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益气活血化痰法对气虚血瘀痰阻型医院获得性肺炎患者炎症因子、动脉血气及免疫功能的影响 *

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摘要 目的:探讨益气活血化痰法治疗气虚血瘀痰阻型医院获得性肺炎(HAP)患者的疗效及其对炎症因子、动脉血气和免疫功能的影响。**方法:**选取2017年1月到2018年1月在我院接受治疗的HAP患者84例,根据随机数字表法将患者分为对照组和观察组,两组均42例。对照组采用常规西医治疗,观察组在此基础上联用益气活血化痰法进行治疗。比较两组患者治疗前后的中医症状积分、急性生理与慢性健康评估II(APACHE II)、动脉血氧分压(PaO₂)、动脉二氧化碳分压(PaCO₂)、超敏C反应蛋白(hs-CRP)、肿瘤坏死因子-α(TNF-α)、白介素-6(IL-6)、降钙素原(PCT)、免疫球蛋白(Ig G、Ig M、Ig A)的水平,比较两组患者的不良反应。**结果:**治疗后两组患者的PaO₂水平明显升高,中医症状积分、APACHE II评分、PaCO₂、hs-CRP、TNF-α、IL-6、PCT水平明显降低($P<0.05$),且治疗后观察组的PaO₂水平高于对照组,中医症状积分、APACHE II评分、PaCO₂、hs-CRP、TNF-α、IL-6、PCT水平低于对照组($P<0.05$);治疗后观察组的Ig G、Ig M水平明显升高,且高于对照组($P<0.05$),两组患者在治疗过程中均未出现明显的不良反应。**结论:**益气活血化痰法可有效治疗气虚血瘀痰阻型HAP患者,能明显改善患者的动脉血气、免疫功能和炎症反应,且无明显不良反应。

关键词:医院获得性肺炎;益气活血化痰法;炎症因子;动脉血气;免疫功能

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Effect of Inflammatory Factors, Arterial Blood Gas and Immune Function on Yiqi Huoxue Huatan Therapy in the Treatment of Patients with Qi Deficiency and Phlegm and Blood Stasis Type Hospital Acquired Pneumonia*

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ABSTRACT Objective: To explore the effect of Yiqi Huoxue Huatan therapy on the treatment of patients with Qi deficiency and phlegm and blood stasis type hospital acquired pneumonia (HAP) and its effect on inflammatory factors, arterial blood gas and immune function. **Methods:** 84 cases of HAP patients who were treated in our hospital from January 2017 to January 2018 were selected. The patients were divided into the control group and the observation group according to the random digital table method, and all the two groups were 42 cases. The control group using conventional western medicine treatment, the observation group on the basis of treatment with Yiqi Huoxue Huatan therapy. The scores of TCM symptom scores, acute physiology and chronic health evaluation II (APACHE II), arterial partial pressure of oxygen (PaO₂), arterial partial pressure of carbon dioxide (PaCO₂), hypersensitive C reactive protein (hs-CRP), tumor necrosis factor -α (TNF-α), interleukin 6 (IL-6), procalcitonin (PCT), immunoglobulin (Ig G, Ig M, I g A) were compared before and after treatment of the two groups, the adverse reactions of the two groups were compared. **Results:** After treatment, the level of PaO₂ in the two groups was significantly higher, and the TCM symptom scores, APACHE II scores, PaCO₂, hs-CRP, TNF-α, IL-6 and PCT were significantly reduced ($P<0.05$). After treatment, the level of PaO₂ in the observation group was higher than that of the control group, the TCM symptom scores, the APACHE II score, PaCO₂, hs-CRP, TNF-α, IL-6 and PCT were lower than those of the control group ($P<0.05$). After treatment, the levels of Ig G and Ig M in the observation group increased significantly, which was higher than that in the control group ($P<0.05$). No obvious adverse reactions were observed in the two groups during the treatment. **Conclusion:** Yiqi Huoxue Huatan therapy can effectively treat HAP patients due to deficiency of vital energy, blood stasis and phlegm type, which can significantly improve arterial blood gas, immune function and inflammatory factors, and has no obvious adverse reactions.

