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Effect of Intracoronary Nicorandil Compared To Nitroglycerin on Coronary Diameter and Hemodynamics Following Balloon Dilatation during Elective PTCA

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Abstract

Introduction: Vasodilators are important drugs to relieve coronary spasm during coronary interventions. Use of Intracoronary (IC) Nitroglycerin (NTG) during PTCA helps to prevent or treat coronary vasospasm, augment coronary collateral flow and also helps in appropriate sizing of stents. Hemodynamic effects of NTG may preclude its use in some patients. Nicorandil (NIC) is used as a coronary vasodilator and has a favourable hemodynamic profile. *Materials and Methods:* 34 patients planned for elective PTCA with coronary stenosis more than 70% were included in the study. Alternate patients received intracoronary administration of 200 microgram of Nitroglycerin (NTG) or 1 mg Nicorandil (NIC). Hemodynamic parameters, TIMI flow grade and coronary diameters were analysedin both groups. *Results:* I.C administration of NTG resulted in significant increase in heart rate (72 ± 10.6 vs 101 ± 9.5 p<0.0001) and a reduction in Mean aortic pressure (80 ± 9.5 vs 69 ± 9.5 p<0.0001). I.C Nicorandil did not produce any significant variation in Heart rate or mean aortic pressures. Both groups showed significant increase in coronary diameters following I.C administration of NTG and Nicorandil (2.02 ± 0.12 and 2.16 ± 0.18 mm respectively). Intracoronary Nicorandil produced a greater coronary vasodilatation than NTG but the values were statistically nonsignificant (2.16 ± 0.18 mm vs 1.83 ± 0.17 mm p=0.05). *Conclusion:* Intracoronary Nicorandil produces a significant increase in coronary diameter following balloon dilatation without adverse effects on hemodynamic parameters compared to nitroglycerine. Nicorandil use was associated with higher TIMI 3 grades. Routine use of Nicorandil may be beneficial as a vasodilatory and cardioprotective agent during PTCA.

Keywords: Coronary diameter; Hemodynamics; Nicorandil; Nitroglycerine; PTCA; TIMI flow grade.

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Introduction

Percutaneous coronary angioplasty (PTCA) has become one of the principal means of revascularization in coronary artery disease (CAD) [1]. 1-5% of balloon angioplasty procedures are complicated by coronary spasm. Predisposing factors include lesions which are not calcified, eccentric lesions, and younger patients [2,3]. Various pathophysiological mechanisms are responsible for coronary spasm. Percutaneous devices cause denudation of coronary endothelium which in turn decreases the nitric oxide levels and an increased sensitivity to various vasoconstrictors like serotonin [4]. Production of norepinephrine and platelet-derived vasoconstrictors (thromboxane, serotonin, platelet-activating factor), changes

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in arachidonic acid metabolism, release of endothelium-derived contractile factor (EDCF), local adrenergic nerve dysfunction, and stimulation of stretch-dependent myogenic tone are other potential mechanisms [5,6].

Coronary vasodilators are used for relieving coronary spasm and its adverse effects during coronary interventions. Intracoronary administration of nitroglycerin (NTG) (200-300 mcg) is often performed to prevent or treat coronary vasospasm, and augment coronary collateral flow during PTCA [7,8]. It can also be helpful in appropriate sizing of balloons and stents. Major adverse effects are fall in blood pressure, reflex tachycardia, headache, and flushing. Patients on nitrates for angina relief without a nitrate-free interval may not respond to intracoronary nitroglycerin (or may require a higher dose), due to nitrate tolerance. Concurrent use of phosphodiesterase-5 inhibitor is also a contraindication for nitroglycerin due to the risk of significant hypotension.

Nicorandil (NIC) is a potassium channel opener with additional nitrate-like effects and is a coronary vasodilator. This agent is used in preventing reperfusion injury and for promoting ischemic preconditioning [9,10]. In addition, nicorandil has no significant adverse reactions, such as significant hypotension, adverse effects on heart rate, or atrioventricular block [11].

Methodology

34 patients planned for elective PTCA with coronary stenosis more than 70% were included in the study after getting informed consent. The study was done in inpatients admitted for PTCA in the department of Cardiology JIPMER. Patients with Left main stenosis, those undergoing rotablation and patients on Intra Aortic Balloon Pump were excluded from the study. After balloon dilatation of the lesion, angiogram was obtained. Alternate patients received 200 microgram of Nitroglycerin (NTG) or 1 mg Nicorandil (NIC) and angiogram repeated. ECG, Heart rate and aortic pressures were constantly recorded. TIMI flow grade and coronary diameters in the segments 5 mm proximal and distal to the lesion were measured by QCA after balloon dilatation and 3 minutes after the administration of the drug.

