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## 补肺通络解毒汤联合培美曲塞治疗肺癌的效果及对患者趋化因子受体的影响\*

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**摘要 目的:**探讨补肺通络解毒汤联合培美曲塞治疗肺癌的效果及对患者趋化因子受体的影响。**方法:**选取2016年4月-2018年5月期间我院收治的肺癌患者78例,依据不同的治疗方法随即分为对照组和研究组,对照组采用培美曲塞+顺铂治疗,研究组在其基础上联合应用补肺通络解毒汤治疗,统计对比两组患者的治疗效果及不良反应的发生情况,对比两组患者治疗前后的生活质量,对比两组患者治疗后癌组织中CCR7和CXCR4的表达情况。**结果:**治疗过程中,研究组患者的头晕头痛、呕吐恶心、肝损伤的发生率低于对照组( $P<0.05$ );治疗前两组患者的生活质量没有明显的差异( $P>0.05$ ),治疗后均得到提高,研究组患者的躯体、生理、心理和社会等功能评分明显高于对照组( $P<0.05$ );治疗后,研究组和对照组患者的缓解率分别为51.28%、28.21%,研究组高于对照组( $P<0.05$ );研究组患者癌组织中趋化因子受体CCR7和CXCR4的阳性表达率低于对照组( $P<0.05$ )。**结论:**采用补肺通络解毒汤联合培美曲塞+顺铂治疗肺癌,可以有效减少患者在治疗过程中发生的不良反应,提高生活质量,改善趋化因子受体的表达,控制和缓解病情。

**关键词:**补肺通络解毒汤;培美曲塞;肺癌;趋化因子受体;效果;影响

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## The Effect of Bufei Tongluo Jiedu Decoction Combined with Pemetrexed in the Treatment of Lung Cancer and Its Effect on Chemokine Receptor\*

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**ABSTRACT Objective:** To explore the effect of Bufei Tongluo Jiedu decoction combined with pemetrexed in the treatment of lung cancer and its effect on chemokine receptor. **Methods:** 78 lung cancer patients admitted to our hospital from April 2016 to May 2018 were selected, according to the different treatment methods, they were divided into control group and study group, the control group treated with pemetrexed and cisplatin treatment, the study group treated with Bufei Tongluo Jiedu decoction on the basis of control group. The treatment effect and adverse reactions of the two groups were compared, the quality of life of the two groups before and after treatment was compared, and the expression of CCR7 and CXCR4 in the cancer tissue of the two groups after treatment was compared. **Result:** The incidence rate of the adverse reactions like dizziness and headache, emesis and nausea and liver injury for study group was lower than that in the control group ( $P<0.05$ ). Before treatment, the life quality for two groups was not significantly different ( $P>0.05$ ), after treatment, the physical function, physiological function, psychological function and social function for study group were significantly higher than that in the control group ( $P<0.05$ ). After treatment, The remission rates of the study group and the control group were 51.28% and 28.21% respectively, the study group was higher than that in the control group ( $P<0.05$ ). The positive expression rate of CCR7 and CXCR4 in cancer tissue of the study group was lower than that of the control group ( $P<0.05$ ). **Conclusion:** Bufei Tongluo Jiedu decoction combined with pemetrexed and cisplatin can effectively reduce the adverse reactions during the treatment, improve the quality of life, improve the expression of chemokine receptor, control and alleviate the disease.

**Key words:** Bufei Tongluo Jiedu decoction; Pemetrexed; Lung cancer; Chemokine receptor; Effect; Influence

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### 前言

肺癌是一种临幊上常见的恶性肿瘤,并且在各种肿瘤中发病率最高,近年来,随着当前人们生活方式的变化以及生活环

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境的恶化,加上社会老龄化问题日益严重,肺癌的发生率也在不断的上升<sup>[1-3]</sup>。临幊上对于肺癌患者通常会采用手术和放化疗等手段进行治疗,但是50%以上的肺癌患者在确诊时疾病就已经发展到晚期,无法采用手术治疗,而大部分的化疗药物都存在一定程度的细胞毒性,在灭杀癌细胞的同时会对机体的骨髓和免疫功能产生抑制,并且治疗后还非常容易出现复发和转移<sup>[4-6]</sup>。因此,加大对于治疗肺癌的临幊研究力度,对于延长患者生存时间,提高生活质量非常关键<sup>[7]</sup>。本研究,针对肺癌患者采用不同的治疗方法,统计对比两组患者的治疗效果、不良反应发生、生活质量变化以及对患者趋化因子受体的影响,报道如下。

