

· 临床研究 ·

国产碘克沙醇对老年冠心病患者肾功能影响的安全性研究

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【摘要】目的 评价国产碘克沙醇注射液对进行经皮冠状动脉介入治疗(PCI)的老年冠心病患者肾功能的影响。**方法** 采用随机分组、单盲设计、阳性对照的多中心研究。于2013年7月至2014年3月在辽宁省5家医院选择60~75岁、拟行PCI的患者88例,随机分为试验组(应用江苏恒瑞医药股份有限公司生产的碘克沙醇注射液,44例)与对照组[应用通用电气药业有限公司生产的威视派克(碘克沙醇商品名),44例]。记录两组术前年龄、性别、体质指数(BMI)及肾功能等基本临床资料,术后48h检测肾功能,从而比较两者对老年冠心病患者肾功能的影响有无差别。**结果** 两组共入选88例患者,试验组与对照组均为44例。88例患者均顺利完成冠状动脉造影与PCI,成功率100%。两组年龄、BMI等基本临床资料无统计学差异($P > 0.05$)。两组PCI前后肾功能指标相比均无统计学差异($P > 0.05$),两组分别有1例患者术后当天出现恶心呕吐,于手术次日恢复正常;两组均未发生对比剂诱发性急性肾损伤及其他不良反应。**结论** 国产碘克沙醇用于行PCI的老年冠心病患者是安全的。

【关键词】 碘克沙醇;经皮冠状动脉介入治疗;对比剂诱发性急性肾损伤;老年人

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Nephrotoxic effects of domestic iodixanol injection in old patients with coronary heart disease

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【Abstract】 Objective To evaluate the nephrotoxic effects of domestic iodixanol injection in the elderly patients with coronary heart disease (CHD). **Methods** A multicenter, single blind, randomized controlled clinic trial was prospectively carried out in 5 hospitals in Liaoning Province from July 2013 to March 2014. Eighty-eight patients of 60 to 75 years old with CHD undergoing percutaneous coronary intervention (PCI) were divided into 2 groups: experimental group (domestic iodixanol injection group, $n = 44$) and control group [Visipaque (trade name of iodixanol) group, $n = 44$]. The clinical information including age, gender, body mass index (BMI), serum creatinine (SCr) and blood urea nitrogen (BUN) was recorded before PCI. Their SCr and BUN were determined in 48 h after PCI for renal function in the patients of the 2 groups. **Results** All of them underwent PCI smoothly, with a successful rate of 100%. There was no significant difference in the age, gender, BMI, SCr and BUN between the 2 groups before PCI ($P > 0.05$). No difference was found in the renal function in the 2 groups before and after PCI ($P > 0.05$). One patient of each group had nausea and vomiting respectively just in the day after operation, and recovered on the next day. None of patient had contrast-induced acute kidney injury or other adverse reactions. **Conclusion** Domestic iodixanol injection is safe for old patients with CHD underwent PCI.

【Key words】 iodixanol; percutaneous coronary intervention; contrast-induced acute kidney injury; aged

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近年来随着我国心血管造影和经皮冠状动脉介入治疗 (percutaneous coronary intervention, PCI) 数量的逐年增长, 含碘对比剂的应用日益广泛, 其不良反应尤其是对比剂诱发性急性肾损伤 (contrast-induced acute kidney injury, CI-AKI) [1,2] 日益受到重视。肾小球滤过率随年龄增长而降低, 故老年人应用对比剂的风险更高 [3]。碘克沙醇 (iodixanol) 因为良好的安全性, 被国内外指南 [4-7] 推荐选用。为评价国产碘克沙醇注射液对老年PCI患者肾功能的影响, 辽宁省5家医院以通用电气药业 (上海) 有限公司生产的商品名为威视派克 (Visipaque) 的碘克沙醇为对照, 进行了前瞻性的多中心单盲随机对照临床研究。现将该研究报道如下。

1 对象与方法

本研究经辽宁省人民医院伦理委员会批准, 由辽宁省人民医院、辽宁医学院附属第一医院、解放军第313医院、沈阳市第一人民医院及辽宁省中医药大学附属医院的心内科, 于2013年7月至2014年3月协作完成。入选患者均签署知情同意书。

