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通脉活血汤联合温针法对高原红细胞增多症患者血液流变学及抗氧化能力的影响

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[摘要] **目的**:观察通脉活血汤联合温针法在高原红细胞增多症(High altitude polycythemia, HAPC)中的临床应用,分析患者治疗前后血液流变学及抗氧化能力的变化。**方法**:将收治的90例HAPC患者按照抽签法随机分为对照组和观察组,其中对照组给予低分子右旋糖酐和卡托普利治疗,观察组在此基础上,辅以通脉活血汤联合温针法治疗,检测所有受试者治疗前后血液流变学及抗氧化指标。**结果**:治疗前,对照组和观察组HAPC患者血液流变学指标水平均无明显差异($P>0.05$)。治疗后,血液流变学相关指标:全血低切还原黏度(ηb低切)、全血高切还原黏度(ηb高切)、血浆黏度(ηP)、血红蛋白(Hb)、红细胞压积(Hct)和红细胞计数(RBC)水平两组均较治疗前显著下降($P<0.05$),且观察组治疗后明显低于对照组治疗后($P<0.05$)。治疗前,对照组和观察组HAPC患者抗氧化指标大小均无明显差异($P>0.05$)。治疗后,两组血清超氧化物歧化酶(SOD)和还原型谷胱甘肽(GSH)含量均高于治疗前各组含量($P<0.05$),而丙二醛(MDA)含量低于治疗前。观察组治疗后血清SOD和GSH含量均高于对照组治疗后,而MDA含量低于对照组治疗后,差异有统计学意义($P<0.05$)。**结论**:西医常规治疗辅以通脉活血汤联合温针法可以更有效降低HAPC患者血红蛋白,改善血液流变学,提高抗氧化能力,是辅助治疗HAPC潜在有效方案之一。

[关键词] 通脉活血汤;血液流变学;抗氧化;温针法;高原红细胞增多症
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Effect of Tongmai Huoxue decoction combined with warm needling therapy on hemorheology and anti-oxidation ability in patients with high altitude polycythemia

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View from specialist: It is creative, and of certain scientific and educational value.

[ABSTRACT] **Objective**: To investigate the curative effect of Tongmai Huoxue decoction combined with warm needling therapy on the treatment of HAPC, and to analyze the changes of hemorheology and anti-oxidation ability before and after treatment. **Methods**: A total of 90 HAPC patients were randomly divided into control group and observation group. Patients in control group were treated with low molecular weight dextran and captopril, while those who were in observation group were treated with Tongmai Huoxue decoction combined with warm needling therapy based on low molecular weight dextran and captopril. Hemorheology and anti-oxidation markers were measured before and after treatment in all subjects. **Results**: Before

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treatment, there were no significant differences in the hemorheology indexes between the control group and the observation group ($P>0.05$). But after treatment, the hemorheology-related indicators of the two groups were significantly lower than those before treatment ($P<0.05$), including whole blood low shear reduction viscosity, whole blood high shear reduction viscosity, plasma viscosity, Hb, Hct and RBC. Besides, the level of the observation group was significantly lower than that of the control group ($P<0.05$). Before treatment, there was no significant difference in antioxidant indexes between the control group and the observation group ($P>0.05$). After treatment, the levels of serum superoxide dismutase (SOD) and glutathione (GSH) in the two groups were significantly higher than those in the pre-treatment ($P<0.05$), while the content of malondialdehyde (MDA) was lower than that before treatment. The levels of serum SOD and GSH in the observation group were higher than those in the control group, and the MDA content was significantly lower than that in the control group ($P<0.05$). Conclusions: Routine treatment of Western medicine supplemented by Tongmai Huoxue decoction with warm needling therapy can reduce hemoglobin, improve hemorheology and increase anti-oxidation ability in HAPC patients. It is one of the potential effective drugs for adjuvant therapy of HAPC.

