

## Comparison of Various Vasodilators Regimen During Radial Coronary Angiogram: A Prospective Randomised Trial

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### Background and Aims:

Coronary intervention through radial artery is a preferred over femoral route. Different vasodilators are used to prevent radial artery spasm. Till date there is no study to compare the effects of various vasodilator regimes during radial coronary angiogram in Nepal. We aim to compare the efficacy of different vasodilator in our patients.

### Methods and Result:

This is a single centre, prospective randomized trial between Verapamil, Nitroglycerine (GTN) and cocktail (Verapamil with GTN). All the patient undergoing coronary angiogram via radial approach, without the contraindication were randomized by a computer generated randomization protocol. Patient undergoing coronary procedures via the radial artery were divided into three groups. Patients in group A received intra-arterial cocktail (2.5 mg of Verapamil plus 100 mcg Nitroglycerine in 10 ml of normal saline), patients in group B received Verapamil (5mg) and patient in group C received Nitroglycerine (200mcg). Heparin of 3000U was given intravenously in all three groups. Altogether 207 patients underwent transradial coronary angiogram, 203 were randomized after exclusion. Over all Radial artery spasm was reported in 28 patients (13.79%). There was no statistically significant difference in spasm between the three regimens however when grading, there was significant higher grade of spasm in Verapamil group (13.23%, P value < 0.05). When comparing Verapamil and GTN separately there was significant higher spasm (21% vs 7%, P value < 0.05) with higher grades of spasm in verapamil group.

### Conclusion:

Intra arterial vasodilators are frequently used as a spasmolytic during Trans-Radial angiogram. Our study showed that there is no difference in spasm when chosen between cocktail, verapamil and GTN. However while grading the spasm; there was greater propensity of high grade spasm among the verapamil users.

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### Keywords

Vasodilators, radial coronary angiogram, nitroglycerine, verapamil

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## INTRODUCTION

First reports of radial coronary angiography was by Lucian Campeau in 1989 and radial percutaneous coronary intervention (PCI) by Ferdinand Kiemeneij in 1992 after which there was an increase in the use of transradial access (TRA) around the world.<sup>1,2,3</sup> Previous studies have shown that transradial artery approach for coronary artery catheterization and intervention to be safe, easy and effective, as well as cost

effective.<sup>4</sup> Patients also prefer transradial route in comparison to the femoral access because of lower incidence of back and access site pain and earlier ambulation.<sup>5,6</sup> The advantages we get from the radial route has some demerits also and it

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is not devoid of complications. The problem which are faced are unsuccessful radial access, coronary catheterization failure, pulse deficit, radial artery occlusion, dissection, and spasm.<sup>1,3,7,8,9</sup> The most common of these is the radial spasm<sup>8,9</sup> causing patient discomfort and even procedure failure. There is high propensity of spasm in the radial artery because of its anatomic property. Its wall is thick and consists of smooth muscle in concentric layer and the cells have high density of alpha-1 receptors. This both properties makes radial artery highly susceptible to spasm.<sup>10</sup> The reported incidence of radial artery spasm ranges from 15-30% even in the centers highly experienced with the procedure.<sup>11</sup> Prevention of the spasm is possible by various premedications.<sup>11</sup> Worldwide there has been a lot of studies of spasmolytics which has shown the benefit.<sup>4,5,6,9,11,12,13,14</sup> Among these studies it has been recommended by Kiemeneij et al.<sup>11</sup> that the spasm is significantly reduced by 34-14% by the use of cocktail with intra-arterial nitroglycerin and verapamil. Radial access for coronary intervention has been in practice in Nepal for last several years there has been no study regarding the different vasodilator regimen for the prevention of radial artery spasm during the procedure. We report a prospectively randomized study to compare the spasmolytic effects on the radial artery with different premedications, with nitroglycerin alone, verapamil alone and nitroglycerin plus verapamil in radial coronary angiogram.

## MATERIALS AND METHODS

Study was conducted for three months from 2015 June 16 to September 17. Altogether 207 patients undergoing elective coronary angiogram from the radial route were randomized into three different vasodilator regimen. All patients above the age of 18 undergoing radial coronary angiogram with hemodynamic stability were included.

Exclusion criteria included:

1. Abnormal Allens test
2. Pregnancy
3. Hemodynamic Instability
4. Acute MI or unstable angina needing emergent cardiac catheterization
5. Hypotension (systolic blood pressure below 90 mm Hg),
6. Significant bradycardia (heart rate below 50 beats/min),
7. Severe left ventricular dysfunction (left ventricular ejection fraction less than 35%)

## 8. Acute lung edema

The baseline characteristics, including patients' age, gender, body weight, body height, serum cholesterol and triglyceride level, the rate of diabetes and smoking, blood pressure, were compared in three groups. Ethical approval was obtained and all patients gave informed consent to this procedure.

Randomization was done by computer generated box randomization protocol. Radial coronary angiogram was performed via right or left route according to the operator's preference. After local anesthetic injection radial artery was punctured and sheath was inserted. Then according to randomization protocol, the patients were divided into three groups of vasodilator regimen. Group A received Cocktail of Verapamil 2.5mg + GTN 100mcg, Group B received Verapamil-5mg and Group C received GTN- 200mcg. All patients in three group received 3000U of heparin via intravenous route.