1.1 研究对象入选标准

- (1) 60~75岁冠心病患者88例, 男女不限;
- (2) 拟行PCI;
- (3) 签署知情同意书。

1.2 排除标准

(1) 受试者既往对碘对比剂及含碘食物有严重不良反应;

(2) 既往甲亢病史者;

(3) 有肾功能障碍, 血清肌酐水平 $\geq 3\text{mg/dl}$ ($265.2\mu\text{mol/L}$);

(4) 3个月内发生过急性肾衰竭和 (或) 接受过血液透析治疗患者。

(5) 接受过肾移植手术的患者;

(6) 严重肝功能不全患者 [丙氨酸氨基转移酶和 (或) 天冬氨酸氨基转移酶 $\geq$ 正常参考值上限2倍];

(7) 受试者不能中断服用盐酸二甲双胍或包含盐酸二甲双胍的药品;

(8) 有急性活动性出血;

(9) 发热, 体温 $\geq 38^\circ\text{C}$;

(10) 严重血液系统疾病患者;

(11) 术前14d内接受过碘对比剂的患者;

(12) 预计术后7d内需要再次接受对比剂的患者;

(13) 有证据显示受试者临床状况不稳定, 包括: 急性心肌梗死 (2周之内); 心源性休克; 充血性心力衰竭或急性肺水肿; 脑卒中 (3个月内);

(14) 既往冠状动脉造影显示为慢性完全闭塞病变、三支弥漫性病变、左主干病变等估计对比剂用量 $\geq 400\text{ml}$ 或 (和) PCI手术风险较高的患者;

(15) 近3个月参加过其他临床研究;

(16) 不具法律能力或法律能力受限者;

(17) 研究者认为不合适参加该临床研究的任何情况。

1.3 方法

患者入选后随机分为试验组 (44例) 与对照组 (44例)。试验组应用江苏恒瑞医药股份有限公司生产的碘克沙醇注射液, 规格为 $100\text{ml}: 65.2\text{g}$ ($100\text{ml}: 32\text{g I}$) /瓶, 批准文号为国药准字 H20103675; 对照组应用通用电气药业 (上海) 有限公司生产的威视派克, 规格为 $32\text{g (I)}/100\text{ml}$ /瓶, 批准文号为国药准字 J20050104。常规进行冠状动脉造影与PCI, 应用阿司匹林、氯吡格雷、他汀类调脂药以及手术前后生理盐水进行水化等治疗。术后随访1周。

1.4 观察指标

记录患者的年龄、性别、身高、体质量、生命体征、伴随疾病、对比剂用量、术前血清肌酐 (serum creatinine, SCr) 与尿素氮 (blood urea nitrogen, BUN)、术后48h SCr与BUN (若升高, 则术后7d复查)、术中术后有无严重心脑血管事件及对比剂引起的不良反应 (包括CI-AKI等)。CI-AKI定义为48h内SCr水平升高 $> 0.3\text{mg/dl}$ 或7d内升高 $> 50\%$ 。计算体质量指数 (body mass index, BMI)、估测肾小球滤过率 (estimated glomerular filtration rate, eGFR) 以及术后eGFR的减少值。 $\text{eGFR}[\text{ml}/(\text{min} \cdot 1.73\text{m}^2)] = 175 \times \text{SCr}(\text{mg/dl})^{-1.234} \times \text{年龄}^{-0.179} \times (0.79\text{女性})^{[8]}$; 术后eGFR的减少值 $[\text{ml}/(\text{min} \cdot 1.73\text{m}^2)] = \text{术前eGFR} - \text{术后eGFR}$ 。

1.5 统计学处理

采用SPSS13.0统计软件进行统计学分析。计量资料以均数 $\pm$ 标准差表示, 两组均数比较采用 t 检验; 计数资料以例数或所占百分比表示, 组间率的比较采用 χ^2 检验。所有的统计检验均采用双侧检验, $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 基本临床资料

88例患者均顺利完成冠状动脉造影与PCI (成功率100%), 随访期间均无死亡、脑卒中、急性心肌梗死、再次血运重建等严重心脑血管事件发生。两组基本临床资料比较, 差异无统计学意义 ($P > 0.05$; 表1)。

2.2 PCI前后肾功能情况

两组PCI前后肾功能指标相比均无统计学差异 ($P > 0.05$; 表2), 两组分别有1例患者术后当天出现恶心、呕吐, 于手术次日恢复正常; 两组均未发生CI-AKI及其他不良反应。