[KEY WORDS] Tongmai Huoxue Decoction; Hemorheology; Anti-oxidation; Warm needling; High altitude polycythemia

高原红细胞增多症(High altitude polycythemia, HAPC)对人体伤害巨大,不仅造成肾、肺、肝等脏器间质水肿或充血,还会影响中枢神经系统,更有甚者威胁患者生命[1,2]。目前,西医防治常以HAPC临床症状为依据[3]:降低血液黏度、减小血流阻力、提升氧饱和度等[4,5],从而缓解HAPC患者临床综合征,降低各种生理病理变化。中医防治以活血化瘀联合补气为主要治则,本文旨探讨在常规西药治疗HAPC患者基础上,加以通脉活血汤联合温针法治疗的临床意义。

1 资料与方法

1.1 一般资料

收治本院2016年3月~2017年4月的HAPC患者90例,按照抽签法随机分为两组,对照组和观察组各45例,其中,观察组男性27例,女性18例,年龄27~53岁;对照组男性29例,女性16例,年龄24~50岁。纳入标准如下[6,7]:(1)一般在高于3 000 m海拔发病;(2)具有耳鸣、气短、头晕、结膜充血、紫绀等临床多血症病状;(3)血液学指标:RBC≥6.5×10^{12}/L,Hb≥200 g/L,Hct≥65%。排除真性红细胞增多症、其他出血性疾病和继发性红细胞增多症。患者及家属知情,且本人签署知情同意书,本研究获得医院伦理委员会批准。

1.2 治疗方法

对照组给予低分子右旋糖酐和卡托普利治疗。观察组在此基础上,加入通脉活血汤联合温针法治疗,具体如下:(1)通脉活血汤配制:丹参和黄芪各30 g,当归和川芎各15 g,生地、桃仁、红花、赤芍和陈皮各10 g,桂枝9 g,炙甘草5 g。我院中药制剂为颗粒剂,开水冲服每日2次。(2)针灸治疗:选取双侧风池、内关、血海、足三里、三阴交,上述穴位常规针刺得气后,施以前后均匀的捻转操作,不疾不徐,均匀一致,角度180°~360°,频率60~90 r/min,反复操作2~3 min后,穴上针柄置1~2 cm艾条,温针灸10~15 min。两组疗程均为4周。

1.3 观察指标

取所有受试者治疗前后空腹静脉血3~4 mL,肝素抗凝,低温离心取上层血清,存于-20℃备用。用赛科希德SA-6000全自动血流变测试仪检测所有受试者血清样本的血液流变学指标:全血低切还原黏度、全血高切还原黏度、血浆黏度、血红蛋白(Hb)、红细胞压积(Hct)和红细胞计数(RBC)[8,9]。采用ELISA试剂盒在分光光度计上检测超氧化物歧化酶(SOD)、丙二醛(MDA)和还原型谷胱甘肽(GSH)含量[10,11]。

1.4 统计学处理

所有数据用软件SPSS20.0分析,计量资料以均数±标准差($\bar{x}\pm s$)表示,组间差异比较采用t检验,$P<0.05$为差异具有统计学意义。

2 结果

2.1 两组治疗对HAPC患者ηb低切、ηb高切和ηP的影响

治疗前,观察组和对照组ηb低切、ηb高切和ηP指标大小无显著性差异($P>0.05$);治疗后,观察组和对照组ηb低切、ηb高切和ηP均低于治疗前($P<0.05$);且治疗后观察组水平显著低于对照组($P<0.05$),见表1。

表1 两组HAPC患者治疗前后ηb低切、ηb高切和ηP的变化($n=45$, mPa.s, $\bar{x}\pm s$)

组别	时间	ηb低切	ηb高切	ηP
观察组	治疗前	55.12±7.65	20.21±5.03	3.11±0.74
	治疗后	43.63±6.24#*	14.03±3.15#*	2.31±0.51#*
对照组	治疗前	56.61±8.34	19.73±4.62	3.53±0.84
	治疗后	48.01±7.19#	17.92±3.86#	2.78±0.67#

注:与治疗前比较,#$P<0.05$;与对照组治疗后比较,*$P<0.05$。

2.2 两组治疗对HAPC患者Hb、Hct和RBC的影响

治疗前,观察组和对照组Hb、Hct和RBC指标大小无显著性差异($P>0.05$);治疗后,观察组和对照组Hb、Hct和RBC数值均低于治疗前($P<0.05$);且治疗后观察组水平显著低于对照组($P<0.05$),见表2。

表 2 两组 HAPC 患者治疗前后 Hb、Hct 和 RBC 的变化($n=45, \bar{x}\pm s$)

组别	时间	Hb(g/L)	Hct(%)	RBC($\times10^{12}$/L)
观察组	治疗前	219.84±19.45	74.57±6.52	7.47±1.15
	治疗后	188.67±15.13#*	61.33±7.87#*	5.86±0.96#*
对照组	治疗前	225.12±20.13	72.71±6.92	7.24±1.23
	治疗后	203.54±18.54#	67.83±6.03#	6.53±1.02#

