Original Article

Periarterial Injections of Nitroglycerin Facilitate Radial Artery Cannulation

Reza Kiani[1], MD ; Mohammad Javad Alemzadeh-Ansari[1], MD; Hamid Reza Sanati[1]*, MD; Reza Hashemi[2], MD; Ata Firouzi[1], MD; Farshad Shakerian[1], MD; Ali Zahedmehr[1], MD; Mohammad Mehdi Peighambari[1], MD; Safar Ali Abdolrahimi[1], MD

ABSTRACT

Background: Facilitating radial artery cannulation is important among patients undergoing cardiac catheterization. The aim of this study was to evaluate the efficacy of periarterial injections of nitroglycerin by inexperienced operators in facilitating radial artery cannulation.

Method: This randomized clinical trial study was conducted on patients who underwent transradial cardiac catheterization for coronary artery disease evaluation. The patients were randomly divided into 2 groups: Group I was the control and Group II received an additional 500 μG of nitroglycerin subcutaneously. The procedure was done by cardiologists trained for the fellowship of interventional cardiology (inexperienced operators). All the participants were monitored for the occurrence of radial artery spasm, number of punctures before successful cannulation, and the radial artery access time.

Results: After the exclusion of 16 patients, 144 patients (118 men and 26 women) at an average age of 55.7 ± 10.2 years were randomly divided into 2 groups: Group I (control, n = 73) and Group II (n = 71). The number of punctures before cannulation was markedly lower in Group II than in the control group (1.9 ± 0.64 vs 2.2 ± 1.04; P = 0.045). The radial artery access time was shorter and radial artery spasm was less prevalent in Group II, but these parameters were not statistically significantly different between the 2 groups.

Conclusions: Periarterial injections of nitroglycerin (500 μG subcutaneously) by inexperienced operators significantly reduced the number of punctures during transradial cardiac catheterization. ***(Iranian Heart Journal 2017; 18(4):6-11)***

KEYWORDS: Nitroglycerin, Radial artery, Angiography

[1]Cardiovascular Intervention Research Center, Rajaie Cardiovascular, Medical, and Research Center, Iran University of Medical Sciences, Tehran, IR Iran
[2] Rajaie Cardiovascular, Medical, and Research Center, Iran University of Medical Sciences, Tehran, IR Iran

***Corresponding Author:** Hamid Reza Sanati, MD; Cardiovascular Intervention Research Center, Rajaie Cardiovascular, Medical, and Research Center, Iran University of Medical Sciences, Tehran, IR Iran.
Email: Sanati.md@hotmail.com **Tel :** 09123765828

Received: May 30, 2017 **Accepted:** September 25, 2017

Cardiac catheterization is a traditional method for diagnosing coronary artery disease (CAD) and providing percutaneous intervention. [1] The most common percutaneous access sites are femoral, radial, and brachial arteries. [2] Although the femoral artery is preferred for coronary procedures because of its larger diameter, this approach has several limitations. It is relatively contraindicated in some circumstances—for instance in patients receiving anticoagulation treatment and in the presence of peripheral arteriopathy. [1, 3]

The transradial access, which was first reported in 1989, seems to be able to overcome most of the problems related to the vascular approach post cardiac catheterization. However, radial artery spasm (RAS), which can occur at any phase of the procedure, is the leading reason for failed artery cannulation and patient discomfort. The rate of RAS incidence ranges from 2% to 34% according to different studies. [4, 5] Accordingly, it is beneficial to prevent RAS and its consequent complications with a view to achieving a successful procedure. A spasmolytic drug is needed to prevent RAS during coronary procedures in the transradial access. [6] It has been documented that RAS during transradial percutaneous intervention is effectively prevented by the administration of antispasmodic agents. [7-9] There are different studies reporting the effects of the intra-arterial application of various vasodilators on reducing the incidence of RAS during radial artery cannulation. Nonetheless, data on the individual efficacy of the subcutaneous administration of this agent are not conclusively established. Nitroglycerine is a low-cost vasodilator with a short half-life and minor side effects; it, therefore, seems an appropriate choice for treatment. [10]

The aim of the present study was to investigate the efficacy of periarterial injections of nitroglycerin in facilitating radial artery cannulation by inexperienced operators (fellows of cardiology) among patients undergoing transradial cardiac catheterization.

