

急性冠状动脉综合征患者初始应用氯吡格雷后换用替格瑞洛的疗效与安全性评价

李晓焯^{1*}, 王齐兵², 吕迁洲^{1#}(1. 复旦大学附属中山医院药剂科, 上海 200032; 2. 复旦大学附属中山医院心内科, 上海 200032)

中图分类号 R969.3 文献标志码 A 文章编号 1001-0408(2016)11-1533-04

DOI 10.6039/j.issn.1001-0408.2016.11.30

摘要 目的: 探讨急性冠状动脉综合征(ACS)患者初始应用氯吡格雷后换用替格瑞洛的疗效与安全性。方法: 采用回顾性分析方法, 收集我院2013年1月—2014年6月初始应用氯吡格雷后换用替格瑞洛的ACS住院患者资料, 根据腺苷二磷酸(ADP)诱导的药物抑制率分为低反应组和反应组。比较两组患者门诊随访1、3、6、9个月后因再发心血管事件的再住院率以及替格瑞洛相关的呼吸困难、出血等不良反应。结果: 入选患者124例, 其中低反应组患者34例, 反应组患者90例。反应组中吸烟患者的比例明显高于低反应组, 低反应组中合并高血压患者的比例明显高于反应组, 差异具有统计学意义($P < 0.05$)。患者在采用替格瑞洛替换氯吡格雷治疗后1、3、6、9个月因再发心血管事件的总体再住院率分别为6.5%、7.2%、8.1%、10.5%, 但两组患者再发心血管事件的再住院率比较, 差异无统计学意义($P > 0.05$)。随访中有12例患者出现呼吸困难, 有3例患者发生牙龈出血。结论: 替格瑞洛能改善氯吡格雷抵抗现象, 降低其因再发心血管事件导致的再住院率; 但应警惕其造成的呼吸困难和再出血风险。

关键词 替格瑞洛; 氯吡格雷抵抗; 再发心血管事件; 再住院率; 药品不良反应

Clinical Efficacy and Safety Evaluation for the Shifting from Clopidogrel to Ticagrelor in Acute Coronary Syndrome Patients

LI Xiaoye¹, WANG Qibing², LYU Qianzhou¹(1. Dept. of Pharmacy, the Affiliated Zhongshan Hospital of Fudan University, Shanghai 200032, China; 2. Dept. of Cardiology, the Affiliated Zhongshan Hospital of Fudan University, Shanghai 200032, China)

ABSTRACT **OBJECTIVE:** To discuss clinical efficacy and safety for the shifting from clopidogrel to ticagrelor in acute coronary syndrome (ACS) patients. **METHODS:** In retrospective study, clinical data of ACS inpatients receiving clopidogrel initially and ticagrelor instead were collected from our hospital during Jan. 2013 to Jun. 2014. They were divided into low response group and response group by inhibition rate of ADP activator. The rehospitalization rate of recurrent cardiovascular events, ticagrelor-related ADR as respiratory depression and bleeding were compared between 2 groups after followed up 1, 3, 6 and 9 months. **RESULTS:** 124 patients were included, among which there 34 patients in low response group and 90 patients in response group. The proportion of smokers in response group was higher than in low-response group, and the proportion of patients with hypertension in low response group was higher in response group, with statistical significance ($P < 0.05$). After using ticagrelor instead for 1, 3, 6 and 9 months, the rehospitalization rates resulting from recurrent cardiovascular events were 6.5%, 7.2%, 8.1% and 10.5%, respectively. There was no statistical significance in rehospitalization rates resulting from recurrent cardiovascular events between 2 groups ($P > 0.05$). In follow-up, 12 patients suffered from dyspnea and 3 suffered from gingival bleeding. **CONCLUSIONS:** Ticagrelor can improve the low platelet response of clopidogrel that could reduce the rehospitalization rates resulting from recurrent cardiovascular events. But should be carefull of the risk of dyspnea and rehaemorrhagia induced by ticagrelor.

