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尼莫地平对动脉瘤性蛛网膜下腔出血脑血管痉挛的临床疗效研究

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摘要 目的: 观察尼莫地平对动脉瘤性蛛网膜下腔出血脑血管痉挛的临床疗效及安全性,为临床治疗提供依据。**方法:** 对我院2010年2月~2013年2月期间收治的92例动脉瘤性蛛网膜下腔出血患者进行随机分为观察组和对照组,每组46例。两组患者入院后均进行常规治疗,绝对卧床休息、镇静、给予氨甲环酸止血、脱水降颅压、防治感染及对症治疗。观察组在上述治疗基础上给予尼莫地平(德国拜耳公司)持续微泵静脉注射20 mg·d⁻¹,连用14 d,后改为口服尼莫地平片40 mg, qid,至第21天,根据监测血压调整剂量。观察两组患者1个月内脑血管发病情况、CT评价情况,并进行对比分析。**结果:** 两组患者治疗后,观察组有效率91.3%;对照组有效率73.91%。两组比较差异明显,观察组疗效明显优于对照组,具有统计学意义($P<0.05$)。两组患者在治疗期间,观察组发生脑血管痉挛4例,占8.7%;对照组发生脑血管痉挛26例,占56.52%,两组比较差异明显,具有统计学意义($P<0.05$)。**结论:** 尼莫地平能够显著降低动脉瘤性蛛网膜下腔出血脑血管痉挛的发生率,对脑血管再出血具有积极防治作用,建议推广应用。

关键词: 尼莫地平;蛛网膜下腔出血;脑血管痉挛;临床疗效

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Study on Clinical Effect of Nimodipine on Cerebral Vasospasm after Aneurysmal Subarachnoid Hemorrhage

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ABSTRACT Objective: To observe the clinical efficacy and safety of nimodipine on cerebral vasospasm after aneurysmal subarachnoid hemorrhage, and to provide basis for clinical therapy. **Methods:** 92 cases of patients with aneurysmal subarachnoid hemorrhage in our hospital from February 2010 to February 2013 were randomly divided into observation group and control group, each with 46 cases. Two groups of patients received conventional treatment, absolute bed rest, sedation, given tranexamic acid hemostasis, lowering the intracranial pressure, prevention of infection and symptomatic treatment. In addition to the above treatment, the observation group received 20mg/d of nimodipine (Bayer company) continued micro-pump infusion for 14 days, and then oral nimodipine tablets 40 mg, qid, until the 21st day, and the dose was adjusted according to the blood pressure monitored. Mobility of cerebral vascular and evaluation of CT were observed and contrastively analyzed. **Results:** After treatment, effective rates of the observation group and the control groups were 91.3% and 73.91% respectively, with significant difference. Clinical efficacy of the observation group was significantly superior that that of the control group, with statistical significance ($P<0.05$). During the treatment, there were 4 cases (8.7%) of cerebral angiospasm in the observation group, and 26 cases (56.52%) in the control group, with statistically significant difference ($P<0.05$). **Conclusion:** Nimodipine can significantly reduce the occurrence rate of cerebral vasospasm after aneurysmal subarachnoid hemorrhage, and has a positive role in the prevention of cerebral vascular hemorrhage, thus is worthy of popularization and application.

Key words: Nimodipine; Subarachnoid hemorrhage; Cerebral vasospasm; Clinical effect

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前言

蛛网膜下腔出血(subarachnoid hemorrhage, SAH)是指脑底部或脑表面的病变血管破裂,血液直接流入蛛网膜下腔引起的一种临床综合征,是临床常见的神经科疾病,临床发病率较

高,占急性脑卒中的10%,是一种非常严重的常见疾病。世界卫生组织调查显示中国发病率约为2.0/10万人年,严重威胁患者的健康及生命安全^[1]。临床表现为突然发生的剧烈头痛、恶心、呕吐和脑膜刺激征,伴或不伴局灶体征。剧烈活动中或活动后出现爆裂性局限性或全头部剧痛,难以忍受,呈持续性或持续进行性加重,有时上颈段也可出现疼痛。其中较为严重的并发症是脑血管痉挛,致残、致死率较高。常规药物经扩容、升压、血管扩张剂应用外,往往还会引发脑梗死导致患者死亡率上升^[2]。近年来,相关资料报道利用尼莫地平治疗蛛网膜下腔出血,能

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够显著降低脑血管痉挛发生率,疗效显著。我们在工作期间对2010年2月~2013年2月期间收治的92例动脉瘤性蛛网膜下腔出血患者进行分组治疗,结果报道如下。

1 一般资料与方法

1.1 临床资料

本组患者共92例,均为我院2010年2月~2013年2月期间收治的动脉瘤性蛛网膜下腔出血患者。其中男56例,女36例。年龄36~78岁,平均 (48.6 ± 3.6) 岁。患者均因突发或持续剧烈头痛伴不同程度意识障碍入院,经头颅CT或腰穿确诊为蛛网膜下腔出血。全部患者临床诊断均符合中华医学会第四届脑血管病会议确定的蛛网膜下腔出血诊断标准,按 Hunt-Hess 分级^[3]。将所有患者随机均分为两组,观察组和对照组各46例。两组患者年龄、性别、病情、发病时间等比较差异无显著,具有可比性。

