

# 活血通络颗粒对缺血性视神经病变的临床研究

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## Clinical studies of Huoxuetongluo granula on the treatment of ischemic optic neuropathy

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### Abstract

• AIM: To evaluate the clinical efficacy of Huoxuetongluo granula on the treatment of qi deficiency and blood stasis type of non-arteritic anterior ischemic optic neuropathy (NAION).

• METHODS: A total of 100 patients with NAION were enrolled in the randomized controlled trial. They were divided into control group (49 cases with 70 eyes) and treatment group (51 cases with 72 eyes). The patients in control group were treated with only injections of compound anisodine (CA) beside superficial temporal artery, 2ml each time, once per day. The patients in treatment group received huoxuetongluo granula, 10g each time, twice per days, besides CA. Patients were followed up for 3mo, and the overall cure effect, visual acuity, mean sensitivity (MS), serum lipid levels and hemorheology indicators were measured and analyzed.

• RESULTS: After treatments, the total effective rate of treatment group were 88.2%, which was significantly higher than that of the control group (71.4%) ( $Z=2.890$ ,  $P=0.004$ ). Compared with the control group, the visual acuity and MS of treatment group were significantly higher and the differences were statistical ( $t=-4.65$ ,  $P<0.0001$ ;  $t=-3.69$ ,  $P=0.0004$ ). The TC, TG and low-density lipoprotein cholesterol (LDL-C) levels were

significantly lower, the high-density lipoprotein cholesterol (HDL-C) significantly increased than those before treatments ( $t=6.25$ ,  $P<0.01$ ;  $t=4.14$ ,  $P<0.01$ ;  $t=4.48$ ,  $P<0.01$ ;  $t=3.76$ ,  $P=0.0003$ ;  $t=-4.31$ ,  $P<0.01$ ). After treatments, the whole blood high shear viscosity, low shear viscosity, plasma viscosity and fibrinogen of the treatment group were significantly lower than those of control group ( $t=3.40$ ,  $P=0.0011$ ;  $t=5.75$ ,  $P<0.01$ ;  $t=3.61$ ,  $P=0.0005$ ;  $t=6.78$ ,  $P<0.01$ ;  $t=3.13$ ,  $P=0.0025$ ).

• CONCLUSION: The combination of CA and huoxuetongluo granula can improve the visual acuity, MS, serum lipid levels and hemorheology indicators significantly.

• KEYWORDS: optic neuropathy; hemorheology; huoxuetongluo granula

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### 摘要

目的:探讨活血通络颗粒对气虚血瘀型非动脉炎性前部缺血性视神经病变的临床疗效。

方法:采用随机对照试验,将100例非动脉炎性前部缺血性视神经病变患者随机分为对照组和治疗组,治疗组51例72眼,对照组49例70眼。对照组给予复方樟柳碱注射液颞浅动脉旁注射,2mL/次,1次/d。在上述治疗的基础上,治疗组患者加用活血通络颗粒(10g/次,口服,2次/d)进行干预。3mo后,观察并分析两组患者视神经病变的总体疗效、视力、视野平均光敏感度、血脂水平及血液流变学指标的改善情况。

结果:治疗后,治疗组患者视神经病变的总有效率为88.2%,显著高于对照组71.4% ( $Z=2.890$ ,  $P=0.004$ );治疗组患者的视力和视野平均敏感度均显著性提高,差异有统计学意义 ( $t=-4.65$ ,  $P<0.01$ ;  $t=-3.69$ ,  $P=0.0004$ );治疗组患者的血清总胆固醇、甘油三酯、低密度脂蛋白胆固醇水平较治疗前均下降,高密度脂蛋白胆固醇较治疗前升高,差异有统计学意义 ( $t=6.25$ ,  $P<0.01$ ;  $t=4.14$ ,  $P<0.01$ ;  $t=4.48$ ,  $P<0.01$ ;  $t=3.76$ ,  $P=0.0003$ ;  $t=-4.31$ ,  $P<0.01$ );治疗组患者的全血高切黏度、低切黏度、血浆黏度和血浆纤维蛋白原均显著降低 ( $t=3.40$ ,  $P=0.0011$ ;  $t=5.75$ ,  $P<0.01$ ;  $t=3.61$ ,  $P=0.0005$ ;  $t=6.78$ ,  $P<0.01$ ;  $t=3.13$ ,  $P=0.0025$ )。