表1 两组基本临床资料表

Table 1 Baseline characteristics of the two groups (n = 44)

Item	Experimental group	Control group
Age(years, $\bar{x} \pm s$)	64.80 $\pm$ 5.40	66.39 $\pm$ 6.23
Males[n(%)]	31 (70.45)	23 (52.27)
BMI(kg/m ² , $\bar{x} \pm s$)	24.56 $\pm$ 1.92	24.22 $\pm$ 2.92
Hypertension[n(%)]	19 (43.18)	21 (47.72)
Diabetes mellitus[n(%)]	6 (13.63)	5 (11.36)
Hyperlipemia[n(%)]	7 (15.90)	9 (20.45)
Contrast dose (ml, $\bar{x} \pm s$)	161.14 $\pm$ 40.07	163.64 $\pm$ 50.18
Success rate of operation[n(%)]	44 (100.00)	44 (100.00)
Rate of statin application[n(%)]	44 (100.00)	44 (100.00)
Application of physiological saline during operation[n(%)]	44 (100.00)	44 (100.00)

BMI: body mass index

表2 两组PCI前后肾功能情况表

Table 2 Comparison of renal function between the two groups (n = 44, $\bar{x} \pm s$)

Index of renal function	Experimental group	Control group
eGFR before operation [ml/(min · 1.73m ²)]	108.08 $\pm$ 31.82	112.73 $\pm$ 39.98
SCr before operation (μmol/L)	72.14 $\pm$ 19.44	70.26 $\pm$ 27.66
BUN before operation(mmol/L)	6.16 $\pm$ 2.00	5.94 $\pm$ 1.86
eGFR after operation [ml/(min · 1.73m ²)]	101.37 $\pm$ 26.63	107.88 $\pm$ 34.58
SCr after operation(μmol/L)	74.82 $\pm$ 18.64	72.10 $\pm$ 28.53
BUN after operation(mmol/L)	5.77 $\pm$ 1.64	5.61 $\pm$ 1.62
Reduction of eGFR after operation[ml/(min · 1.73m ²)]	6.72 $\pm$ 18.79	4.85 $\pm$ 19.47

PCI: percutaneous coronary intervention; eGFR: estimated glomerular filtration rate; SCr: serum creatinine; BUN: blood urea nitrogen

3 讨 论

老年冠心病患者进行PCI治疗的数量逐年增多,而老年患者冠状动脉及全身动脉病理改变较中青年患者更加严重,冠状动脉多存在多支、迂曲和钙化等复杂病变,PCI术中对对比剂需求量相对增多;老年患者肾小球滤过率及心脏储备功能下降,而且合并高血压病、糖尿病、心功能不全的概率增高(本研究中排除了心力衰竭,入选患者合并高血压病、糖尿病的比例仍分别超过40%与10%),肾脏对对比剂不良反应的代偿能力降低。以上因素导致老年患者发生肾功能损害的风险及其危害性增加^[7]。

基础肾功能损害是预测接受碘对比剂检查的患者发生CI-AKI的最重要的标志,因此老年患者PCI术前一定要评价肾功能状态,计算eGFR而不是单纯依据血肌酐水平判断。若eGFR < 60ml/(min · 1.73m²),则视为CI-AKI的高危患者^[9-11]。若老年患者病情需行PCI治疗,在应用他汀类调脂药物^[12],尽量减少对比剂用

量,及术前术后积极有效水化治疗的同时,选择循证医学证实安全的对比剂是非常重要的^[13,14]。等渗对比剂碘克沙醇为非离子型二聚体,其渗透压与血浆渗透压相等^[15],上市后经众多临床研究证实其安全性良好,故被国内外众多指南所推荐^[4-7]。

本研究为前瞻性多中心单盲随机对照临床研究,结果显示在老年冠心病患者进行PCI时应用国产碘克沙醇注射液与威视派克均无CI-AKI等严重不良反应,其他不良反应轻微而发生率相近。因此,国产的碘克沙醇注射液与威视派克相比同样安全,可用于老年冠心病患者的PCI治疗,因其价格更加便宜,值得在临床工作中推广。但本研究样本例数偏小,更加确切的结论有待更大规模的前瞻性随机对照研究来证实。

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