

川芎嗪治疗失代偿期慢性肺心病的临床研究

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内容提要 本文采取自身对照方法,对49例失代偿期慢性肺心病患者观察了用川芎嗪(120mg)静脉滴注治疗一个疗程后的临床疗效。结果表明:川芎嗪能扩张肺血管、降低肺动脉的平均压($\bar{PAP}$)和肺血管阻力(PVR)、增加心输出量、改善右心功能和血液流变性,使临床症状减轻,对动脉血气无明显影响,适于失代偿期肺心病的治疗。

川芎嗪是从中药川芎中提取的有效成份^①。最近邹氏等动物实验的结果表明,川芎嗪可以降低肺动脉高压,提示适于治疗慢性肺心病^②(以下简称肺心病)。本文观察了川芎嗪对失代偿期肺心病患者活血化瘀作用的临床疗效。现将结果报道如下。

对象及方法

一、研究对象:依照肺心病有关诊断标准选取1984年12月~1985年6月间住院的失代偿期患者49例。入院后均经心电图、胸片、心电图向量图或超声心动图及有关实验检查(有38例患者测定血气分析)。凡无肺性脑病和其它肺心病严重并发症者列为研究对象(排除其它对肺血液动力学和血液流变学有影响的疾病)。其中男39例,女10例,年龄30~76岁,平均58.1岁。肺心病病程为1~5年。慢阻肺按Burrows标准^③临床分型:BB型10例。PP型12例,混合型27例。

二、方法

1. 分组:全部患者分为二组,采取治疗前后自身对照方法。甲组(25例)先按一般常规疗法治疗观察5天,作为用川芎嗪前的对照疗程,然后再加用川芎嗪治疗5天,作为治疗疗程。乙组(24例)对照和治疗疗程的安排与甲组相反,甲乙两组的一般常规治疗主要为抗感染和祛痰,两组用药和剂量一致。

2. 用药方法:川芎嗪120mg加入10%葡萄糖250ml内静脉滴注,滴速25~50滴/分,

每天1次,5天为1疗程。为排除平喘利尿、强心、抗凝及其它扩血管药的影响,这些药物在治疗和对照疗程期间一般停用。

3. 观察内容:(1)肺血液动力学和心功能:采用国产HB-3COG型心输出量仪,用阻抗法测定。反映右心功能的肺血流图指标见表2。为排除心率的影响,Q-B和B-Y间期、 H_s 和 α 参数均按公式校正:校正值=实测值/ $\sqrt{\text{心动周期}}$ 。肺动脉平均压($\bar{PAP}$)和肺血管阻力(PVR)按王氏阻抗法公式推算^{④,⑤}。心输出量(CO)采用Kubicek公式推算^⑥。(2)动脉血气分析:采用丹麦产ABL-III型血气分析仪,取股动脉血后立即测定。(3)血液流变学:采用上海医科大学产XN₃型血液粘度计和细胞电泳仪测定有关指标。

4. 观察方法:(1)疗程效果的对比观察:甲乙两组患者分别在治疗1个疗程前后观察肺阻抗血流图(甲组观察21例,乙组观察20例) $\bar{PAP}$ 、PVR、心率(HR)和血液流变学有关指标的变化。部分患者同时观察了CO的变化。对照疗程同上。(2)动脉血气的观察:对6例患者在用川芎嗪前取股动脉血标本,然后立即静脉滴注川芎嗪,待药物滴完之前,再次取股动脉血进行血气分析测定。比较用药前后有关指标的变化。(3)川芎嗪对血液流变性影响的体外试验观察:取肺心病患者静脉血标本12份,随机分为两组。一组加川芎嗪(每毫升血中加0.003ml,含0.03mg)称为加药组,另一组加与前者pH值和剂量相同的溶液,称为对照组。

然后在 24°C 水中浴热 30 分钟, 观察加入药物和溶液前后的血液流变学变化。

结 果

一、甲、乙两组一疗程后各项检查结果对比。

1. 肺血液动力学有关指标的变化: 见表 1。

表 1 甲乙两组疗程前后的肺血液动力学变化 (M±SD)