KEYWORDS Ticagrelor; Low platelet response of clopidogrel; Recurrent cardiovascular events; Rehospitalization rate; ADR

血小板的活化和聚集在动脉粥样硬化血栓形成的发病机制中起着关键作用, 是导致急性冠状动脉综合征(ACS)的直接原因, 其中腺苷二磷酸(ADP)的释放以及通过血小板上的P2Y₁₂受体导致的小血小板聚集是血栓形成的重要因素^[1]。目前, 氯吡格雷为临床最常用的P2Y₁₂受体拮抗药, 但由于其为前体药物, 需经过肝药酶转化为活性物质, 因此遗传基因的多态性直接决定了其抗血小板活性的差异^[2]。一般而言, 血小板对氯吡格雷缺乏反应或反应降低, 称之为氯吡格雷抵抗^[3]。据

文献报道, 支架植入术后发生氯吡格雷抵抗的比例为16.8%^[4]。替格瑞洛无需经过肝药酶代谢转化为活性产物, 因此可作为氯吡格雷抵抗的替代治疗药物^[5]。目前, 相关指南^[6]推荐对于行冠状动脉造影及支架植入术的患者, 可给予氯吡格雷(75 mg, qd)或替格瑞洛(90 mg, bid)抗栓治疗。鉴于此, 本研究应用回顾性分析的方法评估了124名ACS患者采用替格瑞洛替换氯吡格雷后的疗效与安全性。

1 资料与方法

1.1 研究对象

经我院医学伦理委员会批准后, 本研究选取我院2013年1月—2014年6月初始应用氯吡格雷后换用替格瑞洛治疗的行冠状动脉造影以及支架植入术的ACS患者124例进行回顾性

* 主管药师。研究方向: 临床药学。电话: 021-64041990。E-mail: li.xiaoye@zs-hospital.sh.cn

通信作者: 主任药师, 博士。电话: 021-64041990。E-mail: lv.qianzhou@zs-hospital.sh.cn

分析。入选患者均符合2012年欧洲心脏病学会急性ST段抬高性心肌梗死/非ST段抬高性心肌梗死/不稳定心绞痛指南的诊断标准:24 h内均有胸闷、胸痛等症状发作,同时伴有典型的心电图ST-T波和心肌酶学的改变。排除近期内有重大手术、外伤、出血性疾病、脑血管意外和血小板减少症病史(血小板计数 $<100 \times 10^9 L^{-1}$)的患者。

1.2 治疗方法

所有患者入院后即行抗栓、降低心肌耗氧、抑制室重构以及稳定斑块等药物治疗。其中,阿司匹林在经皮冠状动脉介入治疗(PCI)术前给予300 mg负荷剂量,次日开始剂量为100 mg/d,终身服用;氯吡格雷在PCI术前给予300 mg负荷剂量,次日开始剂量为75 mg/d,至少服用1年;低分子肝素(依诺肝素)在PCI围术期给予4 000 IU,q12 h,连续2~8 d;普通肝素在PCI术中给予5 000~10 000 IU。所有患者均为初始应用氯吡格雷后出现血小板抑制率低下及冠状动脉造影结果显示血栓负荷较重,停用氯吡格雷24 h后换用替格瑞洛(瑞典 Astra-Zeneca AB,注册证号:国药准字J20130020,批号:1410129,规格:90 mg),每次90 mg,bid。

1.3 研究指标及测定方法

(1)以ADP来监测氯吡格雷的药物抑制率,患者在服用负荷剂量的氯吡格雷后,对ADP诱导的血小板聚集抑制率 $<30\%$ 定义为氯吡格雷低反应组, $\geq 30\%$ 定义为氯吡格雷反应组^[7]。记录两组患者的性别、年龄、吸烟史、血红蛋白、红细胞压积、血小板计数、治疗药物、合并疾病(包括高血压、中重度肾功能不全、心力衰竭)等,比较两组患者一般资料的差异。(2)通过门诊随访,记录两组患者服用替格瑞洛1、3、6、9个月后因再发心血管事件(包括心血管原因死亡、急性和亚急性支架血栓、再发ACS和缺血性中风)的再住院率。(3)比较两组患者的不良反应发生情况。依据Wallentin L等^[8]关于替格瑞洛与氯吡格雷的对照研究结果,替格瑞洛主要增加的不良反应

