ORIGINAL ARTICLE Effectiveness of Calcium Channel Blockers and Nitrates in Inhibition of Spasm of Radial Artery during Coronary Angiography

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ABSTRACT

Background: The most common issue with transradial cardiac catheterization is radial artery vasospasm. The patient experiences pain and discomfort as a result, the procedure is prolonged, and the interventionist may even be unable to continue.

Aim: The aim of the study is to determine the effectiveness of Verapamil, a calcium channel blocker and nitrate, when used together to prevent radial artery spasm during coronary angiographies.

Methods: This case control study was held in the Cardiology department of Qazi Hussain Ahmed Medical Complex, Nowshera and Peoples University of Medical and Health Sciences for Women PUMHSW (SBA) Nawabshah for six-months duration from July 2021 to December 2021 including 120 cardiac patients undergoing coronary angiography. The patients were selected by non-probability sampling technique. Patients who were enrolled in the study provided written informed consent. Two groups of patients—control (60) and experimental—were formed (60). Heparin/nitrate was administered to one group and labelled as a control group, while heparin/nitrates/verapamil (a calcium channel blocker) was administered to the other group considered as an experimental group. During the angiography procedure, the radial spasm, discomfort, and catheter resistance were assessed in both groups. A predesigned questionnaire was used to collect all other demographic data and patient's history. SPSS version 23.0 was used to collect and analyse the data.

Results: It was found that 68.3% of cardiac patients were over 50 years old, 41.7% of patients were female, and 58.3% of patients were male. Verapamil, a calcium channel blocker, and nitrate did not significantly affect radial spasm, according to this study with a p value of 0.762. According to the study, there was no obvious difference noted in radial spasm, outcome, discomfort, catheter resistance, or procedure time when cases and controls were compared for various variables. However, the test group have a 100% success rate of the procedure compared to the control group's 95%.

Conclusion: Verapamil, a calcium channel blocker when combined with nitrate did not significantly reduce radial spasm during coronary angiography. The theory that calcium channel blockers could prevent radial artery spasm during angiography was nullified. It is best to avoid the financial burden that comes with using calcium channel blockers and nitrate during coronary angiography. Combining nitrate and calcium channel blocker (Verapamil) has no additional advantages.

Keywords: Angiography, catheterization, calcium channel blocker, radial spasm, nitrate, and verapamil are some of the related terms.

INTRODUCTION

A brief and abrupt contraction of the radial artery known as a radial artery spasm (RAS) is typically identified clinically and by an angiographic technique during cardiac catheterization¹⁻². Clinicians diagnose it as forearm pain that worsens when they move the catheter, making it very challenging to manipulate the catheter. Additionally, there is a decrease in arterial pressure and a loss of pulse in the radial artery. A radial arteriogram is therefore obtained in order to confirm radial artery spasm and correspondingly omit vessel injury³. It is crucial to perform angiography because pain may occasionally not be caused by a spasm but rather by coiling or looping in the radial, subclavian, or brachial arteries, which makes it difficult to move the catheter and the patient feels pain. Small artery diameter, diabetes, advanced age, female gender, lower BMI, and first attempt cannula placement failure all contribute to radial artery spasm. Due to diverse definitions being used, a lack of an objective evaluation method, the type of catheter being used, and pre-medications, its incidence rate varies between 2 and 22%. Additionally, it has been suggested that a catheter's length and coating may have an impact on the frequency of RAS⁴⁻ 5. The radial artery is chosen for intrusive monitoring of arterial pressure because it has a lower risk of complications, is simple to insert a cannula, and is easier to access. Radial artery spasm, however, continues to be a significant issue with the transradial technique for percutaneous coronary intervention. Although the initial mechanism of RAS is still not fully understood, it is believed that the process involves the activation of alpha-adrenergic receptors found in smooth muscles⁶. The radial arteries contain a large number of these alpha adrenoreceptors. Additionally, radial arteries have a thicker muscular layer than peripheral arteries, which makes them more prone to spasm. Therefore, it is essential

