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参附注射液联合多西他赛治疗晚期非小细胞肺癌的临床效果观察 *

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摘要 目的：探讨参附注射液联合多西他赛治疗晚期非小细胞肺癌的临床效果和安全性。**方法：**选取 2016 年 1 月 ~2019 年 1 月我院收治的晚期非小细胞肺癌患者 60 例，采用随机数字表法将患者分为两组，每组各 30 例。对照组患者给予多西他赛注射液进行化疗，观察组在对照组的基础上给予参附注射液，比较两组患者治疗后的临床治疗效果，治疗前后免疫功能相关指标、生活质量评分的变化及不良反应的发生情况。**结果：**治疗后，观察组疾病控制率为 86.67%，对照组为 60.00%，观察组显著高于对照组（$P<0.05$）；对照组患者治疗后 $CD3^+$、$CD4^+$ 和 $CD4^+/CD8^+$ 水平显著下降，$CD8^+$ 水平显著升高，观察组患者 $CD3^+$、$CD4^+$ 和 $CD4^+/CD8^+$ 水平显著升高，$CD8^+$ 水平显著下降，观察组患者 $CD3^+$、$CD4^+$ 和 $CD4^+/CD8^+$ 水平显著高于对照组，$CD8^+$ 水平显著低于对照组（$P<0.05$）；两组治疗后的食欲、疼痛、乏力、呼吸困难、痰中带血、咳嗽评分均较治疗前显著下降，且观察组以上指标均显著低于对照组（$P<0.05$）；观察组患者中性粒细胞减少和便秘的发生率均显著低于对照组（$P<0.05$），两组血小板减少、恶心呕吐和神经毒性的发生率比较无统计学差异（$P>0.05$）。**结论：**参附注射液联合多西他赛可显著改善晚期非小细胞肺癌患者的免疫功能和生活质量，提高临床治疗效果，且安全性高。

关键词：参附注射液；多西他赛；晚期非小细胞肺癌；效果

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Clinical Effect of Shenfu Injection Combined with Docetaxel in the Treatment of Advanced Non-small Cell Lung Cancer*

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ABSTRACT Objective: To observe the clinical effect and security of shenfu injection combined with docetaxel in the treatment of advanced non-small cell lung cancer. **Methods:** 60 patients with non-small cell lung cancer were selected from January 2016 to January 2019 in our hospital and divided into two groups according to the random number table method, 30 cases in each group. Patients in the control group were given docetaxel injection for chemotherapy, and those in the observation group were given shenfu injection on the basis of those in the control group. The clinical effect after treatment, changes in immuno-function related indicators, life quality score before and after treatment and adverse reactions were compared between the two groups. **Results:** After treatment, the disease control rate was 86.67% in the observation group and 60.00% in the control group, which was significantly higher than that in the control group ($P<0.05$). After treatment, the levels of $CD3^+$, $CD4^+$ and $CD4^+/CD8^+$ in the control group were significantly decreased, and the levels of $CD8^+$ were significantly increased. The levels of $CD3^+$, $CD4^+$ and $CD4^+/CD8^+$ in the observation group were significantly increased, and the levels of $CD8^+$ were significantly decreased. The levels of $CD3^+$, $CD4^+$ and $CD4^+/CD8^+$ in the observation group were significantly higher than those in the control group, and the levels of $CD8^+$ were significantly lower than those in the control group ($P<0.05$). The scores of appetite, pain, fatigue, dyspnea, bloody sputum and cough in the two groups after treatment were significantly lower than those before treatment, and the above indexes in the observation group were significantly lower than those in the control group ($P<0.05$). The incidence of neutropenia and constipation in the observation group was significantly lower than that in the control group ($P<0.05$), and there was no statistical difference in the incidence of thrombocytopenia, nausea and vomiting and neurotoxicity between the two groups

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(*P*>0.05). **Conclusion:** Shenfu injection combined with docetaxel can significantly improve the immune function and quality of life of patients with advanced non-small cell lung cancer, improve the clinical treatment effect, and have high safety.

