

Efficacy of Nitrates and Calcium Channel Blocker in Prevention of Radial Artery Spasm during Coronary Angiographies

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Abstract

Background: Radial artery vasospasm is the most frequent complication of transradial cardiac catheterization. It causes discomfort and pain to the patient, prolongs the procedure and even makes it impossible for the interventionist to continue the procedure.

Objective: To evaluate the efficacy of combined use of nitrate and calcium channel blocker (Verapamil) in prevention of radial artery spasm during coronary angiographies.

Study design, settings and duration: It was a case control study conducted among 100 cardiac patients undergoing coronary angiography in Rehman Medical Institute (RMI) Peshawar from the duration of January 2016 to December 2016.

Subjects and Methods: Sample selection was done through convenient non probability sampling technique. Written informed consent was taken from the patients included in the study. Patients were divided into two groups control (50) and experimental (50). One group was treated with heparin/nitrate as control group while other group was treated with heparin/nitrates/verapamil (Calcium channel blocker) as experimental group. Both groups were checked for radial spasm, pain and catheter resistance during angiography procedure. All other demography and history were collected through using a predesigned questionnaire. Data was collected, analyzed using SPSS version 16.

Results: It was found that 63% patients were male, 37% were female and 68% cardiac patients were above the age 50 years. The study provided that using Verapamil as calcium channel blockers with nitrate does not put a significant effect on radial spasm with *p* value 0.806. The study provided that in comparison of cases and control for different variable, no significant difference was observed for radial spasm, pain, outcome, catheter resistance and time taken by the procedure. However the outcome of procedure was 100% successful among test group than control (98%).

Conclusion: Calcium channel blocker (Verapamil) use with nitrate provided no significant difference in lowering radial spasm during coronary angiography. The assumption of using calcium channel blocker against radial artery spasm during angiography nullified.

Policy message: Economic burden due to use of calcium channel blockers along with nitrate during coronary angiography should be avoided. There are no additional benefits of using calcium channel blocker (Verapamil) with nitrate.

Key words: Calcium channel blocker, catheterization, angiography, radial spasm, nitrate, verapamil.

Introduction

Radial artery spasm (RAS) is a brief and abrupt contraction of radial artery generally detected clinically and by angiographic method amid cardiac catheterization. In clinics, it is diagnosed as pain in forearm that gets intensified with the movement of the catheter thus causes a great deal of difficulty in catheter manipulation. There is likewise loss of pulse in radial artery and decrease in arterial pressure. Therefore to confirm radial artery spasm and correspondingly omit vessel injury, a radial arteriogram is acquired. It is important to perform

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Received: 19 October 2017, **Accepted:** 25 May 2018,
Published: 29 September 2018

Authors Contribution

US, MK & RF conceptualized the project. US, MK, RF & id the data collection. Literature search was done by US & AK. AK performed the statistical analysis. Drafting, revision and writing of manuscript were done by US, MK, RS & AK.

angiography as it is possible that sometimes pain may not be due to spasm but other reasons such as coiling or looping in radial, sub-clavian or brachial arteries which provide difficulty in moving catheter and cause torment to the patients.¹ Radial artery spasm occurs due to small diameter of artery, diabetes, old age, females, lower BMI, and first attempt failure in cannula placement. Its occurrence rate differs from 2-22% due to different definitions employed, lack of impartial evaluation method, type of catheter utilized and pre-medications.² It is also reported that the properties of catheter such as its length and coating might also influence the frequency of RAS.³ Due to lower complication risk, easiness in cannula placement and ease of access, radial artery is preferred for invasive monitoring of pressure in arteries.⁴ However, radial artery spasm remains a major problem of transradial approach for per-cutaneous coronary intervention.⁵ The original method of RAS is yet to be completely explained, nevertheless it is said that activation of alpha adrenergic receptors present in the smooth muscles are involved in the process.⁶ These alpha adrenoreceptors are present abundantly in the radial arteries. Moreover, these arteries have thick muscular layer in comparison to peripheral arteries which is why radial arteries are more prone to spasm.⁷ Therefore it is imperative to prevent the incidence of RAS and the pain associated with it. For this reason, variety of spasmolytic drugs and assortment of sheaths, guide wires and catheter were taken into consideration to prevent RAS. These investigations were conflicting in techniques and results, particularly with respect to the rate and seriousness of RAS.⁸ Different method utilized to get relieve from RAS consists of utilizing injections of vasodilators and lidocaine (nitroglycerine, calcium channel blockers) within arteries, sympatholytic blocks i.e. brachial plexus block and local warming.^{4,6,9-11} Youn et al. in his studies showed that the provision of topical eutectic blend of prilocaine (2.5%) and lidocaine (2.5%) i.e. EMLA before initiation of transradial coronary angiography can diminish the pain and sympathetic reaction, yet it neglects to demonstrate a statistically noteworthy diminishment in RAS.¹² Ho et al. also proclaimed that RAS occurred in 4-20% of the cases. It was also reported that the utilization of pharmacological agents such as intra-arterial vasodilatory mixtures can be used for the prevention of RAS however caution must be taken when using verapamil for this purpose as it contraindicated in bradycardia and severe left ventricular function.¹ Another report by Kristic et al. combined the findings from 19 studies showed that RAS occurred in 14.7% of the cases. These results were somewhat higher than other

mentioned results.³ He also suggested that when 1.25-5mg of verapamil in combination with 100-200µg of nitroglycerine was used, it can decrease the rate of RAS up to 3.8%.³ Another study by Vuurmans et al. also support this blend.¹³