to stop the occurrence of RAS and the pain it causes. To prevent RAS, a number of spasmolytic medications as well as a selection of sheaths, guide wires, and catheters were considered. In terms of methods and outcomes, these investigations were contradictory, especially when it came to the frequency and severity of RAS. Injections of vasodilators and lidocaine (nitroglycerine, calcium channel blockers) into arteries, sympatholytic blocks, such as brachial plexus block, and local warming are other methods used to treat RAS7. The use of topical eutectic mixtures of prilocaine (2.5%) and lidocaine (2.5%), or EMLA, prior to the start of transradial coronary angiography can reduce discomfort and the sympathetic response, but it fails to show a statistically significant reduction in RAS, according to research by Yousuf et al⁸. RAS was reported in 5-25% of patients, according to Ho et al study. Additionally, it was stated that the use of pharmaceutical substances like intra-arterial vasodilatory combinations could be utilised to avoid RAS. However, verapamil should not be used for this purpose due to its contraindications in bradycardia and severe left ventricular dysfunction. The results of 19 studies by Engin E et al were analyzed revealed that RAS occurred in 15.2% of patients.⁹ These outcomes were a little better than the others that were given. Additionally, he claimed that using 1.25-5 mg of verapamil along with 100-200 g of nitroglycerine could reduce RAS by up to 4.1%. This combination is supported by the study of DeBoard Z et al¹⁰.

Various patients experience strong and diffuse spasms, which are often transient and resolve spontaneously. However, the right medication should be given before beginning the procedure. After sheath insertion, medications that increase radial artery diameter include verapamil and nitrates are given.¹¹ The rate of spasm is reduced when a small hydrophilic catheter, hydrophilic

sheaths, a tapered dilator is used with limited handling and minimum catheter exchange techniques. Verapamil can slow down the rate at which calcium ions enter cells¹². It is well known that this process of calcium ion entrance within the cells plays a crucial part in the contraction of the cardiac cell. Verapamil has been proven to be an efficient spasmolytic in transradial cardiac situations when combined with nitroglycerin. There are alternatives to verapamil; phentolamine is one such alternative¹³. It is a nonselective alpha-adrenergic antagonist that competitively inhibits both pre- and presynaptic adrenergic receptors, favoring vasodilation and lowering peripheral resistance. The use of phentolamine may prove to be a successful strategy because alpha adrenergic receptors are thought to facilitate RAS¹⁴.

This study aimed to determine if nitrate and calcium channel blockers worked together effectively to prevent the onset of radial artery spasm during coronary angiographies. RAS cause discomfort and pain, which extends the time of the treatment.

METHODS

This case control study was held in the Cardiology department of Qazi Hussain Ahmed Medical Complex, Nowshera and Peoples University of Medical and Health Sciences for Women PUMHSW (SBA) Nawabshah for six-months duration from July 2021 to December 2021 including 120 cardiac patients undergoing coronary angiography. The patients were selected by nonprobability sampling technique. Patients with recently diagnosed cardiac issue were referred for an angiography were included in the study, but patients who had already received treatment were excluded. Patients who participated in the study received a brief explanation about the study and were asked to sign written informed permission forms. Two groups of patients-control (60) and experimental-were formed (60). Heparin/nitrate was administered to one group and labelled as a control group, while heparin/nitrates/verapamil (a calcium channel blocker) was administered to the other group considered as an experimental group. A predesigned questionnaire was used to collect all other demographic data and patient's history. Heart blood vessels imaging done with X-ray. The test was typically performed to find blood flow restrictions towards the heart. The procedure of heart catheterization includes a coronary angiography. Cardiac patients were brought in for cardiac catheterization, which involved threading a long, thin tube called a catheter into a blood vessel toward the heart in the blocked artery or vein. Heart conditions were both diagnosed and treated with a coronary angiography. In this technique, patients' blood vessels are injected with dye that can be visualized by an X-ray machine. The X-ray machine quickly take the series of pictures of the blood vessels. During the angiography procedure, the radial spasm, discomfort, and catheter resistance were assessed in both groups.

