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Original Article

Effects of subcutaneously infiltrated nitroglycerin on diameter, palpability, ease-of-puncture and pre-cannulation spasm of radial artery during transradial coronary angiography

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ABSTRACT

Background: The success of transradial catheterization depends on meticulous access of radial artery which in turn depends on palpating a good radial pulse.
Objectives: Our objectives were to analyze the effects of subcutaneously infiltrated nitroglycerin on diameter of radial artery, palpability of radial pulse, ease-of-puncture and pre-cannulation spasm of radial artery during transradial coronary angiography.
Methods: Patients undergoing transradial coronary angiography were randomized to Group NL or Group SL. In Group NL, 3 ml of solution containing nitroglycerin and lignocaine was infiltrated subcutaneously at the site intended for puncture of radial artery. Similarly, saline and lignocaine were infiltrated in Group SL. Diameter of radial artery was objectively assessed by ultrasonography. Measurements were performed at baseline and repeated at 1 min after injecting the solutions. The ease-of-puncture was evaluated by the number of punctures and the time needed for successful access of radial artery.
Results: Both groups had 100 patients each. Baseline diameter of radial artery was similar between two groups. The post-injection diameter of radial artery increased by 26.3% in Group NL and 11.4% in Group SL. Nitroglycerin significantly improved the palpability of radial pulse, reduced the number of punctures and shortened the time needed for successful access of radial artery. Pre-cannulation spasm of radial artery occurred in 1% of Group NL and 8% of Group SL.
Conclusions: Subcutaneously infiltrated nitroglycerin leads to significant vasodilation of radial artery. This avoids pre-cannulation spasm of radial artery, enhances palpability of the radial pulse and thus makes the puncture of radial artery easier.

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1. Introduction

Transradial approach of cardiac catheterization is considered more advantageous than transfemoral approach because it is more comfortable to the patient, associated with lesser incidence of access site complications, reduces the duration and cost of hospitalization.[1–3]

Unlike transfemoral route, transradial approach for coronary angiography requires a longer learning curve.[4] The success of transradial coronary angiography depends on obtaining a meticulous access of radial artery which in turn depends on palpating a good radial pulse. Although spasm of radial artery is usually encountered after cannulation and catheterization of radial artery,[5,6] sometimes it may occur prior to cannulation due to multiple painful punctures.[7] Radial pulse is usually lost with onset of this pre-cannulation spasm necessitating the switching over of approach to transfemoral route. The radial pulse may also become feeble after subcutaneous infiltration of local anesthesia and hence the puncture becomes difficult. This is an important reason for most operators hesitating to infiltrate the site of puncture with adequate local anesthesia, which is usually 2% lignocaine.

Previous studies proved that intravenous,[8,9] topical,[10,11] and intra-arterial[12–14] routes of administration of nitroglycerin lead to vasodilation of radial artery. Very few studies had tested the effect of subcutaneous route of administration of nitrate/nitroglycerin on access of radial artery but they had shortcomings such as subjective endpoints, small sample size and lack of randomization.[7,15,16] We decided to overcome all these shortcomings and hence we undertook our study.

2. Objectives

Our objectives were to analyze the effects of subcutaneously infiltrated nitroglycerin on diameter of radial artery, palpability of radial pulse, ease-of-puncture and pre-cannulation spasm of radial artery during transradial coronary angiography.

3. Materials and methods

This prospective, randomized, double blinded, placebo controlled study was carried out in a single center over a period of 6 months. Patients planned for transradial coronary angiography were included in this study. The exclusion criteria were hypotension (systolic blood pressure <100 mm Hg), prior cannulation of radial artery and abnormal Allen's test. Informed written consent was obtained from the participants and ethical committee approval was obtained from the institute for this study.

The procedure was carried out inside the cath lab just before starting transradial coronary angiography. Using block randomization, patients were allocated into either of the two groups namely (a) Group NL (nitroglycerin + lignocaine) and (b) Group SL (saline + ligocaine). Patients of Group NL received 3 ml of 'Solution A' containing 1 ml of nitroglycerin at a concentration of 500 mcg/ml and 2 ml of 2% lignocaine, while those of Group SL received 3 ml of 'Solution B' containing 1 ml of normal saline and 2 ml of 2% lignocaine. Both these solutions were colorless, odorless and looked similar in appearance.

Baseline diameter of radial artery was assessed by experienced observer using 9 MHz vascular probe and echocardiographic machine. This observer was different from the operator performing the procedure of transradial coronary angiography. The distance between lumen–intima interfaces in the far wall and near wall of radial artery measured at peak of *R* wave of electrocardiogram (ECG) was taken as diameter of radial artery. Three successive measurements were performed and the mean was taken as the diameter of radial artery. Noninvasive blood pressure, ECG and pulse oximetry were continuously monitored during the procedure.