	组别	例数	PAP (mmHg)	PVR (dyn·s·cm ⁻⁵)	HR (beats/min)	CO* (L/min)
对 照	甲	21	27.9 ±9.3	244.6 ±147.5	92.9 ±14.9	3.6 ±0.8
			20.1 ±7.1	146.4 ±100.5	93.9 ±16.7	4.5 ±2.1▲
	乙	20	27.5 ±8.3	226.1 ±168.9	99.5 ±14.6	3.7 ±0.6
			23.6 ±8.1△	182.8 ±121.1	93.6 ±16.7	4.1 ±1.3▲
治 疗	甲	21	27.5 ±8.3	226.0 ±168.9	99.5 ±14.6	3.4 ±1.1
			26.9 ±8.1	217.8 ±158.9	100.7 ±16.2	3.6 ±1.1
	乙	20	20.6 ±5.7△△	138.9 ±70.1△△	91.6 ±18.9△	4.4 ±1.0△
			20.1△△ ±7.1	146.4 ±100.5△	93.9 ±16.7△	4.8 ±1.7△

与疗程前值相比, $\Delta P < 0.05$, $\Delta\Delta P < 0.01$, * 甲组测 10 例, 乙组测 12 例, ▲ 为 6 例测定值

甲、乙两组用川芎嗪治疗 1 个疗程后各项指标均好转 ($P < 0.05 \sim 0.01$), 与此同时心衰和呼衰的症状减轻。而对照疗程后, 甲组的变化无统计学意义 ($P > 0.05$), 乙组部分指标有不同

程度的回升。

2. 肺血流图有关参数的变化: 见表 2。甲乙两组在治疗疗程结束后各指标均明显好转 ($P < 0.05 \sim 0.01$)。而对照疗程后大部分指标有所回升。少数指标有所好转, 但无统计学意义。

3. 血液流变学的变化: 见表 3。甲、乙两组经用川芎嗪治疗后各项指标均好转 ($P < 0.001$), 而对照疗程结束后, 甲组无明显变化 ($P > 0.05$), 乙组红细胞压积、全血(高)和血浆比粘度均回升 ($P < 0.05 \sim 0.01$), 其它指标无明显变化 ($P > 0.05$)。

二、肺心病不同临床类型的血液流变学变化及其与川芎嗪治疗的关系。见表 4。三种临床类型肺心病组与正常人组相比, 各指标均示异常 ($P < 0.05 \sim 0.01$)。三型之间相互比较, 其异常程度依次为: BB 型 > 混合型 > PP 型。

经用川芎嗪治疗 1 疗程后, BB 型、PP 型及混合型各项指标均好转 ($P < 0.005$), 各型依次红细胞压积平均降低 7.70%、4.42%、4.93%, 全血粘度(高)平均降低 2.04、0.93、1.16, 全血粘度(低)平均降低 6.57、2.27、4.23, 血浆粘度平均降低 0.83、0.36、0.53, 红细胞电泳时间平均缩短: 8.99 秒、4.00 秒、6.78 秒。

三、川芎嗪对体外标本的血液流变学的影响: 加川芎嗪组全血比粘度平均降低 0.26(高)、0.77(低), P 值均 < 0.05 , 红细胞电泳时间平均缩短 0.75 秒 ($P < 0.005$)。其余指标无明显变化 ($P > 0.05$)。加对照液组各指标均无明显变化 ($P > 0.05$)。

表 2 甲乙两组疗程前后的肺阻抗血流图有关参数的变化 (M±SD)

	组别	例数	Q-B 间期 (s)	B-Y 间期 (s)	Q-BI	B-YI	Q-B/B-Y	Hs(Ω)	α (s)
对 照	甲	21	0.18±0.03	0.27±0.05	0.22±0.05	0.33±0.08	0.73±0.33	0.12±0.06	0.16±0.04
			0.16±0.03	0.30±0.06	0.20±0.05	0.38±0.08	0.56±0.17	0.19±0.08	0.21±0.06
	乙	20	0.19±0.03△	0.25±0.05	0.24±0.04△	0.32±0.07	0.80±0.33	0.13±0.05	0.17±0.04
			0.18±0.04△△	0.28±0.05△	0.22±0.05△△	0.34±0.07△	0.67±0.23△△	0.16±0.09	0.19±0.04
治 疗	甲	21	0.19±0.03	0.25±0.05	0.24±0.04	0.32±0.07	0.80±0.33	0.13±0.05	0.17±0.04
			0.19±0.03	0.25±0.05	0.25±0.04	0.33±0.07	0.79±0.20	0.13±0.05	0.18±0.05
	乙	20	0.16±0.03△△	0.28±0.04△△	0.20±0.05△△	0.35±0.06△	0.60±0.22△△	0.18±0.07△△	0.19±0.04△△
			0.16±0.03△△	0.30±0.06△△	0.20±0.05△△	0.38±0.08△	0.56±0.17△△	0.19±0.08△△	0.21±0.06△△