为呼吸困难和出血。出血的定义参照心肌梗死溶栓治疗临床试验(TIMI)出血标准^[9],分为大量出血和少量出血:大量出血包括颅内出血或有明显出血使血红蛋白降低 $>50 g/L$;少量出血包括出现肉眼血尿、咯血、消化道出血或黑便等,以及血红蛋白降低 $>30 g/L$ 。

1.4 统计学方法

采用SPSS 19.0软件对数据进行统计分析。计量资料以 $\bar{x} \pm s$ 表示,连续性的变量资料两组间比较采用独立样本 t 检验,方差不齐时采用近似 t 检验(如不符合正态分布则采用Wilcoxon秩和检验)。计数资料以频数和百分率表示,定性资料组间比较采用 χ^2 检验,两组等级资料的比较采用非参数Mann-Whitney秩和检验,两组以上等级资料的比较采用非参数Kruskal-Wallis H 秩和检验。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 患者一般资料

入选患者共124例,其中男性103例(83.1%),平均年龄(60.3 \pm 11.6)岁;女性21例(16.9%),平均年龄(66.7 \pm 9.9)岁。诊断为ST段抬高性心肌梗死(STEMI)者3例(2.4%),非ST段抬高性心肌梗死(NSTEMI)者108例(87.1%),不稳定性心绞痛(UA)患者13例(10.5%);合并有高血压58例、糖尿病34例、高脂血症44例、脑梗死3例、心力衰竭41例、肾功能不全19例。其中,有34例患者(27.4%)ADP诱导药物抑制率 $<30\%$,将其定义为低反应组;有90例患者(72.6%)ADP诱导药物抑制率 $\geq 30\%$,但是由于合并存在多支血管病变或者血栓负荷过重,将氯吡格雷替换为替格瑞洛,将其定义为反应组。两组患者一般资料比较见表1。由表1可知,反应组中吸烟患者的比例高于低反应组,差异具有统计学意义($P < 0.05$);低反应组中合并高血压患者的比例高于反应组,差异具有统计学意义($P < 0.05$)。

表1 两组患者一般资料比较($\bar{x} \pm s$)

Tab 1 Comparison of patients' general information between 2 groups($\bar{x} \pm s$)

| 组别 | 男性,例(%) | 年龄,岁 | 吸烟史,例(%) | 诊断,例(%) | | | 合并症,例(%) | | | | | 血红蛋白, g/L | 红细胞压积, % | 血小板计数, $\times 10^9 L^{-1}$ | 治疗药物,例 | | | | | | |
|------------|----------|-----------------|----------|---------|----------|---------|----------|----------|----------|--------|----------|-----------|--------------|-----------------------------|--------------|-------|-------|---------------|----------|-------|--------|
| | | | | STEMI | NSTEMI | UA | 高血压 | 糖尿病 | 高脂血症 | 脑梗死 | 心力衰竭 | | | | 肾功能不全 | 阿司匹林 | 他汀类 | β 受体阻滞剂 | ACEI/ARB | 硝酸酯类 | 质子泵抑制剂 |
| 低反应组(n=34) | 28(82.3) | 60.0 \pm 12.5 | 11(32.3) | 0 | 30(88.2) | 4(11.8) | 21(61.7) | 8(23.5) | 10(29.4) | 2(5.8) | 9(26.4) | 5(14.7) | 133 \pm 17 | 40.0 \pm 5.0 | 196 \pm 55 | 32 | 33 | 28 | 27 | 28 | 16 |
| 反应组(n=90) | 75(83.3) | 61.9 \pm 11.2 | 49(54.4) | 3(3.3) | 78(86.7) | 9(10.0) | 37(41.1) | 26(28.8) | 34(37.7) | 1(1.1) | 32(35.5) | 14(15.5) | 132 \pm 19 | 39.4 \pm 5.0 | 219 \pm 89 | 85 | 88 | 74 | 71 | 80 | 57 |
| χ^2 | 0.951 | 0.792 | 1.960 | 0.719 | 0.900 | 0.878 | 1.260 | 0.930 | 0.906 | 0.397 | 0.895 | 0.982 | 0.406 | 0.710 | 0.532 | 0.983 | 0.917 | 0.865 | 0.977 | 0.844 | 0.829 |
| P | 0.898 | 0.422 | 0.028 | 0.282 | 0.818 | 0.777 | 0.040 | 0.554 | 0.389 | 0.881 | 0.341 | 0.861 | 0.763 | 0.583 | 0.179 | 0.944 | 0.818 | 0.987 | 0.950 | 0.337 | 0.088 |

