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中药联合放化疗治疗中期非小细胞肺癌的临床疗效 *

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摘要 目的：探讨中药联合放化疗手段治疗中期非小细胞肺癌患者的临床效果。**方法：**选取 2012 年 1 月 -2014 年 1 月陕西中医药大学附属医院肿瘤科、肿瘤科和呼吸科收治的非小细胞肺癌患者 80 例作为本研究的研究对象，按照入院顺序将其随机分为对照组和治疗组。对照组 39 例给予常规放化疗治疗，治疗组 41 例在对照组的基础上给予参芪五味子片进行治疗。比较两组患者的近期疗效、治疗前后卡氏(KPS)评分情况、T 淋巴细胞亚群的变化情况及不良反应的发生情况。**结果：**治疗后，治疗组的总体有效率为 39.02%，与对照组(28.20%)比较差异无统计学意义(P＞0.05)。治疗组患者治疗后的 KPS 评分改善率为 70.70%，明显高于对照组(42.00%，P＜0.05)。两组患者治疗后的 $CD3^+$、$CD4^+$、$CD4^+/CD8^+$ 水平均较治疗前显著升高、$CD8^+$ 水平较治疗前明显降低，且治疗组 $CD3^+$、$CD4^+$、$CD4^+/CD8^+$ 水平显著高于对照组，而 $CD8^+$ 水平明显低于对照组(P＜0.05)。治疗组的各不良反应发生率均显著低于对照组(P＜0.05)。**结论：**中药联合放化疗治疗中期非小细胞肺癌虽不能显著提高临床效果，但可有效缓解放化疗所致的不良反应，提高患者免疫功能，改善患者的生活质量。

关键词：非小细胞肺癌；放化疗；中药联合放化疗

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Clinical Efficacy of Traditional Chinese Medicine Combined with Radiotherapy and Chemotherapy in the treatment of Non-small Cell Lung Cancer*

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ABSTRACT Objective: To explore the clinical effect of traditional Chinese medicine combined with radiotherapy and chemotherapy in the treatment of patients with non-small cell lung cancer at the early and middle stage. **Methods:** 80 patients with non-small cell lung cancer admitted to the Department of Oncology, Oncology and Respiratory Diseases of the Affiliated Hospital of Shaanxi University of Traditional Chinese Medicine from January 2012 to January 2014 were selected as the study subjects. According to the admission order, they were randomly divided into the control group and the treatment group. 39 patients in the control group were treated with conventional radiotherapy and chemotherapy, 41 patients in the treatment group were treated with Shenqi Schisandra tablets on the basis of control group. The short-term efficacy, changes of Kaposr (KPS) score, T lymphocyte subsets before and after treatment and the occurrence of adverse reactions were compared between two groups. **Results:** After treatment, the overall effective rate of treatment group was 39.02%, and there was no significant difference compared with the control group (28.20%) (P>0.05). The improvement rate of KPS score after treatment in the treatment group was 70.70%, which was significantly higher than that in the control group (42.00%, P<0.05). The levels of $CD3^+$, $CD4^+$, $CD4^+/CD8^+$ in the two groups were significantly higher than those before treatment, and the level of $CD8^+$ was significantly lower than that before treatment.The levels of $CD3^+$, $CD4^+$ and $CD4^+/CD8^+$ in the treatment group were significantly higher than those in the control group, while the level of $CD8^+$ was significantly lower than that in the control group (P<0.05). The incidence of adverse reac-

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tions in the treatment group was significantly lower than that in the control group (P<0.05). **Conclusion:** Although traditional Chinese medicine combined with radiotherapy and chemotherapy for the treatment of metaphase non-small cell lung cancer can not significantly improve the clinical effect, it can effectively alleviate the adverse reactions caused by radiotherapy and chemotherapy, improve the patients' immune function and the quality of life.