Key words: Shenfu injection; Docetaxel; Advanced non-small cell lung cancer; Effect

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前言

肺癌是目前世界范围内发病率最高的恶性肿瘤之一,也是肿瘤致死的主要原因,有研究显示肺癌的发病率占全部恶性肿瘤的 20%,死亡率约占肿瘤死亡的 23.8%,非小细胞肺癌是一种常见的肺癌类型,约占肺癌发病率的 80%~85%,且近年来的发病率有明显上升的态势[1-3]。由于肺癌早期没有典型的临床症状,也没有特异性的筛查手段,导致约 60%的患者在确诊时已处于晚期,失去手术治疗的机会,严重影响患者的治疗和预后[4,5]。目前,临床对于晚期非小细胞肺癌的治疗以化疗为主,但化疗会影响患者的免疫功能,且不良反应较多,不仅对患者的生活质量造成影响,也会影响化疗药物的使用和患者的预后[6-8]。

除了延长患者的生存期,改善患者的临床症状和维持较好的生活质量成为恶性肿瘤治疗的目标。祖国传统医学认为正气不足是肿瘤发生的根本原因,晚期非小细胞肺癌主要表现为气虚、脾虚,化疗后虚症进一步加重,损害人体的正气,治疗需以扶正、益气健脾为主[9]。多项研究显示中药在治疗晚期恶性肿瘤中可起到增效减毒的作用,可显著改善患者的生活质量[10]。因此,本研究主要探讨了参附注射液联合多西他赛治疗晚期非小细胞肺癌的效果和安全性,以期为肺癌的临床治疗提供更多的参考依据。

1 资料与方法

1.1 一般资料

选取 2016 年 1 月 ~2019 年 1 月我院收治的晚期非小细胞肺癌患者 60 例, 所有患者均符合《中国常见恶性肿瘤诊治规范》中的相关诊断标准。纳入标准:① 患者均经病理学或细胞学确诊为非小细胞肺癌;② 临床分期为Ⅲ、Ⅳ期;③ 无法进行手术或术后复发者;④ 入组前未接受过相关治疗者;⑤ 预计生存期大于 6 个月者。排除标准:① 合并心、肝、肾等重要器官恶性肿瘤者;② 合并其他严重感染性疾病及造血功能异常者;③ 合并肺部其他疾病者;④ 精神神经异常者;⑤ 不能配合治疗者。

采用随机数字表法将患者分为两组,每组各 30 例。对照组男 18 例,女 12 例;年龄 53~68 岁,平均 60.12± 2.54 岁;肿瘤分期:Ⅲ期 21 例、Ⅳ期 9 例;肿瘤类型:腺癌 16 例,鳞癌 11 例,腺鳞癌 3 例。观察组男 19 例, 女 11 例; 年龄 51~69 岁, 平均 61.05± 2.83 岁;肿瘤分期:Ⅲ期 20 例、Ⅳ期 10 例;肿瘤类型:腺癌 15 例,鳞癌 10 例,腺鳞癌 5 例。两组一般资料比较均无统计学差异(*P*>0.05),具有可比性。

1.2 治疗方法

对照组患者给予多西他赛注射液进行化疗,每个化疗周期的第 1 天静脉注射多西他赛注射液 (上海创诺制药有限公司,国药准字 H20113165),75 mg/m^2,21 天为一个周期。观察组在对照组的基础上给予参附注射液(华润三九(雅安)药业有限公司,国药准字 Z20043117),60~80 mL 加入 250 mL 5%葡萄糖溶液中静脉滴注,1 次 /d,21 天为一个周期。两组患者均连续治疗 2 个周期。治疗期间给予止吐、利尿、PPI、水化等常规对症治疗,并严密监测患者的生命体征。

1.3 观察指标

① 比较两组患者的临床治疗效果。② 比较两组患者的免疫功能,分别于治疗前后抽取两组患者的空腹静脉血 3 mL,采用流式细胞仪测定两组患者的 CD3$^+$、CD4$^+$ 和 CD8$^+$ 水平,并计算 CD4$^+$/CD8$^+$ 值。③ 比较两组患者的生活质量,分别于治疗前后采用肺癌症状量表(LCSS)对两组患者的生活质量进行评估,包括食欲、疼痛、乏力、呼吸困难、痰中带血、咳嗦等,每项总分为 100 分,得分越高表示患者的生活质量越低。④ 比较两组患者不良反应的发生情况。