METHOD

This randomized double-blind clinical trial study was conducted on patients who underwent transradial cardiac catheterization for CAD assessment between April 2012 and January 2013 at Rajaie Cardiovascular, Medical, and Research Center, Iran University of Medical Sciences, Tehran, Iran. The procedure was done by cardiologists trained for the fellowship of interventional cardiology (inexperienced operators).

The exclusion criteria comprised an inadequate ulnar collateral supply (assessed via the Allen test), history of allergy to the agent, and previous treatment via the transradial approach. The patients included were randomly divided into 2 groups. Group I (control) was placed under observation without receiving any additional treatment**,** and Group II received additional nitroglycerin **(**500 μG subcutaneously**)**. Random block sizes were used to conceal the treatment allocation from the patients, and randomization was stratified by the clinical center. Allocation concealment was achieved using the sealed envelope technique. Local anesthesia before cannulation was effected via a subcutaneous injection of lidocaine hydrochloride 2% (10 mg) at about 1 inch above the styloid process (around the radial artery**)**. Group II received an additional 500 μG of nitroglycerin in the syringe containing lidocaine hydrochloride by the nurse. The investigators were blind to the contents of the syringe. All the participants were monitored for the occurrence of RAS and the number of punctures before successful cannulation. RAS was defined as a severe and painful limitation in the maneuvering of the catheter and the flattening of the arterial waves, with or without angiographic confirmation. Additionally, the radial artery access time, success rate of artery cannulation, and hemodynamics were reported. Successful cannulation of the radial artery was considered the primary end point, and other parameters

such as the number of punctures, RAS, hematoma, blood jetting, and radial artery access time were regarded as the secondary end points.

The standard cardiac catheterization technology was utilized. All the patients provided written informed consent for participation in the study, and the study protocol was approved by the Review Board and the Ethics Committee of Iran University of Medical Sciences.

Statistical Analysis

The data are expressed as means ± standard deviations (SDs) for the continuous and as percentages for the discrete variables. The Independent Samples *t* Test or the Mann–Whitney *U* test was used to compare the continuous variables between the groups. The χ^2 test was employed for the statistical analysis of the categorical variables, and the categorical variables were compared using the Fisher exact test, as appropriate. A *P* value less than 0.05 was considered statistically significant. The statistical analyses were conducted using SPSS, version 13.1 (SPSS Inc, Chicago, IL).

RESULTS

Between April 2012 and January 2013, a total of 160 patients, who underwent transradial cardiac catheterization for CAD evaluation, were enrolled into the present study. Of this total, 16 patients with a negative Allen test, history of allergy to the agent, or previous treatment via the transradial approach were excluded. Consequently, 144 patients (118 men and 26 women) at an average age of 55.7 ± 10.2 years were randomly divided into 2 groups. Group I (control, n = 73) was placed under observation without receiving any additional treatment, and Group II (n = 71) was administered nitroglycerin (500 μG subcutaneously) (Fig. 1). The demographic characteristics of the patients, who underwent transradial cardiac catheterization, are shown in Table 1, which demonstrates no significant differences between the 2 groups.

The clinical and procedural characteristics of the patients in the 2 groups are compared in Table 2. Among the 144 patients, cannulation failed in 3 patients. The number of punctures before cannulation was significantly lower in the nitroglycerin-injected patients (Group II; *P* = 0.045) (Fig. 2). In Group II, RAS was observed only in 1 patient, and the time to relieve RAS was 240 seconds. The radial artery access time was faster in the presence of nitroglycerin administration than in the control group; the differences, however, failed to constitute statistical significance. Complications, including radial artery perforation or dissection, were not observed in both groups. In Group II, mild headache was reported in 6 patients and changes in the systolic blood pressure were observed in only 1 patient, which was resolved swiftly.