## 1 资料与方法

### 1.1 一般资料

选取2016年4月-2018年5月期间我院收治的肺癌患者78例,纳入标准:所有患者均符合肺癌的临幊诊断标准;依据国际抗癌联盟的分期标准均为IV期患者;均为腺癌患者;通过MRI、CT等影响学检查发现至少存在一个可以测量的病灶;预计生存期在6个月以上;均知情同意本研究。排除标准:患者的心、肾、肝、脾等脏器存在严重疾病;存在精神功能障碍;存在化疗禁忌症;存在呼吸功能或者心功能不全;存在其他系统肿瘤或者活动性感染;对本研究所使用的药物存在过敏反应;孕妇或者哺乳期的女性患者。依据不同的治疗方法将患者随机分为对照组和研究组,每组39例。对照组男21例,女18例,年龄31-76岁,平均年龄为(53.23±7.61)岁。研究组男22例,女17例,年龄30-75岁,平均年龄为(52.84±7.95)岁。两组患者一般资料比较无统计学差异( $P>0.05$ ),具有可比性。本研究经过医院伦理委员会批准。

### 1.2 方法

对照组采用培美曲塞+顺铂治疗:在治疗的第一天使用注射用培美曲塞二钠(国药准字号:H20123010,由上海凯茂生物医药有限公司生产),按照500 mg/m<sup>2</sup>的剂量对患者进行静脉滴注,同时使用注射用顺铂(国药准字号:H20073652,由齐鲁制药有限公司生产),按照75mg/m<sup>2</sup>的剂量静脉滴注,之后休息20天,21天为1个周期,持续治疗4个周期。研究组采用补肺通络解毒汤联合培美曲塞治疗:患者在对照组的基础上加用补肺通络解毒汤,药方由茯苓30 g、浙贝母30 g、黄芪30 g、白芍20 g、党参20 g、熟地黄20 g、沙参20 g、莪术15 g、太子参15 g、人参15 g、三棱10 g、白朮10 g、丹参10 g、玄参10 g、没药10 g、乳香10 g、山慈姑10 g、法半夏9 g组成,每日一剂,水煎

后取300 mL药液,分早、晚两次服用,每次150 mL,21天为1个疗程,持续服用4个疗程。如果患者存在痰多咳嗽症状,药方中添加杏仁、枳壳、枇杷叶、瓜蒌壳等;如果患者痰内有血,添加三七粉、白茅根、加茜草等;如果患者舌燥口干,添加生石膏、天花粉、麦冬、地黄、石斛、知母等;如果患者存在高烧发热,添加金银花、牡丹皮、生石膏、水牛角、地黄、连翘、知母等;如果存在患者背痛、胸痛,添加郁金、川芎、延胡索等;如果患者呼吸困难,添加车前草、葶苈子、桑白皮、泽泻、猪苓、麻黄等;如果患者大便干结,添加郁李仁、火麻仁、生大黄等。

### 1.3 观察指标

统计对比治疗过程中两组患者的头晕头痛、呕吐恶心、肾损伤、肝损伤发生情况。统计对比治疗前后两组患者的生活质量变化情况。分别在治疗前后采用健康量表(SF-36)对患者的躯体、生理、心理和社会功能进行评估,满分为100分,得分与生活质量成正比<sup>[8]</sup>。统计对比两组患者的治疗效果。治疗后如果患者的肿瘤完全消失,并且能够维持4周以上为完全缓解;患者肿瘤最大径之和的缩小程度大于30%,并且能够维持4周以上为部分缓解;患者肿瘤最大径之和缩小程度≤30%或者增大程度≤20%为无变化;患者肿瘤最大径之和的增大程度大于20%或者有新的肿瘤出现为有进展。缓解率为完全缓解率与部分缓解率之和<sup>[9]</sup>。统计对比治疗后两组患者癌组织中趋化因子受体CCR7和CXCR4的表达情况。采集患者癌组织标本,通过应用Envision二步法免疫组化染色,对标本中的CCR7和CXCR4的表达情况进行检测。如果癌细胞的阳性率大于75%计4分,在51%和75%范围内计3分,在26%和50%范围内计2分,在6%和25%范围内计1分,小于6%计0分;如果癌细胞的染色强烈计3分,中度计2分,微弱计1分,没有染色计0分。结果的判定以染色强度得分和阳性率得分相乘,0为阴性,其余的为阳性<sup>[10]</sup>。