Key words: Non-small cell lung cancer; Radiotherapy and chemotherapy; Chinese medicine combined with radiotherapy and chemotherapy

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前言

肺癌是临床中常见的恶性肿瘤之一,发病率居恶性肿瘤的第一位[1],非小细胞肺癌约占肺癌的 80%。中老年人患者人群比例在肺癌患者中占比较高,大多数患者在确诊时已经为 III、IV 期,病死率较高[2]。老年肺癌患者具有一些共同的临床特征,主要表现为病情发展相对缓慢、临床症状不典型、隐形癌的占比高[3]。放化疗会引起患者带不同程度的不良反应,如骨髓抑制、疲乏等,导致患者身体和精神的双重痛苦[4,5]。

中医药治疗强调整体观念和辩证论治,可以减轻放化疗产生的副作用[6,7]。中药和西药的联合治疗可以兼顾整体和个体治疗观念,能够很好的提高患者的免疫功能、生存质量,同时延缓生存时间,减少患者的痛苦[8,9],中西结合治疗的方法已成为肺癌的主要治疗方式之一[10,11]。本研究通过分析中药联合同期放疗治疗中期非小细胞肺癌的效果,旨在为其临床治疗提供更多的参考依据,具体结果报道如下。

1 材料与方法

1.1 一般资料

选取 2012 年 1 月 -2014 年 1 月陕西中医药大学附属医院肿瘤科及肿瘤科和呼吸科收治的非小细胞肺癌患者 80 例作为本研究的研究对象，纳入本研究的患者符合 2011 年美国国立综合癌症网络对非小细胞肺癌的诊断标准[12]。所有患者首次入院后需进行卡氏 KPS(kamofsky)评分来评估患者的身体体力状态和健康情况。将患者随机分为治疗组和对照组，治疗组 41 例,其中男性 22 例,女性 19 例,平均年龄为 57.3± 7.9 岁;患者中腺癌 21 例,鳞癌 20 例;对照组 39 例,其中男性 19 例,女性 20 例；平均年龄为 58.1± 9.8 岁；患者中腺癌 21 例，鳞癌 18 例。经统计学比较,两组间一般临床资料比较差异无统计学意义(P＞0.05),具有可比性。

1.2 纳入和排除标准

1.2.1 纳入标准 患者符合 2011 年美国国立综合癌症网络中非小细胞肺癌的诊断标准;KPS 评分≥ 60；研究者判断患者的预期生存期至少＞3 个月;患者血、尿常规、心电图、血脂、血糖及肝肾各项功能检查后无严重疾病者；停止其他的抗肿瘤治疗≥ 1 个月,且自愿参加本研究者。

1.2.2 排除标准 具有严重的合并疾病,如高血压等心脑血管疾病、肺结核等呼吸系统疾病、消化系统疾病、糖尿病、血液病或肝肾功能不全等;合并有呼吸、心力衰竭、心肌梗死、心绞痛;对所使用的抗肿瘤药物过敏或禁忌者。

1.3 治疗方法

对照组:给予同步放化疗治疗治疗,其中,化疗方案为:第一天多西他赛(江苏恒瑞医药有限公司,国药准字 H20020543) 75 mg/m^2 持续静脉滴注 1 小时,第 1-5 天顺铂(齐鲁制药有限公司,国药准字 20023465)20 mg/m^2 静脉滴注。为防止患者在治疗过程中发生过敏反应在多西他赛治疗前给予地塞米松、托烷司琼及一些保肝、适度水化治疗。连续治疗 6 周。

放疗方案:采用体架固定体位,经 CT 扫描,设置层厚为 5mm。将扫描图像传送至 CMS Xi O 治疗计划系统,勾画靶区,90%的等剂量线包绕计划靶区 (PTV)。采用多叶光栅技术，西门子 PRIMUS E 直线加速器 6MV X 线放疗,2 Gy/ 次,5 次 / 周,总剂量 DT 40 Gy 时进行 CT 复查，并根据肿瘤的缩小程度重新制定新的放疗方案。