与疗程前值相比, $\Delta P < 0.05$, $\Delta\Delta P < 0.01$

表3 甲乙两组治疗前后的血液流变学变化 (M±SD)

		组别	例数	红细胞压积 (%)	全血比粘度		血浆比粘度	红细胞电泳时间 (s)
					高	低		
对照 治疗 程	前	甲	25	53.76±6.29	7.74±1.16	15.31±5.50	2.36±0.69	31.83±7.48
		乙	24	45.96±6.77	6.51±0.85	10.73±2.82	1.66±0.18	24.25±2.78
	后	甲	25	53.64±5.70	7.72±1.15	15.54±5.67	2.32±0.70	31.97±7.38
		乙	24	47.63±6.33△	6.83±0.92△△	11.31±3.01	1.74±0.23△	24.89±2.71
治 疗 程	前	甲	25	53.64±5.70	7.72±1.15	15.54±5.67	2.32±0.70	31.97±7.38
		乙	24	49.71±5.34	7.71±1.01	14.92±3.76	2.09±0.38	30.59±4.00
	后	甲	25	46.72±6.75*	6.36±1.15*	11.27±4.90*	1.66±0.31*	25.23±5.81*
		乙	24	45.96±6.77*	6.51±0.85*	10.73±2.82*	1.66±0.18*	24.25±2.78*

与疗程前值相比△P<0.05 △△P<0.01 *P<0.001

表4 不同临床类型肺心病(失代偿期)的血液流变学变化 (M±SD)

例数	红细胞压积 (%)	全血比粘度		血浆比粘度	红细胞电泳时间(s)	
		高	低			
(1)BB 型组	10	56.00±3.13△△△	8.45±1.19△△△	18.68±4.96△△△	2.56±0.54△△△	34.13±8.27△△△
(2)PP 型组	12	46.92±4.01△	6.97±0.93△△	11.43±3.60△△	2.00±0.33△△△	27.37±4.18△△△
(3)混合型组	27	52.26±5.85△△△	7.78±0.90△△△	15.66±4.12△△△	2.18±0.63△△△	31.99±4.86△△△
(4)正常人组	10	43.00±2.94	5.66±0.68	7.48±0.84	1.41±0.20	18.31±3.95
各型间比较		(1):(2)<0.01	(1):(2)<0.01	(1):(2)<0.01	各型间皆>0.05	(1):(2)<0.05
P 值		(2):(3)<0.05		(2):(3)<0.05		(2):(3)<0.05

与正常组比△P<0.05, △△P<0.01, △△△P<0.001

四、川芎嗪治疗前后动脉血气的变化。用药前pH为7.33±0.03, PaO₂为50.5±10.7mmHg, PaCO₂为65.2±10.0mmHg, SaO₂为79.8±11.3% 用药后pH7.33±0.03, PaO₂53.1±9.1mmHg, PaCO₂61.3±8.5mmHg, SaO₂82.6±8.5%。仅PaCO₂的变化有统计学意义(P<0.05)。其余指标的变化无统计学意义(P>0.05)。

讨 论

一、川芎嗪对肺血液动力学的作用：本文用阻抗法监测发现，用川芎嗪1疗程后从肺阻抗图上反映出药物扩张肺血管、降低肺动脉压力和肺血管阻力，减轻右心后负荷的作用。从心阻抗图上也反映出川芎嗪增加心输出量、减慢心率的作用。这与邹氏等人的动物实验结果相一致⁽²⁾。说明川芎嗪对肺心病患者有疏通全身血脉、行气活血的效果。对于此作用机理尚不完全清楚。最近王氏等人的动物实验结果表明⁽³⁾：川芎嗪具有典型的钙离子拮抗剂的药理

和电生理作用，能抑制房室传导，选择性松弛血管平滑肌，从而解释了本文用川芎嗪后，肺血管扩张、心率减慢的结果。

二、川芎嗪对右心功能的作用：41例患者用川芎嗪治疗后Q-B间期缩短，B-Y间期延长，Q-B/B-Y比值变小。Q-B和B-Y间期是反映右心室射血前期与射血期时相变化的指标。其中Q-B间期延长在肺动脉高压时多为等容收缩期延长所致，是由于右心室舒张末期之右室压与肺动脉压的压差增大的结果。前述结果已表明川芎嗪有扩张肺血管、减轻右心后负荷的作用，所以可以认为，Q-B间期缩短是由于川芎嗪降低了右心收缩期负荷使等容收缩期缩短所致。同理B-Y间期延长反映了右心后负荷降低使射血时间延长，故每搏心输出量增加。Q-B/B-Y比值变小则进一步说明了右心功能的改善。结合肺心病患者心衰症状的减轻，反映出川芎嗪促进心脏“泵”功能恢复的作用。继之静脉系统瘀血得到改善。显然其效果与“活血”作