The quantitative and qualitative variables. The mean, standard deviation, confidence interval, and maximum and lowest ranges were used to express the quantitative variables. Frequencies were used to express the qualitative characteristics. For each variable, the chi square and p value were calculated in both groups. SPSS 23.0 was used to analyse the data.

RESULTS

The study included 120 cardiac patients who underwent coronary angiography. Two groups of patients—control (60) and experimental—were formed (60). Heparin/nitrate was administered to one group and labelled as a control group, while heparin/nitrates/verapamil (a calcium channel blocker) was administered to the other group considered as an experimental group. It was shown that 68.3% of cardiac patients were older than 50, with 41.7% of patients being female and 58.3% of patients being male. It was shown that 30.8% of cardiac patients had diabetes and 75% had hypertension (Table-1).

Verapamil, a calcium channel blocker, and nitrate did not significantly affect radial spasm, according to this study with a p

value of 0.762. However, it was found that the majority of patients who experienced pain during angiography did not also have radial spasm, with a p value of 0.00, indicating that the cause of the pain was not radial spasm. Results also demonstrated a significant relationship (p value 0.00) between catheter resistance and radial spasm (Table-2).

Table-1: shows the patients demographic features

Group	F	%
Heparin + nitrate+ Verapamil treated patients	60	50.0
(Experiment group)		
Heparin + nitrate treated patients (control group)	60	50.0
Gender	70	58.3
Male		
Female	50	41.7
Age	38	31.7
<50		
>50	82	68.3
Previous MI	59	49.2
Angina	53	44.2
Echo findings	13	10.8
LV function		
Normal	62	51.7
Impaired	45	37.5
Diabetes	37	30.8
Hypertension	70	75
Dyslipidemia	18	15
Social history		
Nil	113	94.2
Smoking	5	4.2
Alcohol	2	1.7
Renal function	112	93.3
Normal		
Impaired	8	6.7

Table-2: shows the Radial spasm comparison with respect to various variables

Group	Radial	Spasm	Chi Sq.	P-value
	Yes	No		
Cases	45	15	0.052	0.762
Control	38	22		
Age Group				
< 50	29	9		
> 50	62	20	0.392	0.627
Gender				
Male	5	65		
Female	3	47	3.042	0.108
Hypertensive				
Yes	7	63		
No	5	45	.067	0.953
Pain				
Yes	8	7		
No	3	102	38.03	0.00
Catheter resistance				
Yes	10	6		
No	4	100	42.83	0.00
Out come				
Successful	10	107		
Abondoned	2	1	13.86	0.00

Table-3:	shows	the	comparison	of	Cases	and	Controls	for	successful
outcome									

	Experiment Group	Control group	P-value	
Out come	60 (100)	57 (95)	NC	
Successful	80 (100)	37 (83)		
Abandoned	0 (0)	3 (5)		
Time taken by procedure (minutes)				
5-10 mints	26 (43.3)	25 (41.6)	0.587	
10-20 mints	29 (48.3)	32 (53.3)		
20-30	5 (8.4)	3 (5)		

According to the study, there was no obvious difference noted in radial spasm, outcome, discomfort, catheter resistance, or

procedure time when cases and controls were compared for various variables.

However, the test group have a 100% success rate of the procedure compared to the control group's 95%.