治疗组在对照组的基础上给予参芪五味子片(康县独一味生物制药股份有限公司,国药准字 Z62020288),口服,0.25 g×50 片,3-5 片 / 次,3 次 / 日,与放化疗同步治疗,连续治疗 8 周。

1.4 疗效判定标准

1.4.1 肺癌疗效评价 参照 RECIST 实体瘤疗效评价标准[13]:分为完全缓解 (CR，肿瘤最大直径及最大垂直直径的乘积缩小＞75%)、部分缓解(PR,肿瘤缩小＞50%,＜75%)、疾病稳定(SD,肿瘤缩小＜50%,增大＜25%)、疾病进展(PD,肿瘤增大＞25%)四个等级。

1.4.2 卡氏评分 Karnofsky 分级标准[14],详情见 KPS 评分表;显效:KPS 评分较用药前提高 20 分；有效:KPS 评分较用药前提高 10 分;稳定:KPS 评分较用药前无明显变化;无效:KPS 评分较用药前下降。

1.4.3 T 淋巴细胞亚群变化情况 应用流式细胞分析仪分别检测两组患者治疗前后的 $CD3^+$、$CD4^+$、$CD8^+$、$CD4^+/CD8^+$ 水平。

1.4.4 不良反应的发生情况 统计并对比两组患者消化道不适症状、脱发、放射性肺纤维化、白细胞下降等毒副反应的发生率。

1.5 统计学方法

采用 SPSS17.0 统计学软件进行数据分析，计量资料以($\bar{x}$± s)表示,组间采用 t 检验,计数资料以[n(%)]表示,组间比较采用 x^2 检验,以 P＜0.05 为差异具有统计学意义。

2 结果

2.1 两组近期疗效的比较

治疗后，治疗组与对照组总体有效率分别为 39.02%和 28.2%,治疗组总体有效率高于对照组,但两组比较差异无统计学意义(P＞0.05),见表 1。

2.2 两组治疗后 KPS 评分改善情况比较

治疗后,治疗组患者的 KPS 评分改善率为 70.70%,明显高于对照组(42.00%,P＜0.05),见表 2。

表 1 两组近期疗效比较(例)

Table 1 Comparison of the clinical efficacy between the two groups(n)

Groups	n	CR	PR	SD	PD	RR(%)
Observation group	41	0	16	20	5	39.02
Control group	39	0	11	20	8	28.20

表 2 两组治疗后 KPS 评分改善情况比较

Table 2 Comparison of the improvement of KPS score between two groups after treatment

Groups	n	Marked effect	Effective	Stable disease	Ineffective	Total effective rate(%)
Observation group	41	14	15	8	4	70.70*
Control group	39	5	11	13	10	42.00

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

2.3 两组治疗前后 T 淋巴细胞亚群变化情况比较

治疗前,两组患者的 $CD3^+$、$CD4^+$、$CD8^+$、$CD4^+/CD8^+$ 水平比较差异无统计学意义 (P>0.05);治疗后,两组患者的 $CD3^+$、$CD4^+$、$CD4^+/CD8^+$ 水平均较治疗前显著升高、$CD8^+$ 水平较治疗前明显降低,且治疗组 $CD3^+$、$CD4^+$、$CD4^+/CD8^+$ 水平显著高于对照组,而 $CD8^+$ 水平明显低于对照组(P<0.05),见表 3。

表 3 两组治疗前后 T 淋巴细胞亚群变化情况比较($\bar{x}\pm s$)

Table 3 Comparison of the changes of T-lymphocyte subpopulations between two groups before and after treatment($\bar{x}\pm s$)