It was observed that large number of patients have intense and diffuse spasm that is usually momentary and sort out spontaneously. However, proper medication before starting the procedures should be administered. Drugs such as verapamil or nitrates are given after sheath insertion systematically which expand the diameter of radial arteries. Utilization of small hydrophilic catheter, hydrophilic sheaths along with tapered dilator and limiting handling and exchange of catheter are associated with decrease in the rate of spasm.^{3,14,15} Verapamil can impede the slow entrance rate of calcium ions into the cells. This mechanism of calcium ion entry within the cells is known to play a vital role in contraction of the heart cell. Verapamil when combined with nitroglycerin ascertained to be effective spasmolyte in transradial cardiac dealings.⁸ Despite the fact that verapamil is most frequently used, it still have certain limitations such as it has lesser vasodilator property of radial artery as compared to other calcium channel agonists.¹⁶ Furthermore, major side effects like bradycardia, ventricular asystole, or persistent hypotension have also been testified in patients with depressed left ventricular function or conduction disturbance, however this occurs rarely.¹⁷ Another complication observed was that the spasm was still reported in 10-20% of the cases even with the utilization of verapamil.^{8,18} Options other than verapamil like Phentolamine is an example of one such option. It is a non-selective antagonist of alpha adrenergic that competitively block both pre and presynaptic adrenergic receptors hence favoring vasodilation and reduces peripheral resistance.¹⁹ Since RAS is considered to be facilitated by alpha adrenergic receptors, the utilization of phentolamine may prove to be an effective option.²⁰ Rafael et al. demonstrated that with the use of phentolamine, the mean radial diameter can be increased significantly thus it is a potent vasodilator similar to verapamil.²¹ The purpose of this study was to determine the efficacy of nitrate and calcium channel blocker in combination to avoid the occurrence of radial artery spasm during the procedure of coronary angiographies. RAS create pain and discomfort which lengthen the duration of the procedure.

Subjects and Methods

It was a case control study conducted among 100 cardiac patients undergoing coronary

angiography in Rehman Medical Institute (RMI) Peshawar from the duration of January 2016 to December 2016. Sample selection was through convenient non probability sampling technique. Newly diagnosed patients referred to angiography were included while already treated follow up patients were excluded from the study. Brief introduction of the study was given and written informed consent was taken from patients participated in the study. Patients were divided into control and experimental groups to check the effect of nitrate and calcium channel blocker in prevention of radial artery spasm during angiography procedure. Control group were treated with heparin/nitrate and test group with heparin/nitrates/verapamil (calcium channel blocker) just before coronary angiography. Both groups were checked for radial spasm, pain and catheter resistance during angiography procedure. All other demography and history were collected using a predesigned questionnaire.

X-ray procedure is used to imaging heart blood vessel. The test was generally used to detect restriction in blood flow going toward heart. Coronary angiogram is part of heart catheterization procedure. Cardiac patients were brought for cardiac catheterization in which a long thin tube called catheter was inserted in an artery or vein in blockage side and threaded through blood vessel toward heart. A coronary angiogram was used to diagnose as well as to treat heart condition. In this procedure, a type of dye that's visible by an X ray machine is injected in blood vessels of patients. The X ray machine rapidly took a series of images of blood vessel. The patients were checked for radial spasm, pain and catheter resistance during the procedure.

The quantitative variables and qualitative variables were separated. The quantitative variables were expressed as mean standard deviation, confidence interval and maximum and minimum range. The qualitative variables were expressed in frequencies. Chi square and p value was calculated using test and control group for each variables. Data was analyzed using SPSS version 16.

Results

A total 100 cardiac patients undergoing coronary angiography were included in the study. Among them 50 patients were taken as control (Heparin + verapamil treated) and 50 as test group (Heparin + verapamil + nitrate treated). It was found that 63% patients were male and 37% were female and 68% cardiac patients were above the age 50 years. It was revealed that 30% cardiac patients were diabetics and 70% hypertensive (Table-1).

Table 1: Frequency of demographic variable of coronary angiographic patients.

