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NT-proBNP 对胺碘酮用于急诊阵发房颤复律疗效的预测价值 *

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摘要 目的:研究 N 末端 B 型利钠肽原(N-terminal pro B-type natriuretic peptide, NT-proBNP)对胺碘酮用于急诊阵发性非瓣膜病心房颤动疗效的预测价值。**方法:**收集 2016-2017 年于宣武医院急诊科诊断为阵发性非瓣膜病房颤(发病 48h 内)的患者共 110 例,记录所有患者入院时一般资料、既往病史、临床症状体征、实验室数据及测定肌钙蛋白 I(Troponin-I, TnI)水平和基线 NT-proBNP 水平,均给予胺碘酮静脉转复治疗。按照胺碘酮转复情况分为成功组和失败组。**结果:**静脉应用胺碘酮成功转复 91 例(82.7%),平均转复时间 8.15 小时 (SD10.16),转复失败者 24 h 内心室率均控制在 100 次/min 以下,均无严重不良反应。成功组血浆基线 NT-proBNP 水平显著低于失败组($P<0.05$);而两组患者性别、年龄、入室血压、心室率、胸痛、房颤持续时间、入室心电图 ST 段压低、TnI 水平、冠心病史、高血压、糖尿病、房颤史比较差异均无统计学意义($P>0.05$)。二元 logistic 回归分析显示 NT-proBNP 的自然对数,即 $\ln(\text{NT-proBNP})$ 为急诊房颤胺碘酮复律疗效的主要影响因素。**结论:**对于非瓣膜病房颤急性发作 <48 h 的患者,胺碘酮转复是安全有效的;基线 NT-proBNP 水平是药物复律成功的重要预测因子,如基线 NT-proBNP 水平较高,则复律成功率低,为了避免药物的不良反应,可考虑控制心室率,而不是复律治疗。

关键词:房颤;复律;胺碘酮;NT-proBNP

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Prognostic Prediction Value of NT-proBNP for the Cardioversion of Recent-onset Atrial Fibrillation by Amiodarone in the Emergency Department*

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ABSTRACT Objective: To analyze the role of N-terminal pro B-type natriuretic peptide (NT-proBNP) in predicting the success of cardioversion of recent-onset atrial fibrillation by Amiodarone in the emergency department. **Methods:** A total of 110 patients with non-valvular atrial fibrillation (within 48 hours) were enrolled in the emergency department of Xuanwu Hospital from 2016 to 2017. A general information, past medical history, clinical symptoms and signs, and laboratory data of Troponin-I (TnI) and baseline NT-proBNP were all recorded. All the patients were treated with intravenous amiodarone. 110 patients were divided into two groups according to cardioversion results: successful group and unsuccessful group. **Results:** Successful conversion rates were 91 (81.67%). The average time was 8.15 hours (SD10.16h), and the ventricular rates were controlled below 100 /min within 24 hours in the unsuccessful group. No serious adverse events were found. Baseline NT-proBNP levels were significantly lower in the successful group than in the unsuccessful group ($P<0.05$); There were no significant differences between the two groups in gender, age, systolic pressure (SYS), ventricular rate, chest pain, duration of atrial fibrillation(AF), ST-segment depression on the initial ECG, TnI levels, the history of coronary artery disease (CAD), hypertension(HTN), diabetes(DM), chronic lung disease and atrial fibrillation ($P>0.05$). According to binary logistic regression analysis, in (Nt-proBNP) was the main predictor for the success of cardioversion using amiodarone. **Conclusions:** Chemical cardioversion using amiodarone is safe and effective in patients with acute non-valvular atrial fibrillation (within 48 hours); baseline NT-proBNP levels are an important predictor of cardioversion. The higher baseline NT-proBNP levels is, the lower conversion rate will be. In order to avoid drug adverse events, a rate control strategy will be better than rhythm control in recent-onset atrial fibrillation with higher NT-proBNP levels.

