.63± 0.92
		After treatment	60.34± 13.89*#	45.71± 5.79*#	2.37± 0.24*#	2.73± 0.45*#	12.09± 2.35*#

表 4 两组的 1 年、2 年和 3 年生存情况对比 [例(%)]

Table 4 Comparison of the 1-year, 2-year and 3-year survival between the two groups [n (%)]

Groups	n	1 year survival rate	2 year survival rate	3 year survival rate
Control group	32	23(71.87)	20(62.50)	16(50.00)
Observation group	31	29(93.55)*	26(83.87)*	24(77.42)*

癌患者经过 2～3 个周期术前新辅助化疗之后瘤体会明显缩小,宫旁组织的浸润程度明显改善,肿瘤的临床分期明显降低,有助于扩大手术的适应证,为手术提供比较满意的条件,降低损伤风险和手术的难度[13-17]。顺铂是铂的一种金属络合物,可以对 DNA 链内和链间交链发挥作用，以进一步形成顺铂 -DNA 的复合物,对 DNA 的复制进行干扰,使模板复制正常的生理学功能得到改变,而且可以改善肿瘤组织中的血供状况,还能促进化疗药物深达患者的肿瘤组织中[18-23]。紫杉醇为一种比较新型的抗微管剂,能在小管 β 位上发生特异性的结合,有效促进微管蛋白二聚体发生进一步的组合,而且抑制微管蛋白二聚体的解聚,而产生稳定微管的效果,使得在有丝分裂过程中不能形成纺锤体的组织结构,可以抑制对有丝分裂期细胞以及分裂间期细胞功能比较重要的微管，发挥抑制细胞分裂增殖的效果[24-28]。但仍存在部分晚期宫颈癌患者疗效不够显著、不良反应较大等问题,因而,还需对术前的治疗方法给予不断的优化。

采取联合应用中药可以有效调整机体的机能，减轻放、化疗所产生的毒副反应,扶正去邪,延长生存期,有助于提高治疗有效率及生活质量。复方菝葜颗粒是由鱼腥草、红土茯苓(菝葜)、猫爪草、款冬花、土鳖虫、大枣(去核)、枸杞组成的一种复方制剂,具有软坚散结、清热解毒、滋阴益气之功效。现代药理学研究发现,土鳖虫具有抑制血小板凝集的效果;菝葜具有镇痛、抗炎、抗氧化和抗肿瘤等多种的生物活性；款冬花有祛痰、止咳、平喘的效果;鱼腥草和猫爪草具有增强免疫功能和镇痛的效果[29]。研究表明,复方菝葜颗粒能明显增加 Bax m RNA 的表达量,减慢细胞增殖的速度,降低 Bcl-2/Bax 比例和 Bcl-2 mRNA 的表达,诱导 A549 细胞凋亡,从而对宫颈癌患者发挥显著的疗效[30]。本研究结果显示治疗后,观察组宫颈癌患者的瘤体最大直径明显低于对照组,的 CD_3^+、CD_4^+、IgM、IgA、IgG 明显高于对照组,1~3 年的生存率明显高于对照组,表明在 PT 新辅助化疗方案的基础上联合使用复方菝葜颗粒可以明显缩小晚期宫颈癌患者的瘤体最大直径,提高远期生存率。分析其机制可能与增加机体的免疫功能相关,这与王静[29]等学者的研究类似,该学者在化疗后应用复方菝葜颗粒,可以显著的发挥抗肿瘤、抗炎、镇痛等作用,通过调节免疫细胞 IgG、IgA、IgM、CD_3^+及 CD_4^+ 水平的表达,改善肿瘤的免疫微环境,增强细胞免疫功能,间接抑制与杀伤肿瘤细胞,从而提高患者的远期生存率。但本研究对于复方菝葜颗粒治疗晚期宫颈癌的具体作用机制未进行研究,后期需要不断的完善上述不足。

综上，复方菝葜颗粒联合 PT 新辅助化疗方案能改善晚期宫颈癌患者的免疫功能,提高远期生存率。

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