经皮腔内冠状动脉成形术对冠心病患者血和尿内皮素的影响

孙　玲[①]　齐国先　吴广成　曾定尹　胡大一[②]　贾三庆[②]　李田昌[②]
(中国医科大学附属第一医院循环内科，沈阳　110001)

Influence of Percutaneous Transluminal Coronary Angioplasty on Endothelin Levels in Patients with Coronary Heart Disease

SUN Ling, QI Guo-Xian, WU Guang-Cheng, ZENG Ding-Yin, HU Da-Yi, JIA San-Qing and LI Tian-Chang
(Department of Circulation, First Affiliated Hospital, China Medical University, Shenyang 110001, China)

ABSTRACT

Aim　The synthesis and release of endothelin (ET) in patients with coronary heart disease undergary percutaneous transluminal coronary angioplasty has not been concluded. This study examined the porsible association between endothelin and coronary atherosclerosis and evaluated the synthesis and release of endothelin in the presence of various stimuli that occur during percutaneous transluminal coronary angioplasty.

Methods　The plasma from femoral artery blood and urinary concentrations of endothelin immunoreactivity in 15 patients and 10 healthy control subjects were measured before and after percutaneous transluminal coronary angioplasty.

Results　The basic plasma and urinary ET-1 level was higher than the control subjects ($P<0.01$). Changes were not detected in peripheral plasma concentrations of ET-1 within 24 h ($P<0.05$), but found increase in urinang ET-1 levels from 50±12 to 274±54 pg/kg of creative a few hours after coronary angioplasty ($P<0.01$). The increase excretion persisted for more than 24 hours. It was found that systolic aortic pressure was correlated with basal uninary excretion of ET-1 within the range of nomal ($r=0.87$, $P<0.01$, $n=15$), but balloon size, dilating times and duration were not associated with ET-1 level.

Conclusion　ET-1 concentration of patients with coronary heart disease was higher than the control subjects. Vascular injury during coronary angioplasty increase urinary ET-1 levels a few hours after the procedure. This increase was not detectable by sampling of femoral artery blood. Systolic aortic pressure was related to urinary ET-1. Larger clinical studies are required to further elucidate the biologic importance of endothelin in patients with coronary heart disease.

KEY WORDS　Percutaneous transluminal coronary angioplasty; Endothelin; Coronary artery disease

摘要　为调查冠心病和内皮素之间存在的联系，并评价经皮腔内冠状动脉成形术过程中各种刺激因素对内皮素水平的影响，观察了15名采取经皮腔内冠状动脉成形术成功的患者股动脉血及尿液的内皮素水平，并与10名健康人作对照。结果发现冠心病患者血、尿基础内皮素值高于正常($P<0.01$)。经皮腔内冠状动脉成形术后股动脉血中内皮素水平无显著增加，尿中内皮素水平却增加3～6倍($P<0.01$)，且持续24 h以上。收缩期主动脉压力与尿中基础内皮素水平呈正相关($r=0.87$, $P<0.01$, $n=15$)。结果表明冠状动脉粥样硬化时内皮素水平高于正常。经皮腔内冠状动脉成形术过程中的血管损伤引起术后内皮素释放，尿内皮素值能较敏感地反映出经皮腔内冠状动脉成形术后内皮素的增加。

关键词　冠状动脉粥样硬化；内皮素-1；经皮腔内冠状动脉成形术

①研究生，现在抚顺市中心医院心内科
②首都医科大学附属红十字朝阳医院心脏中心

内皮素是迄今所知的最强有力的血管收缩肽。近年来发现它可能参与心肌缺血和缺血性心脏病患者的缺血性发作[1~4]。经皮腔内冠状动脉成形术(percutaneous transluminal coronary angioplasty, PTCA)对内皮素水平的影响国外已有报道,但各家取血时间及取血部位不同,其结果也不一致。国内未见有关报道。为评价 PTCA 对内皮素水平的确切影响,本文对冠心病患者 PTCA 术前和术后血浆、尿液的内皮素水平进行测定,评价 PTCA 对内皮素-1 水平的影响。

1 材料与方法

1.1 研究对象

15 名住院患者,年龄 60±9 岁(10 男,5 女),经冠状动脉造影证实为任一支主要冠状动脉病变,常规行 PTCA 成功者作为研究组,急性及近期心肌梗塞者除外。所有入选患者血尿常规及肾功能正常,无其他主要心血管疾病。同时选定 10 名健康人作为对照组(年龄 60±6 岁,5 男,5 女),常规肝肾功能心电图检查正常,近期未服用任何药物。

1.2 心脏导管及标本的采集

经皮腔内冠状动脉成形术(PTCA)采用常规右股动脉穿刺技术,应用 8F 引导管,所有患者均常规使用肝素。患者均于术前及最后一次球囊扩张放气后 2、5、10、15、30、45、60、90 和 120 min 采集股动脉血 2 mL,标本分别注入冰水预冷的含 1×10^{-3} kg/L EDTA 和抑肽酶 300 IU 的试管中,然后在 4℃下以 3 000 r/min 离心 10 min,血浆存于-20℃冰箱备用。病人均于术前禁食水 8 h,术前、术后 3 h 及 24 h 分别留取尿液 2 mL,测定尿肌酐浓度,另取一份留于-20℃冰箱备分析。正常对照组于清晨空腹采集肱动脉血,同时留取尿液,标本处理方法相同。在球囊扩张前记录主动脉收缩压、舒张压和平均压。

1.3 内皮素的测定

血、尿内皮素测定采用放射免疫分析法[5]。试剂盒由解放军总医院免疫技术研究所提供。尿内皮素值以尿内皮素浓度与尿肌酐浓度的比值表示(1 pg/kg of Cr)。

1.4 统计学分析

所有数据以均值±标准差表示,统计学分析采用配对 t 检验。变量间的相关性用直线回归分析,$P<0.05$ 认为有统计学差异。

2 结果

2.1 两组血浆内皮素水平比较

病例组术前血浆 ET-1 水平显著高于正常对照组($P<0.01$)。PTCA 术后血浆 ET-1 无显著增加(表 1, Table 1)。

Table 1. Plasma concentrations of ET in two group of patients before and after PTCA ($\bar{x}\pm s$, ng/L).