Key words: Atrial fibrillation; Cardioversion; Amiodarone; nt-proBNP

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前言

房颤是临床上常见的心律失常;尤其是 60 岁以上,具有冠心病、高血压病、糖尿病、心肌病等器质性心脏病基础的患者发病率更高。其中,40.2%表现为阵发性房颤。一旦出现往往伴有心悸、心绞痛样症状及心功能不全等,应尽快予以转复或控制心室率。急诊室有相当比例有症状阵发性心房颤动患者^[1,2],因为电转复的全身麻醉及不耐受性,目前国内大部分患者接收药物转复或控制心室率。近年来,有关胺碘酮转复窦性心律的临床试验报道较多,但样本多偏少,且研究设计上存在一定差别,转复效果不尽相同,静脉应用胺碘酮对 48h 内新发生的阵发性房颤有效率为 25%-83%^[3,4]。

B 型利钠肽(B-type natriuretic peptide, BNP)和 N 末端 B 型利钠肽原(N-terminal pro B-type natriuretic peptide, NT-proBNP)均是目前管理心功能变化的最佳指标^[5],与高危患者的死亡率增加和再次住院治疗的风险均呈高度相关。近些年的研究表明 BNP 和 NT-proBNP 与房颤的发生发展、分型及预后密切相关^[6-9],不仅能评估房颤患者的心功能状态,还能预测房颤电复律的成功性及复发率^[10-16]。本研究旨在探讨阵发性非瓣膜病心房颤动患者胺碘酮转复疗效及探讨复律成功的预测因素,以期为其临床治疗提供更多的参考依据。

1 研究方法

1.1 研究对象

选取 2016-2017 年于宣武医院急诊诊断为阵发性房颤(发病 48 h 内)的患者 110 例为研究对象,其中男性 48 例,女性 62 例。排除标准:(1)永久性房颤、症状持续 $\geq$ 48h;(2)瓣膜性心脏病;(3)有甲状腺功能亢进病史;(4)血流动力学不稳定;(5)症状性心力衰竭;(6)严重肝、肾功能损伤;(7)急性 ST 段抬高型心肌梗死。

1.2 方法

1.2.1 临床资料 (1)一般资料:包括性别、年龄;(2)既往病史:包括心房颤动、糖尿病、高血压、冠心病、慢性肺部疾病史、射频消融术;(3)临床症状及体征:包括心悸、胸痛、胸闷、乏力及头晕;房颤持续时间;入室血压及心室率;(4)实验室检查:血常规、血生化、甲状腺功能及 12 导联心电图。

1.2.2 TnI 水平检测 急诊入院时采集患者静脉血 5 mL,静置 10 min 后,以 10000 r/min 离心 10 min(离心半径 14 cm),分离血清,采用美国罗氏公司 2010 型电化学发光仪及 TnI 试剂盒检测外周血 TnI 水平,正常值 $<0.023 \mu\text{g/L}$ 。

1.2.3 NT-proBNP 测定 急诊入院时采集患者静脉血 3ml 用乙二胺四乙酸(EDTA)抗凝,采用罗氏 Cardiac reader 快速心动能量检测仪器检测血浆 NT-proBNP 水平。

1.2.4 治疗 所有入组患者予胺碘酮药物转复,一般胺碘酮 150 mg 负荷(静脉注射时间超过 10 min),随后予 1 mg/min 静脉泵入 6 h,如未能转复,调整泵速为 0.5 mg/min,静脉用药时间持续 48 h。在治疗期间持续监测血流动力学和心电图。转复成功者给予胺碘酮口服维持窦律,转复失败者改心室率控制。入院常规予低分子肝素(克赛)抗凝。

1.3 统计学方法

采用 SPSS17.0 软件进行统计学处理,正态分布的计量资料以($\bar{x} \pm s$)表示,组间比较应用独立样本 t 检验;非正态分布的计量资料以 M(QR)表示,组间比较应用 Mann-WhitneyU 检验;计数资料以百分数表示,组间比较应用 χ^2 检验。以 $P < 0.05$ 为差异有统计学意义。

2 结果

本研究患者 110 例,平均年龄 69.9 岁(SD13.8),其中男性 48 例 (43.6%), 女性 62 例 (56.4%);成功转复 91 例 (转复率 82.7%),平均转复时间 8.15 小时(SD10.16),转复失败者 24h 之内心室率均控制在 100 次/min 之内。2 例患者出现一过性低血压,停药或减量后自行缓解;10 例转复窦性心律后出现窦性心动过缓(50-60 次/分)伴或不伴 I 度房室传导阻滞,停药后均自行恢复正常;1 例出现静脉炎,均未发现全身过敏反应、严重心律失常、顽固性低血压、心衰等。