### 1.4 统计学方法

采用SPSS23.0对数据进行统计,计量资料以( $\bar{x} \pm s$ )表示,采用t检验,计数资料以[n(%)]表示,采用 $\chi^2$ 检验,有统计学意义为 $P<0.05$ 。

## 2 结果

### 2.1 两组患者治疗过程中不良反应的发生情况对比

治疗过程中,研究组患者的头晕头痛、呕吐恶心、肝损伤的发生率低于对照组( $P<0.05$ ),两组肾损伤的发生率比较无统计学差异( $P>0.05$ ),具体见表1。

表1 治疗过程中两组患者不良反应的发生情况对比[n(%)]

Table 1 Comparison of adverse reactions between the two groups during the treatment[n(%)]

Groups	n	Dizziness and headache	Emesis and nausea	Renal injury	Liver injury
Control group	39	11(28.21)	15(38.46)	4(10.26)	6(15.39)
Study group	39	3(7.69)	7(17.95)	1(2.56)	1(2.56)
$\chi^2$	/	5.571	4.052	1.923	3.924
P	/	0.018	0.044	0.165	0.048

### 2.2 两组患者治疗前后的SF-36评分对比

治疗前两组患者的生活质量没有明显的差异( $P>0.05$ ),治

疗后两组生活质量评分较治疗前均得到提高,研究组患者的躯体、生理、心理和社会等功能评分明显高于对照组( $P<0.05$ ),具体见表2。

表2 治疗前后两组患者SF-36评分对比(分, $\bar{x}\pm s$ )  
Table 2 Comparison of SF-36 scores between the two groups before and after treatment(scores,  $\bar{x}\pm s$ )

Groups	Times	Physical function	Physiological function	Psychological function	Social function
Control group(n=39)	Before treatment	56.82±4.93	57.41±3.37	52.76±4.51	55.72±3.45
Study group(n=39)		57.24±5.12	58.84±4.18	53.53±4.84	54.94±4.32
t		0.369	1.663	0.755	0.881
P		0.713	0.101	0.452	0.381
Control group(n=39)	After treatment	64.69±4.73*	65.38±3.62*	62.87±3.72*	64.21±3.86*
Study group(n=39)		71.37±4.52*	73.21±3.43*	74.32±5.28*	76.78±4.93*
t		6.376	9.805	11.071	12.537
P		0.000	0.000	0.000	0.000

Note: Compared with before treatment, \* $P<0.05$ .

### 2.3 两组患者的治疗效果对比

见表3。

治疗后,研究组患者的缓解率高于对照组( $P<0.05$ ),具体

表3 两组患者的治疗效果对比[n(%)]  
Table 3 Comparison of treatment effect between the two groups[n(%)]

Groups	n	Complete remission	Partial remission	Unchanged	Progress	Remission rate
Control group	39	0(0.00)	11(28.21)	18(46.15)	10(25.64)	11(28.21)
Study group	39	0(0.00)	20(51.28)	14(35.90)	5(12.82)	20(51.28)
$\chi^2$						4.336
P						0.037

### 2.4 两组患者治疗后癌组织中CCR7和CXCR4的表达情况对比

治疗后,研究组患者癌组织中趋化因子受体CCR7和CXCR4的阳性表达率低于对照组( $P<0.05$ ),具体见表4。

表4 治疗后两组患者癌组织中CCR7和CXCR4的表达情况对比[n(%)]  
Table 4 Expression of CCR7 and CXCR4 in cancer tissues of the two groups after treatment[n(%)]

Groups	n	CCR7		CXCR4	
		Positive	Negative	Positive	Negative
Control group	39	15(38.46)	24(61.54)	13(33.33)	26(66.67)
Study group	39	4(10.26)	35(89.74)	5(12.82)	34(87.18)
$\chi^2$	/		8.419		4.622
P	/		0.004		0.032

### 3 讨论

肺癌是导致患者死亡的一种常见呼吸系统疾病,多发生在60岁以上的老年人群中,患者通常会出现消瘦、咳嗽、胸痛、痰内带血等临床症状,临幊上对于肺癌患者一般会采用手术结合化疗进行治疗<sup>[11,12]</sup>。但是,由于该疾病在体内非常容易发生转移,并且患者在早期不会出现明显的症状,当确诊后往往已经成为中晚期,使其无法进行手术,只能采取保守治疗,导致预后