注:ACEI为血管紧张素转化酶抑制剂;ARB为血管紧张素受体拮抗药

Note: ACEI was angiotensin-converting enzyme inhibitor; ARB was angiotensin receptor antagonist

2.2 以替格瑞洛替换氯吡格雷后患者再发心血管事件的再住院率比较

患者采用替格瑞洛替换氯吡格雷治疗后1、3、6、9个月因再发心血管事件的总体再住院率分别为6.5%、7.2%、8.1%、10.5%。两组患者在不同时间再发心血管事件的再住院率比较见表2。由表2可知,两组患者再发心血管事件的再住院率比较,差异无统计学意义($P > 0.05$)。

2.3 不良反应

患者在采用替格瑞洛替换氯吡格雷治疗后,发生临床不能解释的呼吸困难12例(9.6%),发生牙龈出血3例(2.4%)。发生不良反应的患者均停用替格瑞洛而改用氯吡格雷抗栓治疗。

3 讨论

临床在使用氯吡格雷时,有部分患者出现氯吡格雷抵抗

表2 两组患者在不同时间再发心血管事件的再住院率比较[例(%)]

Tab 2 Comparison of recurrent cardiovascular events resulting from recurrent cardiovascular events between 2 groups at different time points[case(%)]

| 组别 | 治疗后1个月 | 治疗后3个月 | 治疗后6个月 | 治疗后9个月 |
|------------|---------|--------|---------|----------|
| 总体再住院率 | 8(6.5) | 9(7.2) | 10(8.1) | 13(10.5) |
| 低反应组(n=34) | 4(11.7) | 3(8.8) | 4(11.7) | 5(14.7) |
| 反应组(n=90) | 4(4.4) | 6(6.6) | 6(6.6) | 8(8.8) |
| χ^2 | 0.517 | 0.009 | 0.658 | 0.679 |
| P | 0.139 | 0.680 | 0.352 | 0.345 |

现象,尽管长期服用本药,但患者血小板活性并未得到有效控制,从而造成血栓等心血管事件发生率提高^[10]。多项研究结果显示,氯吡格雷的疗效存在广泛的个体差异,主要是由于本药为前体药物,需经过细胞色素P₄₅₀(CYP)2C19代谢后才能转化

为活性产物,因此遗传基因的多态性直接决定了本药抗血小板聚集的活性^[11]。目前采用血栓弹力图可以对凝血过程中的血小板聚集情况进行动态监测^[12],从而用于评估氯吡格雷在支架植入术后抗血小板聚集的反应性。通常当患者服用氯吡格雷达5个半衰期或者负荷剂量后,ADP诱导的药物抑制率<30%,即可认为出现氯吡格雷抵抗现象。