2.1 转复成功组与失败组患者临床资料的比较

依据转复效果分为转复成功组和失败组,两组性别、年龄、入室血压、心室率、胸痛、房颤持续时间、心电图 ST 段压低、TnI 水平、冠心病史、高血压、糖尿病、房颤史比较差异均无统计学意义($P > 0.05$)。两组心悸、NT-proBNP、In(Nt-proBNP)差异具有统计学意义($P < 0.05$),见表 1。

2.2 急诊房颤胺碘酮复律疗效影响因素的二元 logistic 回归分析

初始建模纳入心悸、收缩压、心室率、房颤持续时间及 In(Nt-proBNP),剔除无关因子后,最终结论显示 In(Nt-proBNP)为急诊房颤胺碘酮转复疗效的主要影响因素,即 Nt-proBNP 数值越高,胺碘酮转复成功率越低。

3 讨论

Framingham 心脏研究显示房颤患者发生脑卒中的概率是无房颤患者的 5 倍,死亡风险较无房颤患者高 1.5~1.9 倍。恢复窦性心律可缓解症状、减少血栓栓塞事件、消除或减轻心房电生理重构、并降低死亡率。因此,主张对所有无禁忌证的房颤患者均应给予一次复律治疗^[17,18]。急诊 48 h 内的阵发房颤产生血栓栓塞的危险性低,不需要前期的抗凝治疗即可以直接复律^[19],目前复律手段主要包括电复律和药物复律。电复律虽然快速且成功率高达 94%,但是其有不可忽略的缺点,患者痛苦较大、耐受性低,治疗前需要全身麻醉,反复电复律有皮肤烧伤、缺氧等并发症风险,故除非出现严重的血流动力学障碍,心绞痛心功能恶化或药物复律效果欠佳等需电转复情况外,临床以药物复律为首选。然而,药物复律的成功率相对较低,且可能会诱发心律失常如心动过缓、各种传导阻滞、室性心律失常及抑制心肌收缩^[20,21]。2014 AHA / ACC / HRS 心房颤动管理指南推荐用于复律的药物有氟卡尼、依布利特、普罗帕酮和胺碘酮^[22]。国内常用药物主要为胺碘酮、普罗帕酮。普罗帕酮虽然起效快,作用持久,但因其具有增加室性心律失常的风险及负性肌力作用,故当合并器质性心脏病和心力衰竭时,普罗帕酮则为禁忌,一般使用胺碘酮^[23]。

胺碘酮为多通道的阻滞剂,通过阻断钾、钠、钙等多部位通道,延长各部心肌动作电位时程和不应期,减慢传导速度,有助

于消除折返激动;抑制房室旁路前向传导作用及窦房结、心房和房室结功能,且对冠状动脉及周围血管有直接扩张作用,改善心肌供血,减少心肌氧耗。另外,胺碘酮由于负性肌力作用较弱,能安全地用于各种器质性心脏病及心功能不全者。但胺碘酮转复过程中可出现低血压、心动过缓、静脉炎,长期使用可导致甲状腺功能异常、肺纤维化、肝衰竭等心外副作用^[24]。本组患

者胺碘酮转复有效率达到 82.7%,平均转复时间 8.15 小时,未转复者 24 小时内心室率有明显下降,症状缓解,小部分患者出现一过性低血压、心动过缓、I 度房室传导阻滞及静脉炎等,停药后均自行恢复;未发现严重心律失常、顽固性低血压、心衰等,长期肺外不良反应有待长期追踪观察。

表 1 转复成功组与失败组患者临床资料比较

Table 1 Comparison of the clinical characteristics between successful and unsuccessful group