DISCUSSION

The purpose of the study was to evaluate the effectiveness of the calcium channel blocker (verapamil) in combination with nitrate in preventing radial spasm during coronary angiography¹⁵⁻¹⁶. A significant challenge during the angiography operation that causes the patient pain and discomfort is radial spasm. During the procedure, nitrate is frequently used as an anti-radial spasm agent. Despite utilising nitrate, multiple incidents of radial spasm have been documented¹⁷. Verapamil, a calcium channel blocker, when used with nitrate during the angiography operation did not significantly alter the outcomes. Verapamil does not increase the antagonist effect against radial spasm, despite its relationship with nitrate and the creation of temporary heart block¹⁸⁻¹⁹. In the current study, it was discovered that male patients underwent angiography more frequently than female patients. It was predetermined by a study that compared the frequency of various cardiac procedures done in men and women on a yearly basis. According to the study, 75% of angiography patients had hypertension. Patients with hypertension experience heart complications and cardiac-related disorders²⁰. Due to catheter resistance and severe pain with a substantial p value of 0.00, radial spasm was seen during cardiac catheterization. It has already been established that radial spasm and subsequent catheter resistance are related to catheter pain²¹ ²². The current study found no significant differences between the test and control groups for radial spasm, pain, result, catheter resistance, or procedure time. Another study revealed that the effectiveness of verapamil and nitrate in the long-term therapy of spasm is determined by the length of the treatment.

Due to a low budget and time frame, the study was only conducted at one institute. It should be researched using a large sample size and prolonged treatment. Despite these limitations, the study clearly suggested against using verapamil with nitrate during coronary angiography, while it might be an option in cases of prolonged spasm therapy.

CONCLUSION

Use of Verapamil, a calcium channel blocker, in combination with nitrate did not significantly reduce radial spasm during coronary angiography. The theory that calcium channel blockers could prevent radial artery spasm during angiography was nullified.

REFERENCES

- Gaudino M, Benedetto U, Fremes SE, Hare DL, Hayward P, Moat N, Moscarelli M, Di Franco A, Nasso G, Peric M, Petrovic I. Effect of calcium-channel blocker therapy on radial artery grafts after coronary bypass surgery. Journal of the American College of Cardiology. 2019 May 14;73(18):2299-306.
- Curtis E, Fernandez R, Lee A. The effect of vasodilatory medications on radial artery spasm in patients undergoing transradial coronary artery procedures: a systematic review. JBI Evidence Synthesis. 2017 Jul 1;15(7):1952-67.
 Özdemir HI, van Dijk CH, Özdemir AB, van Straten BH, Haanschoten
- Özdemir HI, van Dijk CH, Özdemir AB, van Straten BH, Haanschoten M, Soliman-Hamad MA. Preventing spasm of the radial artery conduit during coronary artery bypass grafting: Nicardipine versus verapamil. Journal of Cardiac Surgery. 2019 Dec;34(12):1505-10.
- Khan MZ, Patel K, Franklin S, Faruqi A, Ahmad W, Saeed J. Radial artery spasm: reviews and updates. Irish Journal of Medical Science (1971-). 2020 Nov;189(4):1253-8.
- Ruel M, Sun LY. Post-operative calcium-channel blocker use after radial artery grafting: Do we now have a definitive answer?. Journal of the American College of Cardiology. 2019 May 14;73(18):2307-9.