Key words: Hospital acquired pneumonia; Yiqi Huoxue Huatan therapy; Inflammatory factors; Arterial blood gas; Immune function

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医院获得性肺炎(hospital acquired pneumonia,HAP)是指患者入院时不存在感染且不处于感染潜伏期,而在入院 48h 后出现感染性肺炎^[1-3]。伴有多种基础疾病、存在侵入性操作、住院时间长等均是引发 HAP 的危险因素,患者出现 HAP 不但会增加治疗难度,还会加重患者病情、影响患者预后^[4-6]。西医多采用抗菌、抗感染治疗 HAP 患者,然而随着抗菌药物的大量使用,较多致病菌已出现较强的耐药性,单纯的抗菌、抗感染治疗较难获得满意的临床疗效^[7-9]。中医认为 HAP 属于“咳嗽”、“风温”、“喘证”的范畴,患者久病失调、耗伤正气,气虚无力、血阻成瘀,在受到外邪侵袭后肺气被逼、痰浊内生、脾失健运、脾失健运,其发病机制主要为正气亏虚、痰瘀互结,因此宜采用益气活血化痰法进行治疗^[10]。本研究旨在探讨益气活血化痰法治疗气虚血瘀痰阻型 HAP 患者的临床疗效,并分析其对患者炎症因子、动脉血气和免疫功能的影响,以进一步研究益气活血化痰法治疗气虚血瘀痰阻型 HAP 的作用机制,为临床治疗提供参考。现将研究结果整理报道如下。

1 资料与方法

1.1 一般资料

选取 2017 年 1 月到 2018 年 1 月在我院接受治疗的 HAP 患者 84 例,纳入标准:(1)患者均符合 HAP 的临床诊断标准^[11];(2)患者均为气虚血瘀痰阻型 HAP;(3)临床资料齐全;(4)患者及其家属对本研究知情同意,并已签署知情同意书。排除标准:(1)合并有免疫系统疾病、血液疾病者;(2)合并有恶性肿瘤者;(3)对研究药物过敏者;(4)治疗依从性较差者。根据随机数字表法将患者分为对照组和观察组,两组均 42 例。对照组男性 24 例,女性 18 例,年龄 43~74 岁,平均年龄(62.59±6.27)岁,病种:慢性阻塞性肺疾病 14 例,糖尿病 14 例,脑出血 8 例,冠心病 6 例。观察组男性 22 例,女性 20 例,年龄 41~76 岁,平均年龄(62.28±6.24)岁,病种:慢性阻塞性肺疾病 12 例,糖尿病 15 例,脑出血 9 例,冠心病 6 例。两组患者的一般资料比较无明显差异($P>0.05$),可行组间比较。本研究通过了我院伦理委员会的批准。

1.2 诊断标准

HAP 西医诊断标准具体如下^[12]:(1)出现咳嗽、咳痰等症状,呼吸道疾病患者在原症状上加重,并出现脓性分泌物;(2)体温高于 38℃或低于 36℃;(3)肺部可闻干湿啰音;(4)白细胞计数大于 $10 \times 10^9/L$ 或小于 $4 \times 10^9/L$,支气管分泌物培养显示病原菌阳性;(5)X 线显示出现肺内浸润性阴影改变或新的炎症病灶。存在第五项且合并有其他四项中的任意两项则可认定为 HAP。气虚血瘀痰阻型标准如下^[13]:(1)气虚者主证为气短、神疲、乏力、脉虚,次证为自汗、懒言、舌淡,存在两项主证加一项次证则可认定为气虚;(2)血瘀者主证为刺痛、脉络瘀血、癥积、皮下瘀斑、离经之血、舌质紫黯或有瘀斑、脉涩,次证为肢体麻木或偏瘫、狂躁、痴癫、善忘、局部感觉异常、肌肤甲错、外伤史,存在两项主证或一项主证加两项次证则可认定为血瘀;(3)痰阻者主证为喉中痰鸣、咯痰、舌苔腻、脉滑,次证为肥胖、嗜睡、胸闷、恶心呕吐、口眼喎斜、口干不欲饮。存在两项主证、舌苔腻加一项次证、咯痰加两项次证、喉中痰鸣加三项次证、脉滑加三项次证、五项次证,以上条件符合任一则可认定为痰阻。