本研究124例ACS患者中有34例存在氯吡格雷抵抗,为低反应组;余下90例为反应组。其中,反应组中吸烟患者的比例显著高于低反应组。有研究显示,在服用双联抗血小板药物的非搭桥术患者中,吸烟组与非吸烟组发生出血的比例为1.72% vs.1.18%,可能原因是由于吸烟患者的内皮功能受损,需要延长抗血小板药物的治疗时间^[13]。本研究结果还表明,低反应组中合并存在高血压患者的比例显著高于反应组。Akturk IF等^[14]研究发现,在高血压患者中更易导致氯吡格雷抵抗的现象出现,可能原因是由于高血压患者的血流动力学不稳定导致血小板聚集率升高。

替格瑞洛相较于氯吡格雷起效更快,对血小板具有更强的聚集作用。Wallentin L等^[8]的研究结果表明,替格瑞洛能显著降低因心血管事件导致的死亡率、心肌梗死以及脑卒中的风险。同时,RESPOND研究^[15]结果显示,氯吡格雷抵抗患者在换用替格瑞洛后,其血小板聚集率抑制程度得到明显改善,因此相较于氯吡格雷,替格瑞洛具有更强的血小板抑制作用。本研究中,患者在换用替格瑞洛后能使血小板聚集率降低到更低水平,并且在随访的9个月内无明显的因再发心血管事件导致的再住院率增高;同时,在低反应组和反应组之间,换用替格瑞洛后的再发心血管事件导致的再住院率比较差异无统计学意义($P>0.05$)。因此,无论是氯吡格雷抵抗的患者,还是血栓负荷过重的患者,替格瑞洛都能降低其因心血管事件导致的再住院率。

替格瑞洛导致的呼吸困难目前认为主要与其作为腺苷三磷酸类似物有支气管刺激作用有关,此外还与其抑制红细胞再摄取腺苷相关^[16]。在Wallentin L等^[8]的研究中,有0.9%的患者因呼吸困难中断替格瑞洛治疗;而Gaubert M等^[17]研究发现,在服用替格瑞洛的ACS患者中出现呼吸困难的比例为55.6%。本研究结果显示,换用替格瑞洛后出现呼吸困难的患者比例为9.6%。对于各研究中ACS患者服用替格瑞洛后发生呼吸困难比例的差异性,主要原因是发生呼吸困难不仅与替格瑞洛导致的腺苷蓄积有关,还与患者不同严重程度的病变血管导致的胸闷胸痛有关。另外还需注意的是,替格瑞洛在带来更高临床获益的同时增加了出血的风险,本研究中即有2.4%的患者出现牙龈出血,但无大出血事件发生。

本研究为回顾性分析,具有一定的局限性:样本数量有限;缺乏中远期随访结果;由于采用门诊随访方式,缺乏客观实验室检查指标;对于部分再住院患者,其主要病因可能存在多支血管病变,需要多次行冠状动脉造影支架植入手术,但这部分患者却未被剔除。因此,替格瑞洛导致呼吸困难以及出血的不良反应还有待于更大规模的临床试验验证。

参考文献

[1] Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology (ESC), Steg PG, James SK, et al. ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation[J]. *Eur Heart J*, 2012,33(20):2 569.

[2] Garabedian T, Alam S. High residual platelet reactivity on clopidogrel: its significance and therapeutic challenges overcoming clopidogrel resistance[J]. *Cardiovasc Diagn Ther*, 2013,3(1):23.

[3] Guthikonda S, Lev EI, Klieiman NS. Resistance to antiplatelet therapy[J]. *Curr Cardiol Rep*, 2005,7(4):242.

[4] Wang ZJ, Zhou YJ, Liu YY, et al. Impact of clopidogrel resistance on thrombotic events after percutaneous coronary intervention with drug-eluting stent[J]. *Thromb Res*, 2009,124(1):46.

[5] Ferri N, Corsini A, Bellosa S. Pharmacology of the new P2Y₁₂ receptor inhibitors: insights on pharmacokinetic and pharmacodynamic properties[J]. *Drugs*, 2013, 73(15):1 681.