注:与治疗前比较,# $P<0.05$;与对照组治疗后比较,* $P<0.05$。

2.3 两组治疗对 HAPC 患者血清 SOD、GSH 和 MDA 的影响

治疗前,观察组和对照组血清 SOD、GSH 和 MDA 浓度无显著性差异($P>0.05$);治疗后,观察组和对照组 SOD 和 GSH 浓度均高于治疗前($P<0.05$),且治疗后观察组浓度显著高于对照组($P<0.05$);治疗后观察组 MDA 浓度显著低于同期对照组,两组 MDA 浓度均低于治疗前,差异有统计学意义($P<0.05$),见表 3。

表 3 两组 HAPC 患者治疗前后血清 SOD、GSH 和 MDA 含量变化($n=45, \bar{x}\pm s$)

组别	时间	SOD ($\times10^{13}$U/L)	GSH (mg/L)	MDA (μmol/L)
观察组	治疗前	89.67±7.53	90.16±9.13	32.46±3.33
	治疗后	101.07±9.42#*	115.43±8.85#*	24.26±4.75#*
对照组	治疗前	88.35±7.85	89.47±8.35	33.93±3.42
	治疗后	94.33±8.32#	107.58±8.26#	27.81±3.52#

注:与治疗前比较,# $P<0.05$;与对照组治疗后相比较,* $P<0.05$。

3 讨论

HAPC 是由于长期处于低氧环境下造成的,目前研究表明,可能是促红细胞生成素过表达、紊乱的细胞凋亡和增殖、氧自由基代谢异常和强紫外线辐射等诱发 HAPC[12,13]。无论是中医还是西医,目前在缓解 HAPC 临床病理特征上都取得了很大进步。

HAPC 患者伴有耳鸣、气短、指关节麻木、肌肉或关节疼痛、舌质紫色、面部毛细血管扩张充血等组织缺氧症状,这些症状均与血液学变化诱导相关[7,14,15]。低分子右旋糖酐被用于治疗血栓性疾病,能改善微循环,扩充血容量,降低血液黏度[16]。卡托普利主要适用于降血压,通过肾素-血管紧张素-醛固酮系统(RAA 系统),抑制血管紧张素转化酶使血管舒张,降低外周血管阻力[17]。二者被用于西医临床治疗 HAPC 患者,但只能局部改善 HAPC 患者临床疗效。中医理论以"人"为整体,给予中药宏观调理 HAPC 患者气虚血淤体征[18,19]。通脉活血汤能够益气活血,已有报道活血通脉汤加减能够滋阴清热,结合西医常规治疗血管疾病,包括心肌缺血、下肢深静脉血栓、脑血栓等,且临床效果好[20,21]。同时,辅以温针治疗,疏通经络,调节气血。本研究中西医结合:对照组是西医常规治疗,给予卡托普利和低分子右旋糖酐;观察组由西医常规治疗配以中药汤剂和针灸法温治[21]。

血液流变学的变化引起 HAPC 患者组织缺氧[22,23],本研究显示:两组患者治疗前,血液流变学指标无明显差异;治疗后,常规治疗辅以通脉活血汤联合温针法治疗的观察组血液流变学各参数的改善优于对照组:血浆黏度、全血低切还原黏度、全血高切还原黏度、Hb、Hct 和 RBC 均降低更明显。从血液流变学指标参数的显著差异,可推断出辅以通脉活血汤联合温针法治疗,能更有效增加 HAPC 患者血管流动性,降低血红蛋白含量和红细胞压积,改善患者的临床症状。SOD 是人体的一种抗氧化酶;GSH 是一种重要的抗氧化剂,能清除体内多余的自由基;MDA 是脂质氧化的终产物,是常用的过氧化指标[24]。人体正常状态下,这些指标处于平衡。本研究显示:治疗后,HAPC 患者血清 SOD 和 GSH 含量高于治疗前,MDA 含量比治疗前水平低。由于通脉活血汤有活血作用,方中桃仁、当归、红花、丹参、川芎、桂枝活血化瘀;配合黄芪 、陈皮、炙甘草理气补气;生地、赤芍养血滋阴。合理的配伍,增加了汤剂的原有疗效。温针是针刺与艾灸联合,疏通经络,温通气血,祛散寒邪。常规治疗辅以通脉活血汤联合温针法治疗,能有效改善 HAPC 患者血液流变学及抗氧化指标变化。

综上所述,西医常规治疗辅以通脉活血汤联合温针法可以增加 HAPC 患者血管流动性,降低血红蛋白含量和红细胞压积,提高血清 SOD 和 GSH 浓度,降低 MDA 含量,是辅助治疗 HAPC 潜在有效方案之一。

参考文献

1 Julian C G, Gonzales M, Rodriguez A, et al. Perinatal hypoxia increases susceptibility to high-altitude polycythemia and attendant pulmonary vascular dysfunction[J]. Am J Physiol Heart Circ Physiol, 2015, 309(4): 565-573.

