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低频超声治疗动脉粥样硬化性大脑中动脉狭窄急性脑梗死患者的疗效及对炎症指标的影响分析*

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摘要 目的:探讨低频超声治疗动脉粥样硬化性大脑中动脉(MCA)狭窄急性脑梗死(ACI)患者的临床疗效及对炎症指标的影响。**方法:**选取2015年10月至2018年5月华中科技大学同济医学院附属荆州医院收治的动脉粥样硬化性MCA狭窄ACI患者82例,按随机数字表法分为对照组和观察组,每组各41例。对照组行常规治疗,观察组在对照组的基础上行低频超声治疗,对所有患者治疗前及治疗14 d后的神经功能进行评分,低频超声检测MCA狭窄段峰值血流速度(Vs)、微栓子信号(MES)阳性率,比较治疗前、治疗7 d后、14 d后两组患者血清高敏C-反应蛋白(hs-CRP)水平。**结果:**治疗14 d后两组的美国国立卫生研究院卒中量表(NIHSS)评分下降,且观察组较对照组NIHSS评分更低($P<0.05$);治疗14 d后观察组MCA狭窄段Vs低于治疗前($P<0.05$),而对照组与治疗前比较无统计学差异($P>0.05$)。治疗7 d后、14 d后观察组MES阳性率均低于对照组($P<0.05$)。两组治疗7 d后、14 d后hs-CRP水平低于治疗前,且治疗14 d后低于治疗7 d后($P<0.05$);而观察组治疗7 d后、14 d后hs-CRP水平低于对照组($P<0.05$)。**结论:**低频超声治疗动脉粥样硬化性MCA狭窄ACI患者疗效显著,可改善神经功能与炎症反应,减缓Vs,提高动脉粥样硬化斑块的稳定性。

关键词:低频超声;动脉粥样硬化;大脑中动脉;急性;脑梗死;炎症指标;疗效

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Curative Effect of Low Frequency Ultrasound in the Treatment of Atherosclerotic Middle Cerebral Artery Stenosis in Patients with Acute Cerebral Infarction and Its Influence on Inflammatory Markers*

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ABSTRACT Objective: To investigate the clinical effect of low frequency ultrasound in the treatment of atherosclerotic middle cerebral artery (MCA) stenosis in patients with acute cerebral infarction (ACI) and its influence on inflammatory markers. **Methods:** 82 ACI patients with atherosclerotic MCA stenosis treated in Jingzhou Hospital Affiliated to Tongji Medical College of Huazhong University of Science and Technology from October 2015 to May 2018 were selected, they were divided into the control group and the observation group according to the random number table method, 41 cases in each group. The control group received routine treatment, while the observation group accepted low frequency ultrasound based on the control group. The neurological function scores of all patients were evaluated before treatment and 14 d after treatment. MCA stenosis segment peak blood flow velocity (Vs) and micro embolic signal (MES) positive rate were detected by low frequency ultrasound. The levels of serum high sensitive C- reactive protein(hs-CRP) in the two groups were compared before treatment, 7 d, 14 d after treatment. **Results:** The National Institutes of Health Stroke Scale (NIHSS) scores decreased in the two groups at 14 d after treatment, and the NIHSS scores in the observation group were lower than that in the control group ($P<0.05$). 14 d after treatment, MCA stenosis segment Vs in the observation group was lower than before treatment ($P<0.05$), while there was no significant difference between the control group and before treatment ($P>0.05$). 7 d, 14 d after treatment, the positive rate of MES in the observation group was lower than that in the control group ($P<0.05$). 7 d, 14 d after treatment, the level of hs-CRP was lower than before treatment, and at 14 d treatment was lower than that at 7 d after treatment ($P<0.05$). The level of hs-CRP at 7 d, 14 d after treatment in the observation group was lower than that in the control group ($P<0.05$). **Conclusion:** The efficacy of low frequency ultrasound in the

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treatment of atherosclerotic MCA stenosis ACI patients is significant. It can improve the nerve function and inflammatory reaction, slow down the Vs and improve the stability of atherosclerotic plaque.