1.3 治疗方法

对照组患者给予抗感染、化痰、利尿、纠正水电解质平衡等常规西医治疗。观察组在对照组的基础上给予益气活血化痰法治疗,参麦注射液(四川升和药业股份有限公司,国药准字 Z51021264,规格:每支装 10 mL)50 mL 静脉滴注,2 次/d,丹参酮 II A 磺酸钠注射液(上海上药第一生化药业有限公司,国药准字:H31022558,规格:2 mL:10 mg)30 mg 加入 100 mL 生理盐水静脉滴注,1 次/d,痰热清注射液(上海凯宝药业股份有限公司,国药准字 Z20030054,规格:每支装 10 mL)20 mL 加入 250 mL 生理盐水静脉滴注,1 次/d。两组患者均连续治疗 7d。

1.4 观察指标

在治疗前后根据两组患者的相关临床症状进行中医症状积分,其中发热、血气、气喘、咯痰、舌象、脉象、肺部体征均根据严重程度给予 0、2、4、6 分,胸部 X 线、血常规根据严重程度给予 0、2、4 分,另根据是否有神昏、斑疹、厥脱分别给予 3 分或 0 分,分数越高代表病情越严重。两组患者在治疗前后进行急性生理与慢性健康评价 II (acute physiology and chronic health evaluation II,APACHE II),APACHE II 评分只要由急性生理评分、年龄评分和慢性健康评分三部分组成,总分为 71 分,分数越高代表病情越重。在治疗前后抽取两组患者的动脉血 3mL,采用血气分析仪(雷度,ABL800)检测动脉血氧分压(arterial partial pressure of oxygen, PaO_2)和动脉二氧化碳分压(arterial partial pressure of carbon dioxide, $PaCO_2$)。在治疗前后抽取两组患者的静脉血 5 mL,3000 r/min 离心 10 min,提取血清,采用酶联免疫吸附法检测血清中超敏 C 反应蛋白(hypersensitive C-reactive protein,hs-CRP)、肿瘤坏死因子- α (tumor necrosis factor- α ,TNF- α)、白介素-6(interleukin-6,IL-6)、降钙素原(procalcitonin,PCT)的水平,采用速率散射免疫比浊法检测血清免疫球蛋白(Ig G、Ig M、Ig A)的水平,相关试剂盒购于上海酶联生物科技有限公司,严格遵循试剂盒操作指南进行相关操作。比较两组患者治疗过程中出现的不良反应。

1.5 统计学方法

采用 SPSS21.0 进行统计学分析,计数资料以率(%)的形式表示,采用卡方检验,计量资料以($\bar{x} \pm s$)的形式表示,采用 t 检验。以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组患者治疗前后中医症状积分和 APACHE II 评分比较

治疗前两组患者的中医症状积分和 APACHE II 评分比较差异无统计学意义($P>0.05$)。治疗后两组患者的中医症状积分和 APACHE II 评分均明显降低,且观察组的中医症状积分和 APACHE II 评分低于对照组($P<0.05$)。见表 1。

2.2 两组患者治疗前后的动脉血气比较

治疗前两组患者的 PaO_2 和 $PaCO_2$ 水平比较差异无统计学意义($P>0.05$)。治疗后两组患者的 PaO_2 水平明显升高, $PaCO_2$ 水平明显降低($P<0.05$),且治疗后观察组的 PaO_2 水平高于对照组, $PaCO_2$ 水平低于对照组($P<0.05$)。见表 2。

2.3 两组患者治疗前后血清炎症因子水平比较

治疗前两组患者的 hs-CRP、TNF- α 、IL-6、PCT 水平比较差异无统计学意义($P>0.05$);治疗后两组患者的 hs-CRP、

TNF- α 、IL-6、PCT 水平均明显降低,且观察组的 hs-CRP、TNF- α 、IL-6、PCT 水平低于对照组($P<0.05$);见表 3。

表 1 两组患者治疗前后中医症状积分和 APACHE II 评分比较($\bar{x}\pm s$,分)