Time (min)	Control group	CHD group
Pre-operation	24.00±3.20	39.53±14.78[a]
Post-operation		
2	24.00±3.20	38.42±14.09[b]
5	24.00±3.20	37.20±13.49[b]
10	24.00±3.20	36.18±11.91[b]
15	24.00±3.20	38.00±13.58[b]
30	24.00±3.20	38.39±13.01[b]
45	24.00±3.20	36.84±12.30[b]
60	24.00±3.20	37.72±13.55[b]
90	24.00±3.20	36.86±13.38[b]
120	24.00±3.20	37.53±13.29[b]

a: $P<0.01$, compared with baseline level of control group; b: $P<0.01$, compared with baseline level of CHD group.

2.2 两组尿内皮素水平比较

病例组术前尿中内皮素-1 水平显著高于正常对照组($P<0.01$)。PTCA 术后尿内皮素-1 显著增加,并持续至术后 24 h 以上(表 2, Table 2)。

病人中有一名患者 PTCA 术中血管造影显示冠状动脉左前降支内膜撕裂,其尿内皮素-1 于术后增加 6.8 倍(术前 50.66,术后 3 h 达 345.71,术后 24 h 达 250.98×10^{-3} ng/kg),而外周血浆中内皮素-1 水平仅增加 2.5 倍(术前 43,术后 2 min 达到 107 ng/L, 该患者只采集到术后 2 min 的血)。

Table 2. Vrinary ET levels in two group of patients (1 pg/kg of Cr).

Time (h)	Control group	CHD group
Pre-operation	46±24	54±7[a]
Post-operation		
3	46±24	274±54[b]
24	46±24	173±51[b]

a: $P<0.01$, compared with baseline values of control group; b: $P<0.01$, compared with baseline values of CHD group.

2.3 有关变量间的相互关系

经皮腔内冠状动脉成形术(PTCA)过程中记录到15名患者的主动脉压力,发现尿内皮素-1基础水平与主动脉收缩压明显相关($r=0.87$, $P<0.01$, $n=15$)(附图, Figure),而与主动脉舒张压和平均动脉压无关。

患者的年龄、内皮素值、气囊尺寸及扩充时间与血、尿内皮素水平无关。

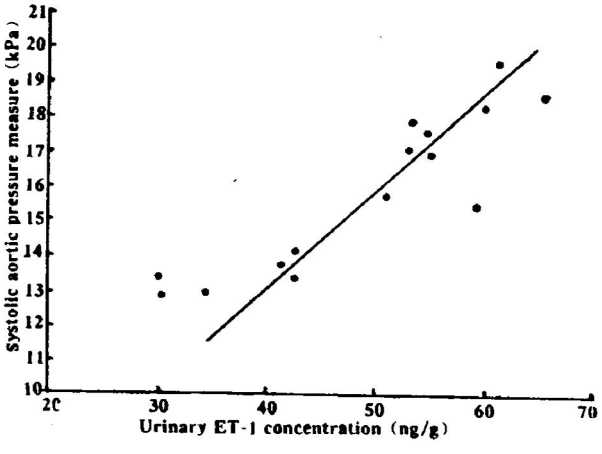

Figure 1. Correlation between the values of urinary ET-1 concentration and systolic aortic pressure measure in 15 patients during PTCA ($r=0.87$, $P<0.01$).

3 讨论

本组病人经术前用药心绞痛已被控制在稳定状态,与正常对照组相比较,PTCA术前血浆及尿液基础内皮素水平均显著增高,提示冠状动脉粥样硬化患者内皮素-1合成和释放增加,与Malatino等[6]报道一致。

病例组术前、术后股动脉血内皮素-1水平无显著差异,术后尿内皮素-1却增加3～6倍,且持续24 h以上,类似于Montalescot等[7]的结果。造成这种PTCA术后尿中内皮素增加、血中内皮素不增加的原因,考虑与血液的全身稀释作用、肺的清除及个体差异有关。以尿内皮素浓度与尿肌酐浓度的比值作为尿内皮素值,这样就排除了血液的全身稀释作用和尿量对尿内皮素浓度的影响,因而说明尿内皮素值的这种检测方法较血浆的检测更为敏感。

病例组中有一名患者术中血管损伤严重,在术后血浆、尿液中均发现内皮素-1增加。相比之下,血管牵张的刺激因素比如气囊尺寸及充气时间与内皮素-1水平不相关,提示血管内膜损伤而非牵张可能参与了内皮素的释放。

在正常范围内主动脉收缩压与尿内皮素-1浓度之间存在明显相关,而与舒张压和平均动脉压不相关,这提示在内皮素和主动脉阻抗及心肌收缩力之间存在着可能的联系[8]。

冠心病病人较正常对照组内皮素-1水平增加。PTCA引起的血管损伤可引起尿内皮素浓度的增加,股动脉采血不能检测出这种增加。收缩期血压与尿内皮素-1浓度相关,有待大规模研究进一步证实内皮素与人冠状血管疾病间的生物学联系。

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