1.2 方法

两组患者入院后均进行常规治疗,绝对卧床休息、镇静、给予氨甲环酸止血、脱水降颅压、防治感染及对症治疗,对于急诊证实颅内动脉瘤行脑血管介入治疗^[4]。观察组在上述治疗基础上给予尼莫地平(德国拜耳公司)持续微泵静脉注射 $20 \text{ mg} \cdot \text{d}^{-1}$,连用14 d,后改为口服尼莫地平片 40 mg, qid ,至第21天,根据监测血压调整剂量。两组经观察治疗1个月记录脑血管痉挛发

生率,病死率等情况。

1.3 脑血管痉挛诊断标准

经治疗后临床症状波动或加重;患者意识由清醒转为昏迷,或反复昏迷、神经系统局灶体征;出现颅内高压症状;排除血肿、脑积水、水电解质紊乱等因素^[5]。具备前述症状4项之一与最后一项即可诊断为脑血管痉挛。或经颅多普勒超声检测大脑中动脉和颅外颈内动脉血流速度比值 >3 。

1.4 疗效评定

经治疗1个月后观察临床疗效及CT结果情况。痊愈:临床症状、体征消失,且无后遗症;无效:死亡或临床症状、体征无改变。

1.5 统计学方法

本组数据均采用SPSS13.0进行统计学分析,计数资料采用 χ^2 检验, $P<0.05$ 表示差异有统计学意义。

2 结果

2.1 两组患者治疗后有效率比较

两组患者治疗后,观察组痊愈26例,好转16例,无效4例,有效率91.3%;对照组痊愈21例,好转13例,无效12例,有效率73.91%。两组比较差异明显,观察组疗效明显优于对照组,具有统计学意义($P<0.05$),见表1。

表1 两组患者治疗后有效率比较
Table 1 Comparison of efficiency between two groups after treatment

组别 Group	例数 The number of cases	无效 Invalid	好转 To become better	痊愈 Recovery	有效率 Efficiency
观察组 The observation group	46	4*	16*	26*	91.3*
对照组 Control group	46	12	13	21	73.91

注:与对照组比较,* $P<0.05$ 。

Note: Compared with the control group, * $P<0.05$.

2.2 两组患者治疗期间脑血管痉挛发生情况

两组患者在治疗期间,观察组发生脑血管痉挛4例,占

8.7%;对照组发生脑血管痉挛26例,占56.52%,两组比较差异明显,具有统计学意义($P<0.05$),见表2。

表2 两组患者治疗期间脑血管痉挛发生情况
Table 2 Incidence of cerebral vascular spasm in the two groups

组别 Group	脑血管痉挛 Cerebral vasospasm	无脑血管痉挛 No cerebral vasospasm	合计 Total	脑血管痉挛发生率/% The incidence of cerebrovascular spasm /%
观察组 The observation group	4*	42*	46	8.7*
对照组 Control group	26	20	46	56.52
合计	30	62	92	32.6

注:与对照组比较,* $P<0.05$ 。

Note: Compared with the control group, * $P<0.05$.

2.3 不良反应情况比较

两组患者在治疗过程中,观察组出现低血压4例,占8.7%,血压最低值为 $80/50\sim 60 \text{ mmHg}$,经调整尼莫地平泵速后好转。

3 讨论

近年来随着我国社会人群结构逐步老龄化,蛛网膜下腔出血的发病率逐年增加,是造成我国中老年致残、致死的重要高

发疾病^[6-10]。而蛛网膜下腔出血 80%是由于患者颅内动脉瘤破裂所致,而引起蛛网膜下腔出血出血较为严重的并发症为脑血管痉挛。截至今日,对于蛛网膜下腔出血后脑血管痉挛的发生机制尚不十分清楚。相关资料^[11-14]报道与物理刺激和化学刺激有关。物理刺激来源于蛛网膜下腔出血后血液对血管壁的机械性刺激有关,化学刺激来源于内皮素、一氧化氮、氧合血红蛋白及各种氧自由基作用。

尼莫地平是近年来常用的治疗脑血管痉挛的有效药物,其脂溶性高、易通过血-脑屏障,拮抗 Ca^{2+} 阻断电位敏感的 L 通道,抑制血管平滑肌外过量的 Ca^{2+} 进入细胞内,从而调节血管张力^[14-17]。通过稳定细胞功能消除各种血管活性物质引起的脑血管收缩。降低脑血管痉挛发生率。本组研究结果显示,观察组痊愈 26 例,好转 16 例,无效 4 例,有效率 91.3%;对照组痊愈 21 例,好转 13 例,无效 12 例,有效率 73.91%。两组比较差异明显,观察组疗效明显优于对照组,具有统计学意义($P < 0.05$)。两组患者在治疗期间,观察组发生脑血管痉挛 4 例,占 8.7%;对照组发生脑血管痉挛 26 例,占 56.52%,两组比较差异明显,具有统计学意义($P < 0.05$)。结果表明,临床作用由于常规治疗方法。患者采用尼莫地平进行治疗,其脂溶性能够迅速通过患者的血脑屏障,继而将细胞膜 L 型 Ca^{2+} 通道阻断,当患者细胞受损时,开放 Ca^{2+} 通道会导致患者细胞内钙含量超载,而尼莫地平能够将上述作用有效减少^[18]。在不良反应观察中,仅有少数存在血压偏低情况,症状轻微,经调节药物后症状缓解。