Key words: Low frequency ultrasound; Atherosclerotic; Middle cerebral artery; Acute; Cerebral infarction; Inflammatory markers; Curative effect

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前言

脑梗死属于神经内科疾病,其发病率较高,患者的主要临床特征为头晕、间歇性肢体麻木、无力等^[1,2]。导致脑梗死形成的一个重要因素为大脑中动脉(middle cerebral artery, MCA)狭窄,脑动脉狭窄的好发部位主要为颈内动脉起始部和椎动脉起始部^[3,4]。以目前临床医疗技术,对动脉粥样硬化性 MCA 狭窄需采用支架置入治疗、药物治疗等,且治疗期间需积极控制导致疾病产生的危险因素^[5-7]。但通常药物治疗无法有效消除动脉粥样硬化斑块,并且对阻碍血栓形成的作用并不理想,而支架置入治疗的适应症存在局限性,治疗具有一定风险性,且治疗费用昂贵^[8,9]。低频超声治疗相比于上述治疗方法具有无创、安全性高等优点,目前正逐渐成为治疗急性脑梗死(acute cerebral infarction, ACI)的新型治疗方式^[10,11]。在本研究中对我院收治的 41 例动脉粥样硬化性 MCA 狭窄 ACI 患者给予低频超声治疗,对比分析常规药物治疗效果。结果报道如下。

1 资料与方法

1.1 一般资料

将华中科技大学同济医学院附属荆州医院 2015 年 10 月至 2018 年 5 月期间确诊的 82 例动脉粥样硬化性 MCA 狭窄 ACI 患者作为本次研究对象。纳入标准:(1)发病 3 日后就诊,符合全国第四届脑血管病学术会议制定的脑梗死诊断标准者^[12];(2)均通过数字减影血管造影、非创伤性血管成像技术及磁共振血管造影检查确诊为脑动脉粥样硬化性 MCA 狭窄;(3)积极配合者;(4)患者或家属均知情同意并签署知情同意书。排除标准:(1)具有严重脑出血病史者;(2)颞窗穿透不良者;(3)由其他原因造成的颅内动脉炎,从而引发颅内动脉狭窄者;(4)MCA 发育异常者;(5)心源性栓塞者;(6)具有颈动脉中重度狭窄者。82 例患者依据随机数字表法分为对照组(41 例)和观察组(41 例),两组一般资料对比,差异无统计学意义($P>0.05$),具有可比性。详见表 1。本研究经华中科技大学同济医学院附属荆州医院伦理委员会审批通过。

表 1 两组患者一般资料对比
Table 1 Comparison of general data between the two groups

Groups	Male/Female	Average age (years old)	Complication			Bad habits			
			Hypertension	Diabetes	Coronary heart disease	Hyperlipidemia	Hyperhomocysteinemia	Smoking	Alcoholism
Control group(n=41)	26/15	61.36± 7.79	20	21	4	13	7	15	17
Observation group(n=41)	28/13	61.74± 8.12	17	23	2	15	4	13	20
t/x ²	0.217	0.216	0.443	0.196	0.719	0.217	0.945	0.217	0.443
P	0.641	0.829	0.506	0.658	0.396	0.641	0.331	0.641	0.506

1.2 方法

两组患者入院后均接受常规药物治疗,主要包括降脂、清除自由基、抗血小板聚集以及脑保护等。观察组在入院后第 2 d 接受低频超声治疗,使用超声溶栓治疗仪(韩国 HANIL-TM 公司生产,型号:H-5212)在血管 MCA 狭窄的一侧颞窗进行治疗。在治疗前使用耦合剂以确保超声探头与皮肤接触有效接触,每次治疗时超声探头所放置位置一致。频率设置为 800 kHz,功率为 0.75 W/cm²,治疗时间为 30 min/d;治疗疗程均为 14 d。

1.3 观察指标

(1)于治疗前及治疗 14d 后对比美国国立卫生研究院卒中量表(National Institutes of Healthy Stroke Scale, NIHSS)评分情况,评分越低则神经功能恢复越好^[13];(2)在治疗前及治疗 14d 后行 TCD 检查,观察且记录 ACI 患者 MCA 狭窄段峰值血流