[6] Kolh P, Windecker S, Alfonso F, et al. 2014 ESC/EACTS Guidelines on myocardial revascularization: The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). Developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI) [J]. *Eur J Cardiothorac Surg*, 2014,46(4):517.

[7] Angiolillo DJ. Variability in responsiveness to oral antiplatelet therapy[J]. *Am J Cardiol*, 2009, 103(3 Suppl): 27A.

[8] Wallentin L, Becker RC, Budaj A, et al. Ticagrelor versus clopidogrel in patients with acute coronary syndromes [J]. *N Engl J Med*, 2009, 361(11):1 045.

[9] Wiviott SD, Antman EM, Gibson CM, et al. Evaluation of prasugrel compared with clopidogrel in patients with acute coronary syndromes: design and rationale for the Trial to assess improvement in therapeutic outcomes by optimizing platelet inhibition with prasugrel Thrombolysis In Myocardial Infarction 38 (TRITON-TIMI 38) [J]. *Am Heart J*, 2006,152(4):627.

[10] Jeong YH, Tantry US, Gurbel PA. Importance of potent P2Y₁₂ receptor blockade in acute myocardial infarction: focus on prasugrel[J]. *Expert Opin Pharmacother*, 2012,13(12):1 771.

[11] Mega JL, Close SL, Wiviott SD, et al. Cytochrome p-450 polymorphisms and response to clopidogrel[J]. *N Engl J Med*, 2009,360(4):354.

[12] Bochen L, Wiinberg B, Kjelgaard-Hansen M, et al. Evaluation of the TEG platelet mapping assay in blood donors[J]. *Thromb J*, 2007,5(3):1.

[13] Cornel JH, Ohman EM, Neely B, et al. Impact of smoking status on platelet function and clinical outcomes with prasugrel vs. clopidogrel in patients with acute coronary syndromes managed without revascularization: insights from the TRILOGY ACS trial[J]. *Am Heart J*, 2014,168(1):76.

[14] Akturk IF, Caglar FN, Erturk M, et al. Hypertension as a risk factor for aspirin and clopidogrel resistance in patients with stable coronary artery disease[J]. *Clin Appl*

益气清肺汤联合化疗用于老年晚期非小细胞肺癌患者的疗效观察

王巧琳*, 邓皖利#, 陆明(新疆医科大学附属中医医院, 乌鲁木齐 830099)

中图分类号 R730.52;R734.2 文献标志码 A 文章编号 1001-0408(2016)11-1536-04

DOI 10.6039/j.issn.1001-0408.2016.11.31

摘要 目的:观察益气清肺汤联合化疗用于老年晚期非小细胞肺癌(NSCLC)患者的疗效。方法:将76例老年晚期NSCLC患者按随机数字表法分为对照组和观察组,各38例。两组患者入院后均给予水化、止吐及托烷思琼+地塞米松治疗,对照组患者第1、8天给予酒石酸长春瑞滨注射液25 mg/m²+0.9%氯化钠注射液125 ml,10 min内ivgtt;第1~3天给予顺铂注射液30 mg/m²+0.9%氯化钠注射液500 ml,3 h内ivgtt。观察组患者在对照组基础上加用益气清肺汤200 ml,每日1剂,分两次服用。两组均治疗2个月。观察两组患者临床疗效及治疗前后凝血状态、T细胞免疫功能、生存时间及生存质量。结果:观察组患者总有效率为63.1%,显著高于对照组的34.2%,差异有统计学意义($P<0.05$)。治疗前两组患者凝血状态及T细胞免疫功能比较,差异无统计学意义($P>0.05$);治疗后,观察组患者纤维蛋白原(FIB)、D-二聚体(D-D)、CD8⁺水平显著降低,CD3⁺、CD4⁺、CD4⁺/CD8⁺水平显著升高,与治疗前及对照组比较,差异均有统计学意义($P<0.05$)。观察组患者中位生存时间为10.2个月,显著长于对照组的7.6个月,差异有统计学意义($P<0.05$)。治疗前,两组患者生存质量评分比较,差异无统计学意义($P>0.05$);治疗后,观察组生存质量评分显著低于对照组,差异有统计学意义($P<0.05$)。结论:益气清肺汤联合化疗能明显改善老年晚期NSCLC患者凝血状态及免疫功能,延长其生存时间,提高其生存质量。