结论:复方樟柳碱注射液联合活血通络颗粒可显著改善NAION患者的视力、视野、血脂水平和血液流变学指标。

关键词:视神经病变;血流变学;活血通络颗粒

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## 0 引言

非动脉炎性前部缺血性视神经病变(non arteritic anterior ischemic optic neuropathy, NAION)是一种50岁以上人群中最常见的急性视神经病变,临床上以无痛性突发视力障碍、视野缺损、视盘水肿或周围神经纤维层出血为主要表现<sup>[1-2]</sup>。该病发病急、短期内视力急剧下降,严重者甚至失明<sup>[3]</sup>。目前,国内在控制原发病的基础上,对NAION治疗多采用复方樟柳碱颞浅动脉旁皮下注射,但疗效尚不尽满意。本研究结合中医辨证思维,旨在探讨复方樟柳碱治疗的基础上应用活血通络颗粒对气虚血瘀型NAION的临床疗效。

## 1 对象和方法

**1.1 对象** 选取2014-02/10在我院眼科门诊及住院的患者100例,其中双眼发病42例,单眼发病58例,共计142眼;男性患者51例,女性患者49例。伴随的全身疾病包括高血压31例44眼,糖尿病27例38眼,冠状动脉硬化29例42眼,无明显诱因13例18眼。纳入标准:符合以下诊断标准,同时自愿配合该项目治疗的患者被纳入为研究对象。参照Hayreh等<sup>[4]</sup>制定的NAION诊断标准:(1)突发视力下降,多在晨起时发生;(2)病史中急性期存在视盘水肿或相关的记录;(3)存在与视盘病变相关的视野缺损;(4)排除其他可以导致视盘水肿和视力下降的神经、系统或眼部疾病。气虚血瘀证型诊断标准<sup>[5]</sup>:视力骤降,心烦郁闷,头目隐痛,胸胁胀满;舌质紫暗或有瘀斑,脉弦数。采用随机对照试验,将100例随机分为治疗组和对照组,其中治疗组51例72眼,对照组49例70眼。两组患者的性别、年龄、病程的差异均无统计学意义( $P>0.05$ ),见表1。

**1.2 方法** 对照组采用复方樟柳碱注射液2mL颞浅动脉旁注射,1次/d。在上述治疗的基础上,治疗组根据韦企平<sup>[5]</sup>主编的《视神经疾病中西医结合诊治》气虚血瘀型方选活血通络方,方药组成:熟地15g、当归、芍药、川芎、鸡血藤、丝瓜络、路路通、女贞子各10g、太子参15g、红花、炒枳壳各6g。上方由北京中医药大学东方医院制剂室制成配方颗粒,每次10g,每天2次早晚饭后服用。两组疗程均为3mo。采用国际标准对数视力表对患者的视力进行检查;采用静态自动电脑Octopus101型视野计检查患者60°范围的视野;眼底荧光血管造影(Fundus fluorescein angiography, FFA)观察眼底血管情况;采用血液流变仪检测血液流变学指标;采用生化分析仪检测血脂、血糖、肝肾功能等指标。记录两组患者用药前后上述指标的变化,并对结果进行比较分析。

疗效标准<sup>[6]</sup>:以视力、视野的改善程度为标准,将疗效分为以下4类:(1)临床治愈:视力 $\geq 1.0$ 或增加4行,从光感提高至0.1,从眼前指数提高至0.2,从0.02提高至0.3,或从0.05提高至0.4,视野缺损面积减少40%以上,或平均视野阈值增加30%以上;(2)显效:视力增加3行,从光感提高至0.05,从眼前指数提高至0.1,从0.01提高至0.2,从0.05提高至0.3,视野缺损面积减少15%~40%或平均视野阈值增加10%~30%;(3)有效:视力增加2行或1行,从光感提高至0.02,从眼前指数提高至0.02~0.05,从0.02提高至0.05~0.1,从0.05提高至