1.4 临床疗效评定标准

完全缓解(CR):肿瘤病灶完全消失,3 个月内未复发;部分缓解(PR):病灶减少>20%,并维持 3 个月;稳定(SD):肿瘤病灶未发生明显变化;进展(PD):肿瘤病灶显著增大。以 CR+PR+SD 计算疾病控制率(DCR)。

1.5 统计学方法

采用 SPSS16.0 对数据进行统计学分析,计数资料以率(%)表示,组间比较行卡方检验,计量资料以($\bar{x}$± s)表示,组间比较行 t 检验,以 *P*<0.05 为差异有统计学意义。

2 结果

2.1 两组临床治疗效果的比较

治疗后,观察组疾病控制率为 86.67%,对照组为 60.00%,观察组显著高于对照组(*P*<0.05),见表 1。

表 1 两组临床治疗效果比较[例(%)]

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

Groups	Cases	CR	PR	NC	PD	DCR
Control group	30	5(16.67)	6(20.00)	7(23.33)	12(40.00)	18(60.00)
Observation group	30	12(40.00)	8(26.67)	6(20.00)	4(13.33)	26(86.67)
x^2						4.322
P						0.036

2.2 两组患者治疗前后免疫功能相关指标的比较

治疗前，两组患者的 $CD3^+$、$CD4^+$、$CD8^+$ 和 $CD4^+/CD8^+$ 水平比较无统计学差异（$P>0.05$），对照组患者治疗后 $CD3^+$、$CD4^+$ 和 $CD4^+/CD8^+$ 水平显著下降，$CD8^+$ 水平显著升高，观察组患者 $CD3^+$、$CD4^+$ 和 $CD4^+/CD8^+$ 水平显著升高，$CD8^+$ 水平显著下降，且两组间比较具有统计学差异（$P<0.05$），见表 2。

表 2 两组患者治疗前后的免疫功能相关指标比较（$\bar{x}\pm s$）

Table 2 Comparison of the immune function related indicators between two groups before and after treatment（$\bar{x}\pm s$）

	Control group(n=30)		Observation group(n=30)	
	Before treatment	After treatment	Before treatment	After treatment
$CD3^+$(%)	52.26± 3.25	50.03± 2.37*	52.06± 3.61	62.89± 5.74*#
$CD4^+$(%)	36.58± 4.13	34.01± 3.64*	35.36± 4.53	39.64± 5.12*#
$CD8^+$(%)	32.51± 3.64	35.26± 5.67*	32.78± 3.91	29.88± 2.36*#
$CD4^+/CD8^+$	1.26± 0.31	0.92± 0.26*	1.27± 0.33	1.49± 0.42*#

注：与治疗前相比，*$P<0.05$；与对照组相比，#$P<0.05$。

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

2.3 两组患者治疗前后生活质量的比较

治疗前，两组患者的食欲、疼痛、乏力、呼吸困难、痰中带血、咳嗽评分比较无统计学差异（$P>0.05$），两组治疗后各项评分均较治疗前显著下降，且观察组以上指标均显著低于对照组（$P<0.05$），见表 3。

表 3 两组患者治疗前后生活质量评分的比较（$\bar{x}\pm s$，分）

Table 3 Comparison of quality of life acore between two groups before and after treatment（$\bar{x}\pm s$）

	Control group(n=30)		Observation group(n=30)	
	Before treatment	After treatment	Before treatment	After treatment
Appetite	89.92± 20.54	78.47± 18.25*	87.03± 20.33	65.43± 12.67*#
Pain	75.61± 15.32	64.65± 11.36*	74.28± 15.06	56.84± 10.49*#
Weak	75.12± 14.15	68.03± 11.37*	72.98± 13.85	56.94± 10.85*#
Dyspnea	87.95± 20.37	75.62± 13.64*	85.16± 18.64	61.38± 11.54*#
Bloody sputum	91.85± 24.37	80.06± 18.12*	90.37± 24.84	71.04± 13.21*#
Cough	58.32± 9.25	50.52± 8.36*	60.04± 9.87	45.86± 6.29*#