2 Xu J, Yang Y Z, Tang F, et al. EPAS1 gene polymorphisms are associated with high altitude polycythemia in tibetans at the Qinghai-tibetan plateau[J]. Wilderness Environ Med, 2015, 26(3): 288-294.

3 Li K, Gesang L, Zeng D, et al. Transcriptome reveals the overexpression of a kallikrein gene cluster (KLK1/3/7/8/12) in the Tibetans with high altitude-associated polycythemia[J]. International Journal of Molecular Medicine, 2017, 39(2): 287-296.

4 Wang T, Xing Z. A fluid-particle interaction method for blood flow with special emphasis on red blood cell aggregation[J]. Biomed Mater Eng, 2014, 24(6): 2511-2517.

5 Freund J B, Vermot J. The wall-stress footprint of blood cells flowing in microvessels[J]. Biophysical Journal, 2014, 106(3): 752-762.

6 祁生贵, 吴天一. 慢性高原病诊断标准及相关研究[J]. 高原医学杂志, 2015, 25(4): 1-11.

7 Jiang C, Chen J, Liu F, et al. Chronic mountain sickness in Chinese Han males who migrated to the Qinghai-Tibetan plateau: application and evaluation of diagnostic criteria for chronic mountain sickness[J]. BMC Public Health, 2014, 14(1): 701.

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motes proliferation, migration, and invasion via negative regulation of MTDH in esophageal squamous cell carcinoma[J]. FASEB J, 2017, 31(5): 2114-2122.
8 Mataki H, Seki N, Mizuno K, et al. Dual-strand tumor-suppressor microRNA-145 (miR-145-5p and miR-145-3p) coordinately targetedMTDH in lung squamous cell carcinoma[J]. Oncotarget, 2016, 7(44): 72084-72098.
9 Shi Z, Tang Y, Li K, et al. TKTL1 expression and its down-regulation is implicated in cell proliferation inhibition and cell cycle arrest in esophageal squamous cell carcinoma [J]. Tumour Biol, 2015, 36(11): 8519-8529.
10 Grimm M, Munz A, Teriete P, et al. GLUT-1(+)/TKTL1 (+) coexpression predicts poor outcome in oral squamous cell carcinoma[J]. Oral Surg Oral Med Oral Pathol Oral Radiol, 2014, 117(6): 743-753.
11 Rehena Z, Ghosh CK, Afroz F, et al. Comparison of Serum CA72-4 and CEA Levels in Patient with Endoscopically Suspected GastricCarcinoma[J]. Mymensingh Med J, 2015, 24(3): 542-549.
12 Song XM, Wang ZJ, Cao WJ, et al. The value of circulating CYFRA21-1 expression in patients with nasopharyngeal carcinoma: a study of 529 subjects [J]. Int J Clin Oncol, 2016, 21 (6): 1038-1045.
13 Sunpaweravong S, Puttawibul P, Sunpaweravong P, et al. Correlation between Serum SCCA and CYFRA 2 1-1, Tissue Ki-67, and Clinicopathological Factors in Patients with Esophageal Squamous Cell Carcinoma [J]. J Med Assoc Thai, 2016, 99 (3): 331-337.
14 Salvatici M, Achilarre MT, Sandri MT, et al. Squamous cell carcinoma antigen (SCC-Ag) during follow-up of cervical cancer patients: Role in the early diagnosis of recurrence[J]. Gynecol Oncol, 2016, 142(1): 115-119.
15 Qin Z, Chen J, Zeng J, et al. Effect of NK cell immunotherapy on immune function in patients with hepatic carcinoma: A preliminary clinical study [J]. Cancer Biol Ther, 2017, 18(5): 323-330.
16 Dolezal JM, Wang H, Kulkarni S, et al. Sequential adaptive changes in a c-Myc-driven model of hepatocellular carcinoma [J]. J Biol Chem, 2017, 292(24): 10068-10086.
17 Tsubaki M, Fujiwara D, Takeda T, et al. The sensitivity of head and neck carcinoma cells to statins is related to the expression of their Ras expression status, and statin-induced apoptosis is mediated via suppression of the Ras/ERK and Ras/mTOR pathways[J]. Clin Exp Pharmacol Physiol, 2017, 44(2): 222-234.
18 Lu C, Xie C. Radiation-induced autophagy promotes esophageal squamous cell carcinoma cell survival via theLKB1 pathway [J]. Oncol Rep, 2016, 35(6): 3559-3565.
19 Ohkawa K, Asakura T, Tsukada Y, et al. Antibody to human α-fetoprotein inhibits cell growth of human hepatocellular carcinoma cells by resuscitating the PTEN molecule: in vitro experiments [J]. Int J Oncol, 2017, 50(6): 2180-2190.