表1 患者的一般情况比较

组别	年龄( $\bar{x}\pm s$ ,岁)	例数(男/女)	病程( $\bar{x}\pm s$ ,mo)
对照组	53.1 $\pm$ 7.9	49(25/24)	9.35 $\pm$ 3.06
治疗组	53.8 $\pm$ 8.67	51(26/25)	10.35 $\pm$ 3.43
$t/\chi^2$	-0.48	0.001	-1.38
$P$	0.6298	0.997	0.1723

表2 治疗组和对照组总体治疗效果的比较

组别	例数	治愈	显效	有效	无效	总有效率(%)
对照组	49(70)	5(7)	8(11)	22(29)	14(23)	71.4
治疗组	51(72)	12(15)	15(21)	18(25)	6(11)	88.2

表3 治疗组和对照组视力和视野平均敏感度的比较

组别	例数	时间	视力	视野平均敏感度
对照组	49	治疗前	0.29 $\pm$ 0.09	16.81 $\pm$ 3.15
		治疗后	0.35 $\pm$ 0.06 <sup>c</sup>	21.89 $\pm$ 3.36 <sup>c</sup>
治疗组	51	治疗前	0.28 $\pm$ 0.08	16.24 $\pm$ 2.84
		治疗后	0.43 $\pm$ 0.09 <sup>a,c</sup>	24.24 $\pm$ 2.22 <sup>a,c</sup>

<sup>a</sup> $P<0.05$  vs 对照组治疗后;<sup>c</sup> $P<0.05$  vs 对照组治疗前;<sup>e</sup> $P<0.05$  vs 治疗组治疗前。

0.12~0.2,视野缺损面积减少15%以下,或平均视野阈值增加10%以下;(4)无效:视力无变化或下降,视野缺损面积不变或增大,或平均视野阈值不变或下降。

统计学分析:采用SPSS 18.0软件进行统计学分析,活血通络颗粒对气虚血瘀型NAION的临床总体疗效采用Wilcoxon秩和检验;两组的视力、视野、血脂和血液流变学指标的治疗前后比较分别采用配对 $t$ 检验,两组之间治疗前后比较分别采用独立样本 $t$ 检验,以 $\bar{x}\pm s$ 表示, $P<0.05$ 有统计学意义。

## 2 结果

**2.1 总体疗效的分析** 治疗后,治疗组患者临床治愈12例15眼(23.5%),显效15例21眼(29.4%),有效18例25眼(35.3%),无效6例11眼(11.8%),有效率为88.2%;对照组患者临床治愈5例7眼(10.2%),显效8例11眼(16.3%),有效22例29眼(44.9%),无效14例23眼(28.6%),有效率为71.4%。两组临床总体疗效比较用Wilcoxon秩和检验差异有统计学意义( $Z=2.890, P=0.004$ ,表2)。

**2.2 视力和视野的改善情况** 治疗后,和对照组比较,治疗组患者的视力显著提高,差异均有统计学意义( $t=-4.65, P<0.01$ );治疗组患者的视野平均敏感度显著提高,差异均有统计学意义( $t=-3.69, P=0.0004$ )。治疗后和治疗前比较,两组患者的视力均提高,差异有统计学意义( $t=-3.86, P=0.0002; t=-7.68, P<0.01$ );两组患者的视野平均敏感度均提高,差异有统计学意义( $t=-6.98, P<0.01; t=-14.03, P<0.0001$ ),见表3。

**2.3 血脂的分析** 治疗前,治疗组与对照组患者的血清总胆固醇(TC)、甘油三脂(TG)、高密度脂蛋白胆固醇(HDL-C)、低密度脂蛋白胆固醇(LDL-C)水平进行比较,均无显著性差异( $P>0.05$ )。治疗后,和对照组比较,

表4 治疗组与对照组血脂水平的比较

 $(\bar{x} \pm s, \text{mmol/L})$ 

组别	例数	时间	TC	TG	HDL-C	LDL-C
对照组	49	治疗前	8.07±1.07	2.43±0.82	1.44±0.30	4.48±1.19
		治疗后	7.59±1.32	2.25±0.48	1.59±0.35	4.25±0.75
治疗组	51	治疗前	8.18±0.93	2.48±0.78	1.40±0.30	4.57±1.08
		治疗后	5.84±1.18 <sup>a,c</sup>	1.79±0.46 <sup>a,c</sup>	1.89±0.30 <sup>a,c</sup>	3.50±1.01 <sup>a,c</sup>