关键词 益气清肺汤;化疗;晚期非小细胞肺癌;老年患者

Efficacy Observation of Yiqi Qingfei Decoction Combined with Chemotherapy in the Treatment of Elderly Advanced Non-small Cell Lung Cancer

WANG Qiaolin, DENG Wanli, LU Ming (The Affiliated TCM Hospital of Xinjiang Medical University, Urumqi 830099, China)

ABSTRACT **OBJECTIVE:** To observe therapeutic efficacy of Yiqi qingfei decoction combined with chemotherapy in the treatment of elder advanced non-small cell lung cancer (NSCLC). **METHODS:** 76 elder patients with NSCLC were randomly divided into control group and observation group, with 38 cases in each group. Both groups were given hydration, antiemetics and tropisetron+dexamethasone therapy. Control group was given Vinorelbine bitartrate injection 25 mg/m²+normal saline diluted to 125 ml, ivgtt within 10 min on the first and eighth day; given Cisplatin injection 30 mg/m²+normal saline 500 ml, ivgtt within 3 h. Observation group was additionally given Yiqi qingfei decoction 200 ml one dose a day, at twice on the basis of control group. Both group were given 2 months of treatment. The clinical efficacy, and blood coagulation, T cell immune function, survival time and survive quality before and after treatment were observed in 2 groups. **RESULTS:** The total effective rate of observation group was 63.1%, which was significantly higher than that of control group (34.2%), with statistical significance ($P<0.05$); there was no statistical significance in blood coagulation and T cell immune function of 2 groups before and after treatment ($P>0.05$); after treatment, fibrinogen (FIB), D-dimer (D-D) and CD8⁺ levels of observation group were significantly reduced, while CD3⁺, CD4⁺ and CD4⁺/CD8⁺ were significantly increased, with statistical significance compared to before treatment and control group ($P<0.05$); median survival time of observation group was 10.2 month, which was significantly longer than that of control group (7.6 month), with statistical significance ($P<0.05$); before treatment, there was no statistical significance in survival quality score between 2 groups ($P>0.05$); after treatment, the survive quality scores of observation group were significantly lower than that of control group, with statistical significance ($P<0.05$). **CONCLUSIONS:** For elder patients with NSCLC, Yiqi qingfei decoction combined with chemotherapy is help to improve the blood coagulation and immune function, extend the survival time, and improve the survive quality.

KEYWORDS Yiqi qingfei decoction; Chemotherapy; Advanced non-small cell lung cancer; Elderly patient

Thromb Hemost, 2014,20(7):749.

- [15] Gurbel PA, Bliden KP, Butler K, *et al.* Response to ticagrelor in clopidogrel nonresponders and responders and effect of switching therapies: the RESPOND study[J]. *Circulation*, 2010,121(10):1 188.
- [16] Ohman J, Kudira R, Albinsson S, *et al.* Ticagrelor induc-

es adenosine triphosphate release from human red blood cells[J]. *Biochem Biophys Res Commun*, 2012, 418(4): 754.

- [17] Gaubert M, Laine M, Richard T, *et al.* Effect of ticagrelor-related dyspnea on compliance with therapy in acute coronary syndrome patients[J]. *Int J Cardiol*, 2014, 173(1):120.

* 主治医师。研究方向:中医药肿瘤防治。电话:0991-5852247。E-mail:9361642@qq.com

通信作者:主任医师,博士。研究方向:中医药肿瘤防治。电话:0991-5852247。E-mail:dwl10707@126.com

(收稿日期:2015-07-31 修回日期:2015-10-31)
(编辑:胡晓霖)