速度(Vs);并且在治疗前、治疗 7 d 后、14 d 后行起源于 MCA 狭窄段的微栓子信号(micro embolic signal, MES)监测。(3)MES 阳性判断标准^[14]:①持续时间低于 300ms;②同背景信号对比,信号强度不低于 3 dB;③血流频谱中出现单项;④低沉劈叭声的音频信号;⑤在心动周期内随意出现;⑥在两个监测深度存在时间延迟。(4)在治疗前、治疗 7 d 后、14 d 后采集两组患者清晨空腹经肘静脉血 10 mL,低温离心 15min,离心速度为 3000 r/min,吸取上清液即得血清,采用免疫比浊法检测血清高敏 C-反应蛋白(high sensitive C-reactive protein, hs-CRP)水平,试剂盒生产厂家为德国罗氏诊断有限公司。

1.4 统计学分析

采用 SPSS 22.0 软件进行数据处理,两组年龄、治疗前后 NIHSS 评分、MCA 狭窄段 Vs 指标及 hs-CRP 水平均以 ($\bar{x} \pm s$)

表示,行 t 检验;两组除年龄外其他一般资料、治疗前后 MES 阳性率用[n(%)]表示,采用卡方检验, $P < 0.05$ 为差异具有统计学意义。

2 结果

2.1 比较 NIHSS 评分、MCA 狭窄段 Vs 指标

表 2 两组治疗前后 NIHSS 评分、MCA 狭窄段 Vs 指标对比($\bar{x} \pm s$)

Table 2 Comparison of NIHSS scores and MCA stenosis Vs before and after treatment between the two groups($\bar{x} \pm s$)

Groups	NIHSS(scores)		Vs(cm/s)	
	Before treatment	14 d after treatment	Before treatment	14 d after treatment
Control group(n=41)	5.89± 1.34	4.75± 1.74*	190.19± 24.57	189.23± 22.65
Observation group(n=41)	5.85± 1.82	3.01± 1.23*	189.97± 28.17	155.62± 33.76*
t	0.113	5.072	0.038	5.294
P	0.910	0.000	0.970	0.000

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

2.2 两组治疗前后 MES 阳性率对比

治疗前两组 MES 阳性率比较无统计学差异 ($P > 0.05$),治

疗前两组的 NIHSS 评分及 Vs 水平比较无统计学差异 ($P > 0.05$);治疗 14d 后两组的 NIHSS 评分下降,且观察组较对照组 NIHSS 评分更低($P < 0.05$);治疗 14d 后观察组 MCA 狭窄段 Vs 低于治疗前($P < 0.05$),而对照组与治疗前比较无统计学差异($P > 0.05$)。详见表 2。

疗 7 d 后、14 d 后观察组 MES 阳性率均低于对照组 ($P < 0.05$)。

详见表 3。

表 3 两组治疗前后 MES 阳性率对比[n(%)]

Table 3 Comparison of MES positive rate before and after treatment between the two groups[n(%)]

Groups	Before treatment	7 d after treatment	14 d after treatment
Control group(n=41)	27(65.85)	12(29.27)	7(17.07)
Observation group(n=41)	30(73.17)	1(2.44)	0(0.00)
χ^2	0.518	11.061	7.653
P	0.472	0.000	0.006

2.3 两组治疗前后炎症指标 hs-CRP 水平对比

两组治疗前 hs-CRP 水平比较,差异无统计学意义($P > 0.05$);两组治疗 7 d 后、14 d 后 hs-CRP 水平低于治疗前,且治疗

14 d 后低于治疗 7 d 后($P < 0.05$);而观察组治疗 7 d 后、14 d 后 hs-CRP 水平低于对照组($P < 0.05$)。详见表 4。

表 4 两组治疗前后炎症指标 hs-CRP 水平对比($\bar{x} \pm s$, cm/s)

Table 4 Comparison of inflammatory markers hs-CRP level before and after treatment between the two groups($\bar{x} \pm s$, cm/s)

Groups	Before treatment	7 d after treatment	14 d after treatment
Control group(n=41)	3.27± 1.65	2.54± 1.08*	1.53± 0.47**
Observation group(n=41)	3.32± 1.75	1.44± 0.69*	0.51± 0.37**
t	0.133	5.496	10.919
P	0.894	0.000	0.000

Note: Compared with before treatment, * $P < 0.05$; Compared with 7 d after treatment, ** $P < 0.05$.