用有关。

三、川芎嗪改善肺心病血液流变学的作用：49例患者用川芎嗪治疗后，血液流变学的异常明显改善。这与在其它疾病中观察结果相似⁽⁸⁾。其作用机理尚不清楚。本文体外观察结果表明：川芎嗪仅直接降低全血粘度和缩短红细胞电泳时间，而对其它指标无影响。推测该药在体内有直接和间接二种作用。直接作用：(1)降低红细胞聚集性，增强其变形性使红细胞电泳时间缩短；(2)降低血小板聚集性⁽⁹⁾，抑制血栓形成⁽¹⁰⁾，使高凝状态减轻，全血粘度降低。间接作用：通过扩张血管，改善循环使各系统和脏器功能恢复，继发性引起血浆粘度和红细胞压积降低。上述作用反映了川芎嗪的“化瘀”功效。

四、川芎嗪对慢阻肺并发肺心病不同临床类型的血液流变学变化的影响：本文对49例慢阻肺并发肺心病患者进行临床分型后发现，血液流变学异常程度依次为：BB型>混合型>PP型。经用川芎嗪治疗后各型均有好转，其程度也依次为：BB型>混合型>PP型。这可能与川芎嗪的作用机理有关。前述川芎嗪的直接作用正是降低红细胞的聚集性和增强其变形能力以及降低全血粘度。所以对全血粘度和红细胞压积较高的BB型改善的幅度就大，“化瘀”效果就好。而对PP型肺心病，由于上述异常变化不明显，故其“化瘀”的幅度就小。上述资料表明，对肺心病进行临床分型，有助于对川芎嗪“化瘀”治疗对象的选择和对疗效的估价。

五、川芎嗪对动脉血气的影响：血管扩张剂治疗肺心病可引起PaO₂和SaO₂降低的副作

用⁽⁵⁾。为此本文观察了6例患者用川芎嗪前后动脉血气的变化。结果表明川芎嗪对PaO₂、SaO₂及pH值无明显影响，仅使PaCO₂轻度降低。这可能是由于：(1)低氧肺泡区通气的改善使PaCO₂降低；(2)心输出量增加，全身循环加速，使氧供增加和改善，代偿了V/Q比值失调所致的SaO₂降低。本文结果提示：川芎嗪无降低PaO₂、SaO₂的副作用，而具有降低PaCO₂的治疗效果并对酸碱平衡无影响。

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诊余漫笔——治小儿感冒一得

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昔年余在某院儿科进修学习，见病儿中不少银翘散证者，田国桢老师每投以定喘汤，而很多咳嗽气喘者又常用桑菊、银翘之类。多数患儿服药两、三剂竟获痊愈，余心中暗自称奇。

一日，诊病稍有空闲，我向田老师探求银翘、定喘二方使用之鉴别要点。田老师说，我是西学中大夫，运用二方，一是要用中医之四诊，辨其是否属风热感

冒，再据肺部听诊，如有干、湿罗音，哮鸣音，即用定喘汤；若听诊正常或仅呼吸音粗，则用银翘等辛凉之品。因很多小儿证似银翘散，但肺部听诊却常常有罗音、哮鸣音或水泡音。此时若用银翘之辛凉解表，则药力轻薄，必治而不效，非定喘汤之清热化痰、降逆平喘以开肺气之闭，则病必不除。寥寥数言，使余顿感豁然。此后，余治小儿感冒每依此法，疗效颇佳。

orange peel, *Perilla frutescens*, *Semen Lepidii apetalum* and *Cortex Mori albae*. To evaluate whether JQDCS has a strong bronchodilative effect or not, the peak expiratory flow rate (PEFR), heart rate (HR) and blood pressure (BP) were measured in eight male patients (20~60 years old) with chronic asthma. Comparative study of JQDCS given orally and single ephedrine administration was performed.

During the consecutive 3-day investigation, routine oral aminophylline or β_2 receptor stimulant were ceased to use in all patients. By the use of single blind method patients received (at random) one of the following drugs at 8:00 A. M. (1) JQDCS granule, (2) ephedrine 36 mg in adjuvant particle, the amount of which was the same as that of JQDCS, (3) placebo. Drug was dissolved in boiling water. PEFR, HR and BP were measured prior and 15', 30', 60', 120' and 180' after medication. Another drug was then given on the second and third day. All parameters were re-measured as before.