<sup>a</sup> $P < 0.05$  vs 对照组治疗后; <sup>c</sup> $P < 0.05$  vs 治疗组治疗前。

表5 治疗组与对照组血流变学指标的比较

 $\bar{x} \pm s$ 

组别	例数	时间	血浆黏度(mP/s)	全血低切黏度(mP/s)	全血高切黏度(mP/s)	红细胞压积(%)	血浆纤维蛋白(mg/dL)
对照组	49	治疗前	1.67±0.29	12.52±1.97	5.66±1.25	47.17±3.30	3.87±0.89
		治疗后	1.55±0.27	11.76±2.84	5.62±1.29	46.12±3.32	3.67±0.90
治疗组	51	治疗前	1.73±0.25	12.43±1.90	5.68±1.25	47.22±3.18	3.92±0.81
		治疗后	1.39±0.15 <sup>a,c</sup>	8.81±1.57 <sup>a,c</sup>	4.77±0.74 <sup>a,c</sup>	41.19±4.63 <sup>a,c</sup>	3.10±0.71 <sup>a,c</sup>

<sup>a</sup> $P < 0.05$  vs 对照组治疗后; <sup>c</sup> $P < 0.05$  vs 治疗组治疗前。

治疗组患者的TC、TG、LDL-C水平较治疗前均下降,HDL-C水平较治疗前升高,差异均有统计学意义( $t = 6.25, P < 0.01; t = 4.14, P < 0.01; t = 4.48, P < 0.01; t = 3.76, P = 0.0003; t = -4.31, P < 0.01$ )。治疗后,和治疗前自身比较,治疗组患者的TC、TG、LDL-C水平较治疗前均下降,HDL-C水平较治疗前升高,差异有统计学意义( $t = 9.83, P < 0.01; t = 4.78, P < 0.01; t = 4.58, P < 0.01; t = 7.22, P < 0.01$ )。对照组患者的上述指标比较,无显著性差异( $t = 1.77, P = 0.0807; t = 1.25, P = 0.2153; t = 1.04, P = 0.3038; t = -1.89, P = 0.0629$ ),表4。

**2.4 血流变学的分析** 治疗前,治疗组与对照组患者的血浆黏度、全血高切黏度、低切黏度、红细胞压积指数及血浆纤维蛋白原水平进行比较,均无显著性差异( $P > 0.05$ )。治疗后,和对照组比较,治疗组患者的血浆黏度、全血高切黏度、低切黏度、红细胞压积指数及血浆纤维蛋白原水平均下降,差异有统计学意义( $t = 3.40, P = 0.0011; t = 5.75, P < 0.01; t = 3.61, P = 0.0005; t = 6.78, P < 0.01; t = 3.13, P = 0.0025$ )。治疗后,和治疗前进行自身比较,治疗组患者的上述指标较治疗前均下降,差异有统计学意义( $t = 7.51, P < 0.01; t = 9.30, P < 0.01; t = 3.98, P = 0.0002; t = 6.78, P < 0.01; t = 4.79, P < 0.01$ )。对照组患者的上述指标进行比较,无显著性差异( $t = 1.90, P = 0.0606; t = 1.40, P = 0.1660; t = 0.16, P = 0.8744; t = 1.42, P = 0.1602; t = 1.02, P = 0.3120$ ),见表5。

### 3 讨论

NAION是50岁以上人群中最常见的急性视神经病变,血流动力学异常、血液黏稠度改变、眼灌注压较低为其病理生理学基础<sup>[7-8]</sup>。活血通络颗粒由熟地、当归、芍药、川芎、鸡血藤、丝瓜络、路路通、女贞子、太子参、红花、炒枳壳组成,具有益气活血、通络明目的功效。该配方符合气虚血瘀型NAION患者的恢复期的证候特点,具有多向调节功能。