Table1. Demographic characteristics of the patients, who underwent transradial cardiac catheterization

Demographic Characteristics	Group I (n=73)	Group II (n=71)	*P*
Age (y)	56.2±10.9	55.1±9.5	0.516
Male	60 (82.2%)	58 (81.7%)	0.938
Diabetes	15 (20.5%)	11 (15.5%)	0.430
Smoking	23 (31.5%)	24 (33.8%)	0.769
BMI (kg/m^2)	28.1±15.5	27.3±4.4	0.166

Values are expressed as mean ± SD or n (%).
BMI, Body mass index

Table 2. Clinical and procedural characteristics of the patients, who underwent transradial cardiac catheterization

Clinical and Procedural Characteristics	Group I (n=73)	Group II (n=71)	*P*
Successful cannulation of the radial artery	71 (97.26%)	70 (98.59%)	0.576
Number of punctures	2.2±1.04	1.9±0.64	0.045
Radial artery spasm	3 (4.11%)	1 (1.41%)	0.324
Hematoma	1 (1.37%)	1 (1.41)	0.984
Blood jetting	32 (43.83%)	34 (47.79%)	0.626
Radial artery access time (s)	241.2±72.2	228.7±62	0.290

Values are expressed as mean ± SD or n (%).

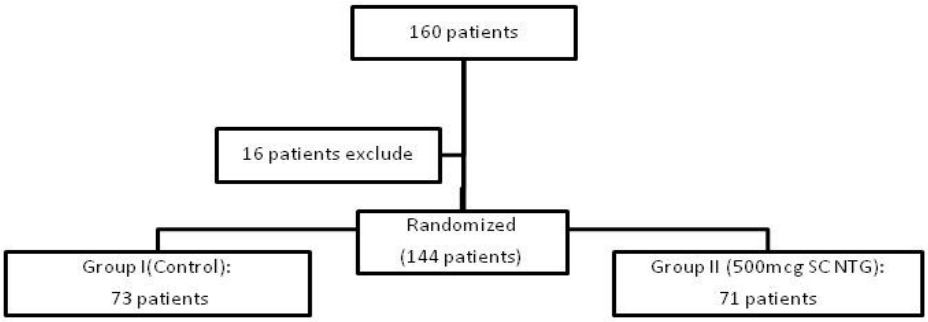

Figure 1. Study design

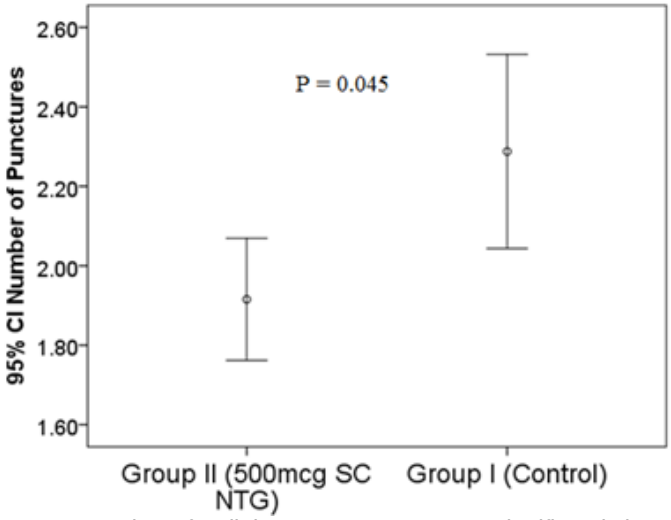

Figure 2. Number of radial artery punctures was significantly lower in the patients receiving additional nitroglycerin (500 µG subcutaneously).