较差<sup>[13,14]</sup>。随着社会的发展,肺癌患者的数据也在不断的增加,对患者的身体健康和生命安全造成严重影响。培美曲塞是一种新型的抗肿瘤代谢药物,能够对叶酸的多个靶点产生拮抗,通过对细胞复制的过程产生干扰,抑制叶酸的代谢合成<sup>[15,16]</sup>。此外,培美曲塞还可以有效抑制甘氨酰胺核苷甲酰基转移酶、胸苷酸合成酶以及二氢叶酸还原酶等的活性,降低嘌呤核苷酸和胸腺嘧啶的合成量,阻断肿瘤细胞DNA和RNA的合成,使肿瘤细胞的增殖在S期停止,进而发挥抗肿瘤效果<sup>[17,18]</sup>。顺铂是一

种具有双功能的烷化剂,能够对DNA的复制过程产生抑制,损害细胞膜的结构,进而发挥抗肿瘤的效果<sup>[19,20]</sup>。两种药物联合使用能够在一定程度上控制和缓解肿瘤患者的病情,延长患者的生存时间<sup>[21,22]</sup>。但是,由于大部分的化疗药物都存在一定程度的细胞毒性,长期使用会使患者出现头晕头痛、呕吐恶心、骨髓抑制、免疫力降低等不良反应,甚至还会对肾、肝等脏器功能造成损伤,给患者造成很大的痛苦<sup>[23,24]</sup>。

中医学认为,肺癌是由于胸中聚邪、气道壅塞、气机不通、为痰为血,正邪相搏,胜既败,遂形结块,不论是脏腑失调、内虚正气,还是寒热太过、侵袭外邪,均经肺气积聚成痰。亏虚元气,运化失职而致气虚、气滞,遂毒积、饮止、血瘀等证候标实<sup>[25]</sup>。治病时应以扶正益气、化瘀活血、化痰散结解毒为主,培元固本,驱除外邪。本研究中,研究组采用补肺通络解毒汤联合培美曲塞治疗,药方中党参既可补脾气,帮其健运,又可补肺气,助其疏散;人参可补元气,固体扶正;丹参可化瘀活血;玄参可散结消坚、清热养阴;沙参、太子参既可养肺阴又可补肺气。6参共用本标兼顾、攻补兼备,可以扶正益气、培元固本,驱邪而不伤正<sup>[26]</sup>。研究显示,治疗过程中,研究组患者的头晕头痛、呕吐恶心、肝损伤的发生率低于对照组;治疗前两组患者的生活质量没有明显的差异,治疗后均得到提高,研究组患者的躯体、生理、心理和社会等功能评分明显高于对照组,表明采用补肺通络解毒汤联合培美曲塞+顺铂治疗肺癌,可以有效减少患者在治疗过程中发生的不良反应,提高生活质量。药方中没药、乳香、三棱、莪术可化瘀活血;熟地黄、白芍可补血养精;山慈姑、浙贝母、法半夏可散结消瘤,药方集活血、益气、养阴、生血、解毒、散结等为一体,可使化生有余,扶正而不促邪,真正达到健体养身、驱邪治病的目的<sup>[27]</sup>。研究显示,治疗后,研究组和对照组患者的缓解率分别为51.28%、28.21%,研究组高于对照组,表明采用补肺通络解毒汤联合培美曲塞+顺铂治疗肺癌,可以有效控制和缓解患者的病情。

趋化因子是一种促炎细胞因子,能够趋化和激活白细胞,通过与其受体相互结合可以对细胞骨架的重排以及靶细胞的迁移产生诱导和趋化,进而使内皮细胞和靶细胞的粘附能力增强,参与细胞的生长发育以及分化凋亡等多个过程,尤其是在肿瘤细胞的转移、侵袭、生殖过程中发挥非常重要的作用<sup>[28,29]</sup>。研究证实,趋化因子受体CCR7和CXCR4阳性的表达率与肿瘤的临床分期和浸润程度有关,并且具有非常高的准确性,对于临幊上及时调整患者的治疗方案十分重要<sup>[30]</sup>。本研究显示,研究组患者癌组织中趋化因子受体CCR7和CXCR4的表达情况优于对照组,表明采用补肺通络解毒汤联合培美曲塞+顺铂治疗肺癌,可以有效防止患者疾病的复发和转移。

综上所述,临幊上针对肺癌患者采用补肺通络解毒汤联合培美曲塞+顺铂治疗,可以有效提高患者的生活质量,减少不良反应的发生,控制和缓解病情,防止复发和转移,治疗效果更加安全有效。

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