综上所述,尼莫地平能够显著降低动脉瘤性蛛网膜下腔出血脑血管痉挛的发生率,在临床治疗过程中应注意血压偏低情况,提高对脑血管再出血的积极防治作用,建议推广应用。

参考文献(References)

- [1] Fernandez-Ortiz A, Pan M, Alfonso F, et al. Comment on the ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. A report of the Task Force of the Clinical Practice Guidelines Committee of the Spanish Society of Cardiology[J]. Rev Esp Cardiol, 2012, 65(2):125
- [2] Iversen AZ, Galatius S, Abildgaard U, et al. Intracoronary compared to intravenous abciximab in patients with ST segment elevation myocardial infarction treated with primary percutaneous coronary intervention reduces mortality, target vessel revascularization and reinfarction after 1 year [J]. Cardiology, 2011, 120(1):43
- [3] Wang Lei, Zhang Min-zhou. Progress of traditional Chinese medicine treatment of coronary artery disease after percutaneous coronary intervention[J]. Chinese Journal of Integrated Traditional and Western Medicine, 2010, 20(4):444-446
- [4] Altay H, Pehlivanoglu S. Management of acute coronary syndromes in patients presenting without persistent ST segment elevation: What has changed in the new European Society of Cardiology guideline[J]. Turk Kardiyol Dern Ars, 2012, 40(1):1-5
- [5] Merchant FM, Weiner RB, Rao SR, et al. In-hospital outcomes of emergent and elective percutaneous coronary intervention in octogenarians [J]. Coron Artery Dis, 2009, 20(2): 118-123
- [6] Levine GN, Bates ER, Blankenship JC, et al. 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention. A report of the American college of cardiology foundation/american heart association task force on practice guidelines and the society for cardiovascular angiography and interventions[J]. J Am Coll Cardiol, 2011, 58(24): e44-e122
- [7] Chandra YO, Michael KPO, Stacy CB, et al. The mechanisms linking health literacy to behavior and health status [J]. Am J Health Behav, 2011, 35(1):118-128
- [8] Wright RS, Anderson JL, Adams CD, et al. 2011 ACCF/AHA focused update of the guidelines for the management of patients with unstable angina/non-ST-elevation myocardial infarction (Updating the 2007 guideline) [J]. Circulation, 2011, 123(22): 2022-2060
- [9] Gryglewska B, Sulicka J, Fornal M, et al. Women with prehypertension in primary care-Risk profile on the basis of selected cardiovascular risk factors[J]. Blood Press, 2009, (3): 99-104
- [10] Thiele H, Wöhrle J, Hambrecht R, et al. Intracoronary versus intravenous bolus abciximab during primary percutaneous coronary intervention in patients with acute ST-elevation myocardial infarction: a randomised trial [J]. Lancet, 2012, 379(9819):923
- [11] Chandra YO, Kerri C, Kenneth AW, et al. Self-efficacy links health-literacy and numeracy to glycemic control [J]. J Health Commun, 2010, 15(2):146-158
- [12] Hamm CW, Bassand JP, Agewall S, et al. ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: The task force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC)[J]. Eur Heart J, 2011, 32(23):2999-3054
- [13] Bennett I, Chen J, Orzoi J, et al. The contribution of health literacy to disparities in self-rated health status and preventive health behaviors in older adults[J]. Ann Fam Med, 2009, 7(3):204-211
- [14] Li CY, Lee O, Shin GS, et al. Health Literacy and health status of Korean-Chinese elderly people living in Yanbian China [J]. J Korean Acad Nurs, 2009, 39(3):386-392
- [15] Nitin-Mahajan, Namita Malik, Ajay Bahl, et al. Correlation among soluble markers and severity of disease in nondiabetic subjects with premature coronary artery disease [J]. Mol Cell Biochem, 2009, 330: 201-209
- [16] Su Hyun Kim, Xu Yu. The mediating effect of self-efficacy on the relationship between health literacy and health status in Korean older adults: a short report [J]. Aging and Mental Health, 2010, 14(7):870-873
- [17] Ishikawa H, Yano E. The relationship of patient participation and diabetes outcomes for patients with high vs. low health literacy[J]. Patient Educ Couns, 2011, 29(1):1-5
- [18] Muller C. New ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation[J]. Swiss Med Wkly, 2012, 142:1-7