DISCUSSION

Since the human radial artery has a high receptor-mediated vasodilation and vasoconstriction capability, it exhibits more spastic characteristics. The latter supports the necessity of utilizing pharmacologic intervention to relieve spasm during cardiac catheterization. [11, 12] A large-scale study on the predictors of RAS showed that female gender, small radial artery diameter, diabetes, and unsuccessful access at first attempt were the independent predictors of RAS. [13] It has been documented that the mechanism of RAS is mediated by circulating hormonal factors, which via stimulating some specific receptors regulate the tonic contraction of the radial artery smooth muscle layer. [4] Failure to puncture the radial artery, dissection, and RAS are the common causes of unsuccessful cannulation of coronary arteries. [3, 14]

In our study, radial artery puncture was done by cardiologists trained for the fellowship of interventional cardiology (inexperienced operators). We found that among the patients who were subcutaneously injected with nitroglycerin, the number of the punctures before cannulation was markedly less than that in the control group (1.9 ± 0.64 vs 2.2 ± 1.04; *P* = 0.045). Furthermore, the radial artery access time was shorter and RAS was less prevalent in the nitroglycerin-administered group, but these

parameters were not statistically significantly different between the 2 groups.

Candemir and colleagues [15] reported no significant changes in their nitroglycerin-administered patients with respect to the number of punctures before cannulation. The authors demonstrated that the radial artery access time improved significantly after the application of nitroglycerin. However, RAS was insignificantly less frequently observed in their patients.

A prophylactic intra-arterial administration of vasodilators and spasmolytic agents has been shown to significantly reduce RAS. In a study, the rate of RAS was reduced from 20.4% to 4% with an intra-arterial administration of nitroglycerin alone or in conjunction with verapamil. [16] Also, nitroglycerin safely and without affecting blood pressure increases the radial artery diameter and, thus, facilitates radial artery catheterization. [15, 17]

Some studies have evaluated the effects of the periarterial injection of antispasmodic agents in addition to intra-arterial spasmolytic cocktails. Ouadhour et al [18] demonstrated that the subcutaneous application of 0.5 mg of isosorbide dinitrate, as an adjunctive drug to local anesthesia in the radial area, facilitated the artery puncture without increasing patient discomfort. Ezhumalai et al [19] reported that subcutaneously infiltrated nitroglycerin conferred significant vasodilation in the radial artery, reduced pre-cannulation spasm, and enhanced the palpability of the radial pulse. Accordingly, the authors concluded that subcutaneously infiltrated nitroglycerin facilitated the puncture of the radial artery.

According to Pancholy et al, [12] a subcutaneous administration of nitroglycerin is more advantageous than its sublingual application in terms of facilitating radial artery cannulation. This observation supports the theory that periarterial (local) injections of nitroglycerin have fewer systemic side effects and may improve successful cannulation during radial cardiac catheterization. Turan et al [20] in a recent study showed that all adverse events allied to transradial angiography—including multiple punctures, RAS, access site crossover, hypotension, and bradycardia—were associated with nitroglycerin and radial artery occlusion was very similar in both intra-arterial and sublingual groups. [20]

CONCLUSIONS

Periarterial injections of nitroglycerin (500 μG subcutaneously) by inexperienced operators significantly reduced the number of punctures during transradial cardiac catheterization and, thus, facilitated radial artery cannulation.

Conflict of Interest: None declared.