Group	F	%
Heparin + nitrate+ Verapamil treated patients (cases)	50	50.0
Heparin + nitrate treated patients (control)	50	50.0
Sex		
Male	63	63.0
Female	37	37.0
Age		
< 50	32	32.0
> 50	68	68.0
Diagnosed		
Previous MI	53	53.0
Angina	47	47.0
Echo findings		
LV function	8	8.0
Normal	55	55.0
Impaired	37	37.0
Diabetes		
Yes	30	30.0
No	70	70.0
Hypertensive		
Yes	70	70.0
No	30	30.0
Dyslipidemias		
Yes	9	9.0
No	91	91.0
Social history		
Nil	90	90.0
Smoking	9	9.0
Alcohol	1	1.0
Renal function		
Normal	96	96.0
Impaired	4	4.0

The study provided that using verapamil as additional calcium channel blockers with nitrate do not put a significant effect on lowering radial spasm with p value 0.806. However it was observed that pain during angiography are not due to radial spasm as relation between pain and radial spasm showed that majority patients were with pain having no radial spasm with p value 0.00. Results also showed that catheter resistance was due to radial spasm with significant relation p value 0.00 (Table-2). The study provided that in comparison of cases and control group for different variable, no significant difference was observed for radial spasm, pain, outcome, catheter resistance and time taken by the procedure.

Table 2: Comparison of radial spasm with different variable.

Group	Radial Spasm		Chi Sq.	p value
	Yes	No		
Cases	39	11	.060 ^a	.806
Control	40	10		
<i>Age Group</i>				
< 50	24	8	.454 ^a	.501
> 50	55	13		
<i>Gender</i>				
Male	2	61	2.410 ^a	.121
Female	4	33		
<i>Hypertensive</i>				
Yes	4	66	.034 ^a	.854
No	2	28		
<i>Pain</i>				
Yes	5	6	34.113 ^a	.000
No	1	88		
<i>Catheter resistance</i>				
Yes	5	3	49.218 ^a	.000
No	1	91		
<i>Out come</i>				
Successful	5	94	15.825 ^a	.000
Abandoned	1	0		

Table 3: Comparison of Cases and Controls for different variable N (%).

Variable	Groups		p value
	Cases	Controls	
<i>Radial spasm</i>			
Yes	3 (6)	3 (6)	NC
No	47 (94)	47 (94)	
<i>Pain</i>			
Yes	4 (8)	7 (14)	.338
No	46 (92)	43 (86)	
<i>Catheter resistance</i>			
Yes	3 (6)	5 (10)	.461
No	47 (94)	45 (90)	
<i>Out come</i>			
Successful	50 (100)	49 (98)	NC
Abandoned	0 (0)	1 (2)	
<i>Time taken by procedure (minutes)</i>			
5-10	22 (44.9)	23 (46)	0.4778
10-20	22 (44.9)	25 (50)	
20-30	5 (10.2)	2 (4)	

However the outcome of procedure was 100% successful among test group than control (98%) (Table-3).

Discussion

The study was carried out to determine the significant of calcium channel blocker (verapamil) when use with nitrate against radial spasm during coronary angiography. Radial spasm is a major hindrance during the angiography procedure,²² make patient discomfort and painful. Nitrate generally used against radial spasm during the procedure²³ however many cases of radial spasm are observed inspite of using nitrate. Calcium channel blocker (Verapamil) used with nitrate during the angiography procedure does not put a significant difference on the results (Table-3). Verapamil associated with the development of transient heart block²⁴ and its association with nitrate does not enhance the antagonist effect against radial spasm. It was found in present study that male patients were frequently undergoing angiography than females (Table-1). It was predetermined by a study carried out for comparison of men and women regarding the frequency with which they underwent various cardiac procedures.²⁵ The study provided that 70% patients undergoing angiography were hypertensive (Table-1). Hypertensive patients develop cardiac problems and cardiac related complication.^{26,27} Radial spasm in case of cardiac catheterization was observed due to catheter resistance and severs pain having a significant *p* value 0.00 (Table-2). It is already determine that catheter pain is associated with radial spasm and subsequent catheter resistant.²⁸ The present study revealed no major difference for radial spasm, pain, outcome, catheter resistance and time taken by the procedure between test and control group (Table-3). Other study provided that long term treatment of verapamil and nitrate is affected against spasm and their treatment is influenced with duration of treatment.²⁹

The study was restricted to Rehman Medical Institution due to limited budget and time. It needs to be studied among large sample size with prolong treatment. In spite of these limitation the study clearly provided an idea not to use verapamil with nitrate at the time of coronary angiography but in case of long spasm treatment, it may be a treatment choice.

Calcium channel blocker (Verapamil) use with nitrate provided no significant difference in lowering radial spasm during coronary angiography. The assumption of using calcium channel blocker against radial artery spasm during angiography nullified.

Acknowledgement

The Authors are grateful to the Rehman Medical Institute (RMI) staffs and managements for their consent to carry out this research and their time to time support. Special thanks to Mr. Aftab Khan and Janat Sher of Pakistan Health Research Council (PHRC Research Centre KMC) for helping in data analysis, proof reading and compilation of this paper.

Conflict of interest: None declared.

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