Results

19 patients received NTG and 15 NIC. Mean age of the patients were 58 ± 6 years in the NTG group and 56 ± 8 years in the NIC group. None of the patients were on calcium channel blockers. 42% (n=8) of patients were diabetics in NTG group and 46% (n=7) in NIC group. 20 patients underwent PTCA of LAD, 10 of LCX and 4 of RCA (Table 1).

Table 1: Baseline characteristics

Parameter	Group I (NTG) (n=19)	Group II (NIC) (n=15)	p value
Age (Yrs)	58 ± 6	56 ± 8	0.76
Gender (M:F)	13:6	10:5	0.89
Diabetes Mellitus (%)	8 (42)	7(46)	0.72
Hypertension (%)	10(52)	8(53)	0.88

Table 2: Hemodynamic change

Parameter	Group I (NTG) (n=19)			Group II (NIC) (n=15)		
	Baseline	After NTG	p value	Baseline	After NIC	p value
Heart rate (beats/minute)	72 ± 10.6	101 ± 9.5	< 0.001	76 ± 11.1	81 ± 10.3	0.54
Mean Aortic Pressure (mmHg)	80 ± 9.5	69 ± 9.5	< 0.001	78 ± 8.9	76 ± 9.1	0.67

Table 3: Change in coronary diameter

Parameter	Group I (NTG) (n=19)			Group II (NIC) (n=15)		
	Baseline	After NTG	p value	Baseline	After NIC	p value
Coronary diameter (mm)	1.80 ± 0.16	2.02 ± 0.12	< 0.001	1.83 ± 0.17	2.16 ± 0.18	< 0.001

Heart rate increased significantly after NTG (72 ± 10.6 vs 101 ± 9.5 p<0.0001) but did not show a significant variation after Nicorandil (76 ± 11.1 vs 81 ± 10.3 p-NS). Mean aortic pressure decreased significantly in the NTG group (80 ± 9.5 vs 69 ± 9.5 p<0.0001). Aortic pressures did not vary significantly in the Nicorandil group (78 ± 8.9 vs 76 ± 9.1) (Table 2). All patients in the NIC group had TIMI 3 flow whereas 2 patients in the NTG group had TIMI 2 flow and one patient TIMI 1 flow. The mean coronary diameter after balloon dilatation was 1.80 ± 0.16 mm in NTG group and 1.83 ± 0.17 in NIK group. Both groups showed significant increase in coronary diameters following I.C administration of NTG and Nicorandil (2.02 ± 0.12 and 2.16 ± 0.18 mm respectively). Intracoronary Nicorandil produced a greater coronary vasodilatation than NTG though the values did not reach statistical significance (2.16 ± 0.18 mm vs 1.83 ± 0.17mm p=0.05) (Table 3).

Discussion

This study was done in 34 patients undergoing elective PTCA to study the effect of intracoronary nitroglycerin and nicorandil. Nitroglycerin causes relaxation of vascular smooth muscle and consequent dilatation of peripheral arteries and especially veins. Venodilatation reduces left ventricular preload. Arteriolar relaxation results in lowering of systemic vascular resistance, systolic arterial pressure, and hence the afterload. The study by BG Brown et. al., showed that after intracoronary NTG, luminal caliber dilated in the normal and diseased arterial segments, with an average 40 ± 26% reduction ($p < 0.05$) in predicted stenosis flow resistance [12]. NTG use can result in significant fall in mean arterial pressure and tachycardia during PTCA and may preclude use of further doses. Nicorandil is a coronary vasodilator and has no significant effects on heart rate and blood pressure.

In this study both nicorandil and NTG resulted in coronary dilatation. Patients who received Nitroglycerine had a significant fall in the mean arterial pressure. Administration of Nicorandil resulted in coronary vasodilatation without adversely affecting the hemodynamics. Though Nicorandil produced a greater increase in coronary diameter compared to NTG, it was not statistically significant.

Nicorandil is a K-ATP channel opener, and dilates resistance arteries less than 100 µm in diameter [13]. It reduces the production of reactive oxygen species in cardiac mitochondria, and attenuates ischemia/reperfusion induced polymorphonuclear leukocytes activation via nitric oxide donation [14]. Various studies have shown a reduction in the frequency of no-reflow or slow flow phenomenon in patients with acute coronary syndrome in patients who received intracoronary or intravenous nicorandil [15,16]. In this study all patients who received nicorandil had TIMI 3 flow after stenting but in the NTG group 2 patients had TIMI 2 flow and one patient TIMI 1 flow. This could be explained as due to the protective effects of Nicorandil on the microcirculation, on which NTG does not have any role.

Conclusion

Intracoronary Nicorandil produces a greater increase in coronary diameter following balloon dilatation without significantly affecting hemodynamic parameters. Nicorandil use was associated with higher TIMI 3 grades. Routine use of Nicorandil may be beneficial as a vasodilatory and cardioprotective agent during PTCA.

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