- Gaudino M, Fremes S, Schwann TA, Tatoulis J, Wingo M, Tranbaugh RF. Technical aspects of the use of the radial artery in coronary artery bypass surgery. The Annals of Thoracic Surgery. 2019 Aug 1;108(2):613-22.
- Schwann TA, Gaudino M, Baldawi M, Tranbaugh R, Schwann AN, Habib RH. Optimal management of radial artery grafts in CABG: Patient and target vessel selection and anti-spasm therapy. Journal of cardiac surgery. 2018 May;33(5):205-12.
- Audisio K, Halbreiner MS, Chadow D, Gaudino M. Radial artery or saphenous vein for Coronary artery bypass grafitng. Trends in Cardiovascular Medicine. 2021 Sep 23.
- Engin E, Yildirim Fİ, Durman DK, Ömeroğlu SN, Göksedef D, Teskin Ö, Balkanay OO, İpek G, Doğan BS. Relaxant effect of the prostacyclin analogue iloprost on isolated human radial artery: An approach for the reversal of graft spasm. Prostaglandins & Other Lipid Mediators. 2017 Nov 1;133:35-41.
- DeBoard Z, Kim HC, Brevig JK. Outcomes of Radial Artery Grafts Without Postoperative Calcium Channel Blocker Administration. Authorea Preprints. 2021 Dec 22.
- 11. He GW. Pharmacology to prevent spasm in conduits. State of the Art Surgical Coronary Revascularization. 2021 Feb 4:299.
- Shipulin V, Kozlov B, Nasrashvili G, Zatolokin V, Kuznetsov M, Panfilov D, Afanas' ev S. Intraoperative chlorpromazine treatment for prevention of radial artery spasm in aortocoronary bypass grafting. Interactive CardioVascular and Thoracic Surgery. 2017 Sep 1;25(3):493-5.
- Gürbak İ, Güler A, Panç C, Güner A, Ertürk M. Impaired Heart Rate Recovery May Predict Radial Artery Spasm in Patients Undergoing Coronary Angiography Via Radial Access. Koşuyolu Heart Journal. 2021;24(3):238-44.
- 14. Tatoulis J, Schwann TA. Long term outcomes of radial artery grafting in patients undergoing coronary artery bypass surgery. Annals of cardiothoracic surgery. 2018 Sep;7(5):636.
- Vefali V, Sariçam E. The comparison of traditional radial access and novel distal radial access for cardiac catheterization. Cardiovascular Revascularization Medicine. 2020 Apr 1;21(4):496-500.
- Eslami G, Golshani S, Moosazadeh M, Shadfar F. Intra-Arterial Labetalol and Nitroglycerin in Preventing Radial Artery Spasm Following Transradial Angiography: A New Approach. Pharmaceutical Sciences. 2020 Jun 27;26(2):142-9.
- 17. Mason PJ, Shah B, Tamis-Holland JE, Bitti JA, Cohen MG, Safirstein J, Drachman DE, Valle JA, Rhodes D, Gilchrist IC, American Heart Association Interventional Cardiovascular Care Committee of the Council on Clinical Cardiology; Council on Cardiovascular and Stroke Nursing; Council on Peripheral Vascular Disease; and Council on Genomic and Precision Medicine. An update on radial artery access and best practices for transradial coronary angiography and intervention in acute coronary syndrome: a scientific statement from the American Heart Association. Circulation: Cardiovascular Interventions. 2018 Sep;11(9):e000035.
- Tamim M, Alexiou C, Al-Hassan D, Al-Faraidy K. Prospective randomized trial of endoscopic vs open radial artery harvest for CABG: clinical outcome, patient satisfaction, and midterm RA graft patency. Journal of Cardiac Surgery. 2020 Sep;35(9):2147-54.
- patency. Journal of Cardiac Surgery. 2020 Sep;35(9):2147-54.
 19. Sandoval Y, Bell MR, Gulati R. Transradial artery access complications. Circulation: Cardiovascular Interventions. 2019 Nov;12(11):e007386.
- Wada K, Otani N, Toyooka T, Takeuchi S, Tomiyama A, Mori K. Superficial temporal artery to anterior cerebral artery hemi-bonnet bypass using radial artery graft for prevention of complications after surgical treatment of partially thrombosed large/giant anterior cerebral artery aneurysm. Journal of Stroke and Cerebrovascular Diseases. 2018 Dec 1;27(12):3505-10.
- Chen Y, Ke Z, Xiao J, Lin M, Huang X, Yan C, Ye S, Tan X. Subcutaneous injection of nitroglycerin at the radial artery puncture site reduces the risk of early radial artery occlusion after transradial coronary catheterization: a randomized, placebo-controlled clinical trial. Circulation: Cardiovascular Interventions. 2018 Jul;11(7):e006571.
- 22. Raelson C, Ahmed B. Prevention and Management of Radial Access Complications. Current Treatment Options in Cardiovascular Medicine. 2020 Apr;22(4):1-2.