REFERENCES

1. Hamel WJ. Femoral artery closure after cardiac catheterization. Critical Care Nurse. 2009;29(1):39-46.
2. Schneider P. Endovascular skills: guidewire and catheter skills for endovascular surgery: 3rd ed. Informa Healthcare, CRC Press, Boca Raton, FL; 2008.
3. Archbold RA, Robinson NM, Schilling RJ. Radial artery access for coronary angiography and. BMJ. 2004;329:443-6.
4. Shivaraju A, Shroff A. Radial artery spasm: pick the right cocktail and relax. The Journal of invasive cardiology. 2011;23(10):405-6.
5. Kristić I, Lukenda J. Radial artery spasm during transradial coronary procedures. The Journal of invasive cardiology. 2011;23(12):527-31.
6. Dharma S, Shah S, Radadiya R, Vyas C, Pancholy S, Patel T. Nitroglycerin plus diltiazem versus nitroglycerin alone for spasm prophylaxis with transradial approach. J Invasive Cardiol. 2012;24(3):122-5.
7. Coppola J, Patel T, Kwan T, Sanghvi K, Srivastava S, Shah S, et al. Nitroglycerin, nitroprusside, or both, in preventing radial artery spasm during transradial artery

catheterization. The Journal of invasive cardiology. 2006;18(4):155-8.

8. Varenne O, Jégou A, Cohen R, Empana JP, Salengro E, Ohanessian A, et al. Prevention of arterial spasm during percutaneous coronary interventions through radial artery: the SPASM study. Catheterization and cardiovascular interventions. 2006;68(2):231-5.

9. Kiemeneij F, Vajifdar BU, Eccleshall SC, Laarman G, Slagboom T, Wieken Rvd. Evaluation of a spasmolytic cocktail to prevent radial artery spasm during coronary procedures. Catheterization and cardiovascular interventions. 2003;58(3):281-4.

10. Marsh N, Marsh A. A short history of nitroglycerine and nitric oxide in pharmacology and physiology. Clinical and Experimental Pharmacology and Physiology. 2000;27(4):313-9.

11. He G-W, Yang C-Q. Radial artery has higher receptor-mediated contractility but similar endothelial function compared with mammary artery. The Annals of thoracic surgery. 1997;63(5):1346-52.

12. Pancholy SB, Coppola J, Patel T. Subcutaneous administration of nitroglycerin to facilitate radial artery cannulation. Catheterization and cardiovascular interventions. 2006;68(3):389-91.

13. Jia D-a, Zhou Y-j, Shi D-m, Liu Y-Y, Wang J-L, Liu X-l, et al. Incidence and predictors of radial artery spasm during transradial coronary angiography and intervention. Chinese medical journal. 2010;123(7):843-7.

14. Talwar S, Owens P, Motwani J, editors. The ulnar artery revisited: a useful alternative access site for coronary angiography and intervention. Heart; 2003:89 (Suppl. 1): A 18.

15. Candemir B, Kumbasar D, Turhan S, Kilickap M, Ozdol C, Akyurek O, et al. Facilitation of radial artery cannulation by periradial subcutaneous administration of nitroglycerin. Journal of Vascular and Interventional Radiology. 2009;20(9):1151-6.

16. Chen C-W, Lin C-L, Lin T-K, Lin C-D. A simple and effective regimen for prevention of radial artery spasm during coronary catheterization. Cardiology. 2005;105(1):43-7.

17. Majure DT, Hallaux M, Yeghiazarians Y, Boyle AJ. Topical nitroglycerin and lidocaine locally vasodilate the radial artery without affecting systemic blood pressure: a dose-finding phase I study. Journal of critical care. 2012;27(5):532. e9-. e13.

18. Ouadhour A, Sideris G, Smida W, Logeart D, Stratiev V ,Henry P. Usefulness of subcutaneous nitrate for radial access. Catheterization and cardiovascular interventions. 2008;72(3):343-6.

19. Ezhumalai B, Satheesh S, Jayaraman B. Effects of subcutaneously infiltrated nitroglycerin on diameter, palpability, ease-of-puncture and pre-cannulation spasm of radial artery during transradial coronary angiography. Indian heart journal. 2014;66(6):593-7.

20. Turan B, Daşlı T, Erkol A, Erden İ. Effectiveness of sublingual nitroglycerin before puncture compared with conventional intra-carterial nitroglycerin in transradial procedures: a randomized trial. Cardiovascular Revascularization Medicine. 2015;16(7):391-6.