## Definitions

Spasm was graded according to the operative perceived resistance, Maneuverability of the catheters and degree of pain perception by the patients.

Pain score was defined as the patient's assessment of pain during radial artery sheath removal, where I denote nothing felt; II, noticeable sensation but no pain; III, mild pain; IV, significant pain; and V, unbearable pain.<sup>11</sup>

## Statistical Analysis

Variables were presented as mean  $\pm$  standard deviation. ANOVA was used for analysis of the difference in the rate of radial spasms between the three groups. An SPSS software program was used for performing the analysis. A p value <0.05 was considered statistically significant.

## RESULTS

Altogether 214 coronary angiograms were performed. Seven underwent angiogram via femoral route. Two hundred seven underwent angiogram via radial route and four were rejected due to abnormal anatomy and radial loop. Two hundred and three patients were randomized into three vasodilator regimens. Sixty five were included in group A, 68 in group B and 70 in group C.

Table 1 shows the baseline characteristics, including patients' age, gender, serum cholesterol and triglyceride level, the rate of diabetes and smoking, blood pressure and rate of right and left handed approach. No significant difference in baseline parameters was found between these three groups. Overall radial artery spasm was noted in 14% of the patients. Nine

patients in group A (13.8%), 14 patients in group B (20.5%) and 5 patients in group C (7%) showed radial spasms. The spasm difference noted was not statistically significant. There was high rate of spasm in female as compared to male (20% vs 9%,  $P < 0.05$ ). There is no statistically significant difference of radial spasm between groups A and B ( $p > 0.05$ ) and groups A and C ( $p > 0.05$ ); however there is strong statistically significant difference between groups B and C ( $p < 0.05$ ). When grading spasm significant higher grade of spasm was noted in group B as compared to group A and group C ( $p < 0.05$ ). Regarding the pain during sheath removal more pain was noted in group B as compared to group A and group C ( $p < 0.05$ ).

Table 1: Baseline characteristics

	Group A (Cocktail Regimen)	Group B (Vera- pamil)	Group C (GTN)	p-value
Mean	55.96 ± 10.1	54.57 ± 10.9	56.37 ± 9.0	> 0.05
Male	44	43	37	> 0.05
Female	21	25	33	
Hypertensive	29	31	37	> 0.05
Normotensive	36	37	33	
Diabetic	11	5	15	> 0.05
Non Diabetic	54	63	55	
Present	4	6	6	> 0.05
Absent	61	62	64	
Smoker	15	15	19	> 0.05
Non Smoker	50	53	51	
Right	62	66	69	> 0.05
Left	3	2	1	
Mean	92.47 ± 15.89	88.48 ± 12.34	88.30 ± 18.74	> 0.05

Patients in group A received, 100 mcg of nitroglycerin and 2.5 mg of verapamil via sheath, group B received 5mg of verapamil and group C 200mcg.

## DISCUSSION

Due to the presence of dual blood supply to the hand, radial route for coronary catheterization and intervention is relatively

safe.<sup>3,5,13,15,16</sup> Prevention is better than cure and when it comes to radial artery spasm it holds true. The prevention of spasm is easy than to control when it occurs.<sup>8</sup>

He and yang classification classifies the radial artery into type III artery graft with high propensity for spasm and also as stated above due to abundance of the alpha receptors slight catecholamine release during pain or anxiety can induce radial spasm.<sup>17</sup> Many studies done in the past have used different spasmolytic regimens.<sup>5,8,9,16</sup> In one of the similar studies published by Kiemeneij et al.<sup>14</sup> which was a prospective study proved that intra-arterial administration of 5 mg of verapamil and 200 mcg of nitroglycerin reduced the occurrence and severity of radial artery spasm. The data showed the evidence of benefit of verapamil in the prevention of spasm but concern still remains regarding the negative inotropic and chronotropic effects of verapamil. The VITRIOL study<sup>18</sup> states that The preventive use of verapamil may be unnecessary for transradial procedures. The omission of prophylactic verapamil may not only reduce the rate of potential complications related to the drug but also allow the safe extension of the transradial method to those with contraindications to verapamil. So there has been a lot of reluctance in the use of verapamil as spasmolytics. Study done by Chen et al showed that nitroglycerine alone is also effective as compared to placebo in prevention of radial artery spasm.<sup>19</sup> Mechanism by which the nitroglycerine causes vasodilation is by activating guanylyl cyclase and increasing cGMP.<sup>20</sup> Nitroglycerine has also been compared with the diltiazem and was found to be more effective.<sup>21</sup> Our data showed that the nitroglycerine is more effective than verapamil and the cocktail of both in preventing spasm. In this study more spasm was found among the female which may be due to the hormonal effect or due to the low pain threshold but the exact cause is still not known. Further larger study requires confirming this.

## Study Limitations

There are few limitations of this study:

1. Not placebo controlled
2. Operators not blinded
3. Due to the different threshold of pain there might be difference in spasm and grading of spasm
4. This is a single center study
5. The follow up of the patient was not done

In conclusion, we recommend that the nitroglycerine be used a preferred spasmolytics during radial coronary angiogram. However larger study using large population in multicenter setting is required to confirm the findings of this study.

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