(上接第 2039 页)

8 马婕, 崔森, 冀林华,等. 高原红细胞增多症发病基因的研究进展[J]. 山东医药, 2017, 57(10):112-114.
9 Ainslie P N, Subudhi A W. Cerebral blood flow at high altitude [J]. High Alt Med Biol, 2014, 15(2):133-40.
10 Bailey D M, Rimoldi S F, Rexhaj E, et al. Oxidative-nitrosative stress and systemic vascular function in highlanders with and without exaggerated hypoxemia[J]. Chest, 2013, 143(2):444-451.
11 Jiang C, Cui J, Liu F, et al. Mitochondrial DNA 10609T promotes hypoxia-induced increase of intracellular ROS and is a risk factor of high altitude polycythemia[J]. Plos One, 2014, 9 (1):e87775.
12 Bigham A W, Lee F S. Human high-altitude adaptation: forward genetics meets the HIF pathway[J]. Genes & Development, 2014, 28(20):2189-2204.
13 Julian C G, Vargas E, Gonzales M, et al. Sleep-disordered breathing and oxidative stress in preclinical chronic mountain sickness (excessive erythrocytosis)[J]. Respir Physiol Neurobiol,2013,186(2):188-196.
14 Leónvelarde F, Villafuerte F C, Richalet J P. Chronic mountain sickness and the heart [J]. Prog Cardiovasc Dis, 2010,52(6): 540-549.
15 陈浩, 次仁罗布, 刘金风,等. 益心康泰胶囊对高原红细胞增多症患者血液流变学的影响[J]. 西藏医药, 2010, 31(4):1-3.
16 陆阳, 曾慧琳. 丹参联合低分子右旋糖酐在妊娠晚期合并下肢静脉血栓患者中的治疗效果[J]. 哈尔滨医药, 2017, 37(2): 101-103.
17 Hoiland R L, Bain A R, Rieger M, et al. Hypoxemia, oxygen content, and the regulation of cerebral blood flow[J]. Am J Physiol Regul Integr Comp Physiol.2016 ,310(5):R398-413.
18 仁桑. 藏中医结合治疗高原红细胞增多症的疗效观察[J]. 中国民族医药杂志, 2014, 20(5):27-28.
19 Zhu H L, Nie H J, Pei-Bing L I, et al. The physiological effects of resveratrol and its potential application in high altitude medicine[J]. Chin J Appl Physiol, 2015, 31(6):498-503.
20 臧奉娇, 王树庆, 王念德,等. 活血通脉颗粒对真性红细胞增多症患者血栓弹力图 K 值的影响[J]. 安徽中医药大学学报, 2017, 36(2):22-25.
21 邓树荣, 王贤明, 李洪韬,等. 中西医结合治疗对急性缺血性脑卒中的临床综合干预效果评价[J]. 海南医学院学报, 2013, 19 (4):470-473.
22 Guo L, Chughtai A R, Jiang H, et al. Relationship between polycythemia and in-hospital mortality in chronic obstructive pulmonary disease patients with low-risk pulmonary embolism [J]. Journal of Thoracic Disease, 2016, 8(11):3119-3131.
23 Ainslie P N, Subudhi A W. Cerebral blood flow at high altitude [J]. High Alt Med Biol, 2014, 15(2):133-40.
24 Basang Z, Wang B, Li L, et al. HIF2A variants were associated with different levels of high-altitude hypoxia among native tibetans[J]. Plos One, 2015, 10(9):e0137956.