3 讨论

导致脑梗死形成的主要原因与动脉粥样硬化性血管狭窄具有显著相关性^[15]。有调查研究表明^[16],欧美脑梗死患者主要为颅外血管病变,而我国主要为颅内血管病变,其原因与种族不同相关。MCA 具有三个近直角转角,发生湍流的概率较高,从而引发血流剪切力产生的血管保护性一氧化氮显著降低,最终形成 MCA 狭窄,病情严重者会出现 MCA 闭塞^[17]。目前临床上治疗症状性 MCA 狭窄的治疗效果仍然不佳,患者具有较高死

亡率,而存活的患者出现偏瘫等后遗症的概率较高^[18]。以目前医疗技术主要可采用药物治疗、支架植入治疗等方式,但常规药物治疗对于逆转 MCA 狭窄的作用甚微,并且患者经治疗后无法避免病情复发^[19]。Tsuda K 等人的相关研究表明^[20],脑卒中复发的原因与 MCA 狭窄具有显著相关性。支架置入治疗虽具有一定疗效,但虹吸段的迂曲度较大,严重影响支架的输送;不仅如此,MCA、外膜肌层薄弱,在给予支架植入治疗后容易损坏血管,导致穿支血管闭塞等现象,在治疗后发生过度灌注、再狭窄等概率较高,并且支架置入治疗的手术费用昂贵,所以此

类治疗方式具有一定局限性^[21,22]。

目前随着临床医疗技术的不断发展,低频超声治疗逐渐被运用于动脉粥样硬化性颅内、外动脉狭窄的治疗中。本研究结果显示,观察组治疗后 NIHSS 评分低于对照组,说明低频超声治疗可明显改善患者神经功能。原因主要在于此治疗方法能够通过生物-物理作用有效提高动脉狭窄部位血栓的溶解效果,并且帮助建立侧支循环,从而起到促进脑血液循环、改善脑细胞代谢水平,促进患者脑功能恢复^[23]。MCA 狭窄段治疗前 Vs 升高,存在湍流或涡流,部分频谱紊乱,声频粗糙、伴特殊乐音样或低沉浑浊杂音,且频窗消失,包络线不光滑、低频超声治疗几个疗程后 Vs 减缓,且逐渐平稳,频谱形态较前明显改观。本研究中,观察组治疗 14 d 后 MCA 狭窄段 Vs 低于对照组,说明低频超声治疗能够有效降低血流流速。原因主要为患者经低频超声治疗后可显著提高动脉粥样硬化 MCA 狭窄段的管腔横截面积,并且对于消除动脉粥样斑块及血栓的效果显著。稳定动脉粥样硬化性 MCA 狭窄患者几乎不存在 MES 阳性因子,而不稳定者则存在,且出现脑缺血的概率较高^[24]。本研究中,观察组治疗 7 d 后、14 d 后 MES 阳性率低于对照组,说明低频超声治疗对降低 MES 效果更为显著。原因与此治疗方式能有效提高动脉粥样硬化斑块的稳定性相关。这提示在 MCA 型脑梗死患者中血小板数量及血管狭窄程度与 MES 密切相关。有研究还表明,MES 阳性患者较 MES 阴性患者卒中复发率明显增高,MES 是 MCA 型脑梗死患者卒中复发的独立危险因素,本次研究样本数量有限,验证该结论需进一步扩大病患^[25]。

动脉粥样硬化的产生与机体存在慢性炎症具有显著相关性^[26]。hs-CRP 是机体受到外界细菌或病毒入侵后造成组织损伤等炎症刺激后,肝细胞合成急性相蛋白,是一种慢性炎症标志物^[27,28]。有研究表明^[29,30],hs-CRP 水平与脑卒中事件具有显著相关性,hs-CRP 越高,则脑梗死患者病情越严重、脑梗死范围更大,如果 hs-CRP 水平显著提高则可能脑梗死患者死亡率及不良预后的概率更高。在本研究中,两组治疗后 hs-CRP 均低于治疗前,而观察组治疗 7 d 后、14 d 后 hs-CRP 低于对照组($P < 0.05$)。进一步表明低频超声治疗可显著缓解局部脑组织受到的损伤,提高药物治疗对动脉粥样硬化斑块的稳定效果。其原因可能为低频超声可穿透颅骨进入患者脑组织,由机械及空化作用从而缓解动脉粥样硬化斑块及血栓。

综上所述,低频超声治疗动脉粥样硬化性 MCA 狭窄 ACI 患者可明显提高疗效,促进神经功能恢复,降低患者 MCA 狭窄段 Vs 和 MES 阳性率,减轻炎症反应。

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