Table 1 Comparison of TCM symptom scores and APACHE II scores between the two groups before and after treatment($\bar{x}\pm s$, scores)

Groups	Times	TCM symptom scores	APACHE II scores
Control group(n=42)	Before treatment	35.52 $\pm$ 7.51	26.75 $\pm$ 7.18
	After treatment	19.57 $\pm$ 4.73*	17.16 $\pm$ 4.93*
Observation group(n=42)	Before treatment	34.98 $\pm$ 7.67	26.37 $\pm$ 7.46
	After treatment	15.24 $\pm$ 5.22* [#]	14.25 $\pm$ 4.68* [#]

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

表 2 两组患者治疗前后的动脉血气比较($\bar{x}\pm s$, mmHg)

Table 2 Comparison of arterial and blood gas between the two groups before and after treatment($\bar{x}\pm s$, mmHg)

Groups	Times	PaO ₂	PaCO ₂
Control group(n=42)	Before treatment	52.31 $\pm$ 5.54	60.23 $\pm$ 7.46
	After treatment	71.64 $\pm$ 7.64*	47.19 $\pm$ 5.43*
Observation group(n=42)	Before treatment	52.69 $\pm$ 5.38	60.84 $\pm$ 7.52
	After treatment	76.97 $\pm$ 8.01* [#]	40.25 $\pm$ 5.21* [#]

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

表 3 两组患者治疗前后血清炎症因子水平比较($\bar{x}\pm s$)

Table 3 Comparison of serum inflammatory factors between the two groups before and after treatment($\bar{x}\pm s$)

Groups	Times	hs-CRP(mg/L)	TNF- α (ng/L)	IL-6(ng/L)	PCT(ng/L)
Control group(n=42)	Before treatment	95.48 $\pm$ 18.65	202.41 $\pm$ 48.63	27.69 $\pm$ 9.46	3.92 $\pm$ 1.08
	After treatment	53.44 $\pm$ 15.64*	109.58 $\pm$ 24.26*	14.33 $\pm$ 3.68*	2.41 $\pm$ 0.96*
Observation group (n=42)	Before treatment	96.15 $\pm$ 17.93	199.94 $\pm$ 45.58	27.28 $\pm$ 9.52	3.94 $\pm$ 1.13
	After treatment	43.58 $\pm$ 13.23* [#]	84.65 $\pm$ 20.47* [#]	10.21 $\pm$ 3.05* [#]	1.54 $\pm$ 0.97* [#]

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

2.4 两组患者治疗前后免疫球蛋白水平比较

治疗前两组患者的 Ig G、Ig M、Ig A 水平比较差异无统计学意义($P>0.05$);治疗后对照组的 Ig G、Ig M、Ig A 水平与治疗

前比较差异无统计学意义($P>0.05$);治疗后观察组的 Ig A 水平与治疗前比较差异无统计学意义($P>0.05$);治疗后观察组的 Ig G、Ig M 水平明显升高,且高于对照组($P<0.05$);见表 4。

表 4 两组患者治疗前后免疫球蛋白水平比较($\bar{x}\pm s$, g/L)

Table 4 Comparison of immunoglobulin levels between two groups before and after treatment($\bar{x}\pm s$, g/L)

Groups	Times	Ig G	Ig M	Ig A
Control group(n=42)	Before treatment	11.23 $\pm$ 1.15	0.95 $\pm$ 0.21	2.57 $\pm$ 0.56
	After treatment	11.64 $\pm$ 1.27	1.01 $\pm$ 0.26	2.53 $\pm$ 0.48
Observation group(n=42)	Before treatment	11.21 $\pm$ 1.08	0.94 $\pm$ 0.24	2.61 $\pm$ 0.52
	After treatment	13.62 $\pm$ 1.23* [#]	1.42 $\pm$ 0.27* [#]	2.56 $\pm$ 0.51

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

2.5 两组患者不良反应比较

两组患者在治疗过程中均未出现明显的不良反应。

3 讨论

HAP 是医院感染的常见类型,是由真菌、细菌、病毒、支原体或原虫等病原体引起的肺实质炎症,患者主要表现为精神萎靡、呼吸困难加重、发热、呼吸道脓性分泌物增多等症状,且 X