注：与治疗前相比，*$P<0.05$；与对照组相比，#$P<0.05$。

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

2.4 两组患者不良反应发生情况的比较

两组患者的不良反应主要表现为骨髓抑制、胃肠道反应和神经毒性等。观察组患者的中性粒细胞减少和便秘的发生率显著低于对照组（$P<0.05$），两组血小板减少、恶心呕吐和神经毒性的发生率比较无统计学差异（$P>0.05$），见表 4。

表 4 两组患者不良反应发生情况比较[例(%)]

Table 4 Comparison of the incidence of adverse reactions between two groups[n(%)]

Groups	Neutropenia	Thrombocytopenia	Nausea and vomiting	Constipation	Peripheral neurotoxicity
Control group	26(86.67)	5(16.67)	17(56.67)	23(76.67)	8(26.67)
Observation group	19(63.33)	3(10.00)	13(43.33)	11(36.67)	6(20.00)
x^2	4.356	0.577	1.067	9.774	0.373
P	0.037	0.706	0.302	0.002	0.542

3 讨论

晚期非小细胞肺癌的治疗以化疗为主，多西他赛是一种常用的化疗药，也是临床公认的治疗非小细胞肺癌的一线或二线用药[11-13]。但其不良反应较多，可降低患者的免疫功能，使患者的服药依从性下降，进而影响其预后和生活质量[14-16]。多西他赛是新一代的紫杉醇类抗肿瘤药物，可作用于细胞周期的 M 期，减少微管数量，破坏微管的网状结构，进而发挥抗肿瘤作用，且

是目前临床治疗非小细胞肺癌的最有效的药物之一[19-21]。但化疗药物在杀灭肿瘤细胞的同时对机体的正常细胞也会产生影响，可显著抑制患者的免疫功能[22,23]。

$CD4^+/CD8^+$ 是反映机体细胞免疫功能的重要指标，当 $CD4^+/CD8^+$ 值较低时，表示机体的免疫应答能力减弱[17-19]。本研究结果显示观察组患者治疗后的 $CD3^+$、$CD4^+$ 和 $CD4^+/CD8^+$ 水平显著升高，$CD8^+$ 水平显著下降，与对照组相比具有统计学差异，说明参附注射液联合多西他赛可显著提高晚期非小细胞肺癌患者的免疫功能。参附注射液来源于著名方剂 " 参附汤 "，主要由红参和黑附片提取精制而成，有效成分为人参皂甙、人参多糖和水溶性乌头类生物碱等，具有补气温阳、救逆固脱的功效，主要用于治疗元气不足、阳气虚脱之症。现代药理研究表明，人参皂甙具有杀伤肿瘤细胞和调节机体免疫力的作用，乌头类生物碱可直接抑制或杀灭肺癌细胞[24,25]。因此，参附注射液不仅具有直接抑制肿瘤的作用，还能够显著改善患者的免疫功能。

有研究显示具有两种或以上症状的非小细胞肺癌患者症状负担可显著影响患者的生活质量，常见的症状为疼痛和呼吸困难，另外乏力、气促、咳嗽、痰中带血、食欲不振等在晚期非小细胞肺癌患者中出现的比例也比较高 [26-28]。本研究采用 LCSS 评分法对患者的症状负担进行评分，以评估患者的生活质量，结果显示治疗后两组患者的 LCSS 评分均显著下降，且观察组显著低于对照组，说明参附注射液联合多西他赛可显著改善晚期非小细胞肺癌患者的临床症状，提高患者的生活质量，这可能与参附注射液可显著提高患者的免疫功能，减少化疗过程中的不良反应有关[29,30]。本研究结果还显示参附注射液可显著降低多西他赛化疗的晚期非小细胞肺癌患者的不良反应。这是可能由于参附注射液可促使肿瘤细胞更早、更多的凋亡，促进造血干细胞的增殖，改善患者骨髓微环境，从而减轻不良反应。

综上所述，参附注射液联合多西他赛可显著改善晚期非小细胞肺癌患者的免疫功能和生活质量，提高临床治疗效果，且安全性高。

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