Type	Observation group		Control group	
	Prior treatment	Post treatment	Prior treatment	Post treatment
$CD3^+$/%	50.2± 2.6	63.2± 3.9*#	49.3± 2.1	57.2± 3.1*
$CD4^+$/%	29.3± 4.1	40.1± 3.1*#	28.7± 3.8	34.5± 4.1*
$CD8^+$/%	28.3± 3.6	23.0± 3.5*#	27.5± 2.7	24.9± 3.3*
$CD4^+/CD8^+$	1.4± 0.4	1.9± 0.6*#	1.4± 0.3	1.7± 0.5*

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

2.4 两组不良反应发生情况比较

治疗组患者的消化道不适症状、脱发、放射性肺纤维化、白细胞下降等不良反应的发生率均显著低于对照组(P<0.05),见表 4。

表 4 两组不良反应发生情况的比较

Table 4 Comparison of the incidence of adverse reactions between the groups

Groups	n	Gastrointestinal discomfort	Alopecia	Radiation pulmonary fibrosis	Leukopenia
Observation group	41	6(14.6)*	2(4.9)*	5(12.2)*	0(0.0)*
Control group	39	15(38.5)	10(25.6)	16(41.0)	6(15.4)

Note: compared with control group, *P<0.05.

3 讨论

根据世界卫生组织(WHO)的评估,2000 年中国世界人口肺癌中男性发病率占比较女性高,其中男性约为 4%,女性约为 1.3%[15],预计到 2025 年中国癌症患者中的肺癌患者将会达到 100 万,中国会成为世界第一肺癌大国。根据分化程度和形态特点,肺癌主要分为两种类型,即非小细胞肺癌(NSCLC)和小细胞肺癌(SCLC)[16-18]。放化疗是目前非小细胞肺癌治疗的重要手段之一,但是放化疗所致的不良反应给患者带来了很大的痛苦,而中药与放化疗治疗相结合可以在有效治疗患者的同时降低放化疗的不良反应[19-21]。

肺癌的症状体征在中医中表现主要归属为肺积、痞癖、咳嗽、咳血、胸痛等,发病原因主要为正气虚损、邪气侵肺及痰瘀内聚导致。中医认为放化疗过程会损伤人体气血及精液,导致患者免疫功能降低、困乏等。中医药在治疗 NSCLC 时以病灶稳定率较高、患者的生存期较长及患者生活治疗较好为主要特征,同时在癌细胞抗复发和转移方面有一定的作用。临床上,中药联合放化疗治疗肿瘤患者时,常使用健脾和胃、益气养血、除湿化痰及滋补肝肾等以扶正固本或扶正祛邪为目的[22,23],以升高患者白细胞,增强机体免疫力来改善癌症患者的症状。现代研究表明[24]西洋参等中药中含有的人参皂苷可以抑制细胞生长因子和肿瘤转移及生长。黄芪中的多糖能够增强 NK 细胞活性,提高患者的机体免疫力。五味子中的五味子素可以促进组织再修复。因此,在肺癌患者的临床治疗中,权衡扶正祛邪可使患者治疗效果达到最佳[25]。

本研究使用的参芪五味子片可以提高疗效、保护造血系

统、减轻毒性、改善免疫功能及提高生活质量[26,27]。从本研究的治疗总体有效率来看，治疗组总体有效率高于对照组，说明中药可以很好的辅助癌症的放化疗治疗提高患者的治疗效果。此外，中药联合放化疗治疗手段可以很好的改善患者的生活质量，提高患者免疫功能[28,29]。参芪五味子片有助于抑制肿瘤生长，稳定病灶，改善机体免疫功能，且减少放化疗所致的不良反应，提高患者的生活质量。也有学者等通过研究发现中药治疗老年非小细胞肺癌患者，在改善患者生存质量、延长患者寿命、减轻化疗的毒副作用等方面明显优于联合化疗[30]。

因此，中药联合放化疗治疗中期非小细胞肺癌虽不能显著提高临床效果，但可有效缓解放化疗所致的不良反应，提高患者免疫功能，改善患者的生活质量。

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