Variable	Categories	Successful	Unsuccessful	P-Value
Gender	Male	40(83.3%)	8(16.7%)	0.882
	Female	51(82.3%)	11(17.7%)	
Palpitation	Yes	83(85.6%)	14(14.4%)	0.031
	No	8(61.5%)	5(38.5%)	
Chest pain	Yes	15(88.2%)	2(11.8%)	0.514
	No	76(81.7%)	17(18.3%)	
Known AF	Yes	51(79.7%)	13(20.3%)	0.320
	No	40(87.0%)	6(13.0%)	
DM	Yes	22(88.0%)	3(12.0%)	0.428
	No	69(81.2%)	16(18.8%)	
HTN	Yes	56(82.4%)	12(17.6%)	0.895
	No	35(83.3%)	7(16.7%)	
Known CAD	Yes	38(84.4%)	7(15.6%)	0.692
	No	53(81.5%)	12(18.5%)	
ST depression	Yes	22(84.6%)	4(15.4%)	0.771
	No	69(82.1%)	15(17.9%)	
TnI	Positive	11(84.6%)	2(15.4%)	0.848
	Negative	80(82.5%)	17(17.5%)	
Age		79.8(12.9)	70.6(17.6)	0.855
SYS		127(20.5)	138(18.9)	0.052
Heart rate		126.5(25.9)	120.4(20.8)	0.276
Duration of AF		3h*	6h*	0.099
Nt-proBNP		644*	2730*	0.006
In(Nt-proBNP)		2.77(0.52)	3.24(0.85)	0.01

Note: The numbers marked * is the median, using Mann-Whitney U test; In (Nt-proBNP) is the natural logarithm of Nt-proBNP.

表 2 二元 logistic 回归模型分析胺碘酮复律疗效影响因素

Table 2 Binary logistic regression model for the successful of amiodarone for cardioversion

	B	S.E.	Wald	Exp(B)	(95%CI)	P Value
In(Nt-proBNP)	-1.419	0.577	6.036	0.242	(0.078-0.751)	0.014

B 型利钠肽主要在心室合成,随心室容量扩增及压力负荷反应而分泌并释放入血^[25],B 型利钠肽原(proBNP)在内切酶的作用下裂解为有利钠、利尿、扩血管等生物活性的 BNP 和无生物活性的 N 末端 B 型利钠肽原 (NT-proBNP),BNP 和 NT-proBNP 均是目前管理心功能变化疾病的最佳指标^[5]。其中,NT-proBNP 在血清及血浆中均能测定,清除半衰期长,可累积较高浓度,因此能更灵敏的反映心脏功能的状态和变化。近些年的研究表明 BNP 和 NT-proBNP 与房颤的发生发展、分型

及预后密切相关^[6-9],不仅能评估房颤患者的心功能状态,还能预测房颤电复律的成功性及复发率^[10-16]。陈俊等^[26]研究 68 例接受射频消融治疗的房颤患者并发现,房颤患者血浆 BNP 水平升高,原因与房颤造成心房牵张和容量负荷过重相关。经射频消融治疗后,BNP 水平会下降,同时 BNP 浓度同射频消融术后房颤复发有关,如射频消融后 BNP 水平持续升高,提示房颤复发风险大。Amin A 等^[27]入组 112 例阵发房颤患者,使用氟卡胺药物复律,研究结果亦表明低水平 BNP 浓度者房颤复律成功

率明显增高。以上结论与本研究结果一致。根据本研究结果,初始 NT-proBNP 水平是房颤患者胺碘酮转复成功的一个重要预测因子,胺碘酮转复成功者血浆 NT-proBNP 水平显著低于转复失败者。

既往研究^[28-31]表明房颤复律(电复律或药物复律)成功率与患者年龄,既往心脏器质性疾病,左心房大小,房颤持续时间及血浆 C-反应蛋白(C-reactive protein, CRP)水平相关,亦有研究结论不一致者^[32]。我们的研究纳入的均为 48h 内阵发性房颤患者,未发现药物转复率与房颤持续时间相关,同时既往冠心病史、高血压、糖尿病、慢性肺部疾病、房颤病史对转复率亦无明显影响。快速房颤患者因心室舒张期缩短,同时心肌耗氧增加,冠脉血管相对供血不足,出现胸痛等心绞痛样症状,心电图表现为 ST 段压低、肌钙蛋白水平增高,本研究未发现房颤药物转复率与心室率、胸痛、心电图 ST 段压低及 TnI 水平相关;复律后患者心绞痛样症状缓解,ST 段回到基线水平,提示药物转复为此类患者重要治疗方法之一。

综上所述,对于房颤急性发作 <48 h 的患者,胺碘酮的转复是安全有效的;基线 NT-proBNP 水平是胺碘酮复律成功的一个重要预测因子,如基线 NT-proBNP 水平较高,则复律成功率低,为了避免药物的不良反应,可考虑控制心室率,而不是复律治疗。

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