PEFR (246 ± 66 L/min) showed no change except for that at 180' (increased by 10.8%, $P < 0.05$) in the placebo group. A significant increase of mean PEFR at the above time interval by 7.1%, 20.3%, 29.0%, 40.3% and 37.6% respectively (comparing with premedicative determination 298 ± 96 L/min, $P < 0.01 \sim 0.05$) were shown in ephedrine administration, and by 12.6%, 23.9%, 30.3%, 41.1% and 61.0% respectively (as compared with the value of premedication 236 ± 68 L/min, all $P < 0.01$) in JQDCS administration. The improvement rate of PEFR at 180' in JQDCS group was significantly higher than that in ephedrine group (61.0% vs 37.4%, $P < 0.05$). There was no change of BP, HR after placebo administration. BP increased slightly but significantly (8~10 mmHg of systolic pressure) at 30' and returned to normal at 180' after giving ephedrine orally. Also, a significant increase of HR, 6~10 beats/min, was shown from 60'~180' after ephedrine administration. JQDCS had the same effect on BP and HR as that of ephedrine. We conclude that JQDCS has a better and longer bronchodilative effect as compared with ephedrine without increasing side effect.

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Clinical Study of Ligustrazini in Treating Chronic Cor Pulmonale

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Self-contrasted method was used in observing 49 patients with advanced cor pulmonale. They were divided into two groups, A and B groups (A group: control period followed by course of treatment; B group: vice versa). Before and after intravenous administration of ligustrazini (120 mg), pulmonary hemodynamic, right cardiac function, hemorheology and arterial blood gas were determined in these patients. After one course of treatment, A and B group showed that: Pap decreased by 6.84 and 6.73 mmHg respectively. PVR lowered for 87.08 and 71.34 $\text{dyn} \cdot \text{s} \cdot \text{cm}^{-5}$, CO elevated for 1.05 and 1.23 L/min., HR reduced for 7.9 and 6.8 beats/min., Q-B interval shortened for 0.03 and 0.03 sec., B-Y interval prolonged for 0.03 and 0.05 sec., Q-B/B-Y ratio, Q-BI and B-YI improved, H_s elevated by 0.05 and 0.06 Ω , α time prolonged by 0.02 and 0.03 sec.; the whole blood viscosity (high) decreased for 1.36 and 1.20, whole blood viscosity (low) reduced for 4.27 and 4.19; plasma viscosity lowered for 0.66 and 0.43, RBC electrophoretic time shortened by 6.74 and 6.34 sec., hematocrit decreased for 6.92 and 3.75% respectively. These changes of parameters were significant in the course of treatment with ligustrazini ($P < 0.05 \sim 0.01$), but not significant in the control period of treatment. Arterial blood gas changes were observed in 6 patients. After treatment with ligustrazini, results showed that the PaCO_2 was significantly reduced from 65.2 ± 10.0 to 61.3 ± 8.5 mmHg ($P < 0.05$). Except that, the pH, PaO_2 and SaO_2 did not significantly change. These results showed the ligustrazini was effective in "promoting the blood circulation and removing the blood stasis", namely, in dilating the pulmonary vessels, decreasing Pap and PVR, and improving right cardiac function as well as hemorheological quality in treating patients with cor pulmonale.

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Relationship between Tongue Picture and Epithelial Cells of Tongue in Patients with Gastric Cancer

—An Analysis of 50 Cases

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In this paper, tongue picture and the smear of tongue fur in 50 patients with gastric cancer were observed. It was compared with those in 27 healthy persons. Cytology of the tongue picture mainly observes the keratinization of epithelial cells of the tongue and its morphology.

The result showed that most of the epithelial cells in the healthy persons were pro-keratotic, while those in the patients with gastric cancer were keratotic and hyperkeratotic. Many keratotic cells with smaller size and dark color could be seen. Different coated tongues were different in cytological picture of the tongue. About thick fur, there were many epithelial cells, leucocytes, bacteria and dirty background; about exfoliative fur, sparse epithelial cells and fairly numerous middle layer epithelial cells were seen.

The result also showed the keratinization of epithelial cells of tongue was relevant to the thickness and color of fur, but had nothing to do with the changes of the tongue proper. When the fur thickened, the level of keratinization of the cells increased, which was higher in yellowish fur than that of white fur.

The paper explores preliminarily on the cytological characteristics of the tongue picture in gastric cancer patients, and the pattern of cytological changes in different tongue pictures.

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