本研究结果显示:治疗组患者的视力、视野改善情况总有效率(88.2%)高于对照组患者(71.4%)。该结果和常永业等<sup>[9]</sup>的研究结果基本一致。另外,治疗组患者视力和视野平均敏感度均较对照组显著性提高。上述结果提示:在采用复方樟柳碱注射液治疗的基础上,联合应用活血通络颗粒,在一定程度上可以改善NAION患者的视力、

视野。该治疗效果与活血通络颗粒的成分密切相关。活血通络颗粒中的多种成分:地黄<sup>[10-11]</sup>、川芎<sup>[12-13]</sup>、芍药<sup>[14]</sup>、鸡血藤<sup>[15]</sup>和枳壳<sup>[16]</sup>中有效成分可以调节多种血管活性物质的释放,对抗交感神经的缩血管作用,有扩张微血管、改善视网膜缺血后再灌注产生的损伤。川芎中川芎嗪<sup>[17-18]</sup>、地黄中梓醇和毛蕊花糖苷<sup>[19-21]</sup>、红花中红花黄色素<sup>[22-24]</sup>和羟基红花黄色素A<sup>[25-26]</sup>、芍药中芍药苷<sup>[27-30]</sup>、太子参中皂苷<sup>[31]</sup>以及枳壳中柚皮素<sup>[32]</sup>和橙皮苷<sup>[33-34]</sup>均对神经均有一定的保护作用。

本研究结果显示:治疗组患者的血清总胆固醇、甘油三脂、低密度脂蛋白胆固醇水平较对照组均下降,高密度脂蛋白胆固醇水平较对照组升高,差异有显著性意义。该结果可能与活血通络颗粒组方中地黄<sup>[35]</sup>、红花<sup>[36]</sup>、女贞子<sup>[37]</sup>、太子参<sup>[38]</sup>、和丝瓜络<sup>[39]</sup>中多种有效成分均可以降低血清胆固醇、甘油三脂、低密度脂蛋白的水平 and 升高高密度脂蛋白的水平。

另外,本研究结果显示:治疗组患者的血浆黏度、全血高切黏度、低切黏度和血浆纤维蛋白原水平较对照组均显著下降。该结果可能因为活血通络颗粒配方中地黄的有效成分5-羟甲基糠醛<sup>[40-41]</sup>、川芎和赤芍中有效成分<sup>[42]</sup>、枳壳中柚皮素<sup>[16]</sup>、鸡血藤和红花中有效成分<sup>[43]</sup>均具有抑制血小板及红细胞凝聚,降低血液黏滞度,促进纤溶活性,抑制血管内凝血,扩张血管,改善微循环和细胞代谢,增加动脉血流量,降低外周血管阻力的作用。

结合中医辨证论治,活血通络颗粒中熟地、当归、太子参养血活血,补气生津,使脉充血行,共为主药;赤芍活血化瘀,白芍柔肝益阴,川芎为血中气药,可行气走窜通络,其辛香善行之力可直达头目巅顶,鸡血藤养血活血,红花活血化瘀,通络开闭,四药同为辅药;佐以枳壳调理气机,疏解气滞,丝瓜络味甘、辛平,路路通味苦、辛平,二药合并可增强其通经活络功效,性味平缓,毒性小,可持久应用;女贞子性味平和,可“强阴,健腰膝,变白发,明目”,加入本方有滋阴增液,生津润络之效,为使药。全方以活为要,以补助通,药性和缓,可长服久用。以上诸药具有益气养阴、活血化痰通络的作用。

活血通络颗粒以中医辨证论治和整体观念为指导,对NAION患者视功能的保护作用可能是通过中药内多成分、多重途径、多个靶点共同实现的。总之,本研究采用复

方樟柳碱注射液治疗的基础上,联合应用活血通络颗粒,进一步改善了NAION患者的视力、视野、血脂水平及血液流变学指标,在用药过程中无明显不良反应,具有一定的临床借鉴意义。

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