线可显示出肺内浸润性阴影改变^[14-16]。目前西医治疗 HAP 的主要思路是抗感染、化痰、利尿、纠正水电解质平衡等,但其临床疗效欠佳^[17]。周妍卉等人^[18]的研究显示,清肺化痰方联合活血化痰法可有效提高 HAP 的治疗效果,且可有效降低患者体内的炎症反应。气虚血瘀痰阻型 HAP 是 HAP 常见的中医证型,中医认为 HAP 的发病机理为正气亏虚、外邪侵袭,进而导致痰瘀互结、胶结难愈,其中正气亏虚主要表现是气阴两伤,痰瘀互

结、胶结难愈则为瘀血内阻,津聚成痰,两者相互胶结,滞于体内,因此其治疗思路为益气、活血、化痰^[19]。

益气活血化痰法是参麦注射液、丹参酮 II A 磺酸钠注射液、痰热清注射液等制剂联合使用的治疗方案,具有益气、活血、化痰的功效。其中参麦注射液的主要成分为红参、麦冬,红参具有补气、滋阴、益血、强心的功效,麦冬具有润肺生津、化痰止呕的功效,两者并用共奏益气固脱、养阴生津的效果^[20]。丹参酮 II A 磺酸钠注射液的主要成分是丹参酮 II A,其水溶性和脂溶性较好,具有活血化痰的功效,能增加血流量、改善器官微循环^[21]。痰热清注射液主要由黄芩、熊胆粉、山羊角、金银花、连翘等药物组成,其中黄芩清热去燥、润肺止咳,熊胆粉清热、明目,山羊角清热散瘀,金银花清热解毒,连翘散结消肿,多药并用共奏清热、化痰、解毒^[22]。本研究结果显示,治疗后两组患者的中医症状积分和 APACHE II 评分均明显降低,且观察组的中医症状积分和 APACHE II 评分低于对照组 ($P<0.05$),这说明观察组患者的治疗效果更佳,提示益气活血化痰方可有效提高临床疗效。动脉血气分析是判断机体缺氧程度和酸碱平衡情况的常用方法,HAP 患者由于气道炎症、呼吸道粘液增加、肺功能下降等原因,可导致肺的通气、换气功能下降,出现 CO_2 滞留。本研究结果显示,治疗后两组患者的 PaO_2 水平明显升高, PaCO_2 水平明显降低 ($P<0.05$),且治疗后观察组的 PaO_2 水平高于对照组, PaCO_2 水平低于对照组 ($P<0.05$),这说明益气活血化痰方可有效改善患者的动脉血气,提高肺的通气、换气功能。炎症反应和免疫功能障碍是引发 HAP 的重要原因,hs-CRP、TNF- α 、IL-6、PCT 均是常见的炎症因子,可反映机体炎症反应程度,免疫球蛋白免疫活性分子中的一类,可反映机体的免疫功能。本研究结果显示,治疗后两组患者的 hs-CRP、TNF- α 、IL-6、PCT 水平均明显降低,且观察组的 hs-CRP、TNF- α 、IL-6、PCT 水平低于对照组 ($P<0.05$);治疗后观察组的 Ig G、Ig M 水平明显升高,且高于对照组 ($P<0.05$),这说明益气活血化痰方可有效降低 HAP 患者体内的炎症反应,提高患者的免疫力^[23]。现代药理证明,参麦注射液具有改善机体免疫功能、降低炎症反应的作用,而丹参酮 II A 具有活血化瘀,改善器官微循环的作用,痰热清注射液具有增加免疫功能和抗菌的作用。因此三药联合使用可明显降低患者的炎症反应,提高免疫功能,改善肺功能和动脉血气^[24,25]。此外,两组患者在治疗过程中均未出现明显的不良反应,这说明益气活血化痰方安全性较好。

综上所述,益气活血化痰方可有效改善气虚血瘀痰阻型 HAP 患者的临床症状、免疫功能和动脉血气,降低患者体内的炎症反应,且无明显的副作用。

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