Transradial coronary angiography was performed by well experienced operator in this study. The operator assessed the baseline palpability of radial artery pulse and subcutaneously infiltrated 3 ml of local anesthetic solution at the site of maximal radial pulse just proximal to the wrist in the lateral aspect of the right forearm of patients using 26G hypodermic needle. One minute after the injection of local anesthetic solution, the diameter of radial artery was assessed again by the same observer. Then the operator reassessed the radial pulse and graded the change in palpability of radial pulse from 0 to 4 as follows:

- Grade 0: radial pulse not palpable after the injection
- Grade 1: radial pulse became feeble after the injection
- Grade 2: palpability of radial pulse remained the same after the injection
- Grade 3: radial pulse became better palpable after the injection
- Grade 4: radial pulse became bounding after the injection.

Radial artery was then punctured by the operator using 20G cannula. The ease-of-puncture was evaluated by (i) the number of punctures needed for successfully puncturing radial artery and (ii) the time needed for successful access of radial artery. The latter is defined as the period from the injection of local anesthetic solution to the successful insertion of sheath into radial artery. Pre-cannulation spasm was defined as spasm of radial artery occurring prior to insertion of sheath.

Statistical analyses were performed using SPSS software (SPSS Inc. Released 2007. SPSS for Windows, Version 16.0. Chicago: SPSS Inc). All statistical analyses were carried out for 5% level of significance and two-tailed p value < 0.05 was considered significant for all tests in this study.

4. Results

Out of 200 patients included in this study, 100 patients were randomly allocated to each of the two groups. The clinical profile of these patients is mentioned in Table 1. Patients included in the both the groups were age and sex matched. The risk factors for coronary artery disease such as obesity, diabetes mellitus, hypertension, smoking and dyslipidemia were also matched between the two groups. The assessment

Table 1 – Clinical profile of patients.

Parameters	Group NL $n = 100$	Group SL $n = 100$	p Value
Age in years (mean ± SD)	53.1 ± 9.1	55.1 ± 9.6	0.12*
Males	61 (61%)	58 (58%)	0.77†
Females	39 (39%)	42 (42%)	0.77†
Obesity	37 (37%)	33 (33%)	0.66†
Hypertension	43 (43%)	49 (49%)	0.48†
Diabetes	58 (58%)	63 (63%)	0.56†
Dyslipidemia	78 (78%)	70 (70%)	0.26†
Smoking	36 (36%)	32 (32%)	0.65†

Note:†Chi-square test; NL: nitroglycerin + lignocaine; SL: saline + lignocaine; SD: standard deviation; *Student's unpaired t test.

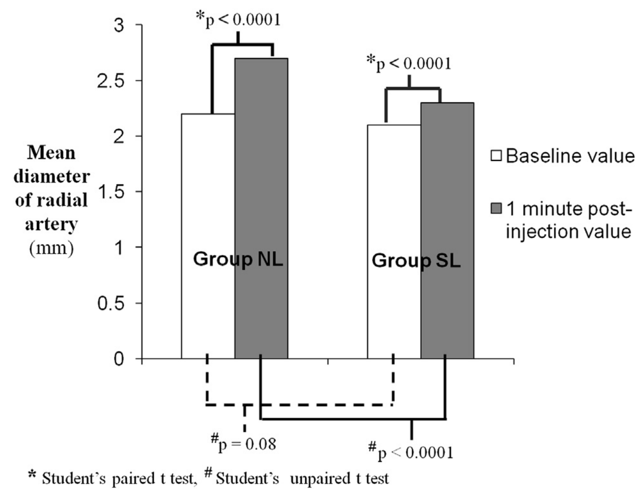

Fig. 2 – Comparison of diameter of radial artery: graph shows comparison of mean diameter of radial artery between Group NL and Group SL. Graph also shows comparison between baseline and 1 min post-injection values of mean diameter of radial artery in each group.

of diameter of radial artery using vascular probe is shown in Fig. 1. The mean values of baseline diameter of radial artery between Group NL & Group SL were similar (2.2 ± 0.3 mm and 2.1 ± 0.4, $p = 0.08$; Student's unpaired t test; see Fig. 2). One minute after the injection of local anesthetic solutions, diameter of radial artery increased by 26.3% from baseline (2.7 ± 0.4 mm from 2.2 ± 0.3 mm, $p < 0.0001$, Student's paired t test) in Group NL while it increased by 11.4% from baseline (2.3 ± 0.4 mm from 2.1 ± 0.4 mm, $p < 0.0001$, Student's paired t test) in Group SL. The post-injection diameter of radial artery was significantly higher in Group NL compared with Group SL (2.7 ± 0.4 mm vs. 2.3 ± 0.4 mm, $p < 0.0001$, Student's unpaired t test).

Pre-cannulation spasm of radial artery occurred in 1% of Group NL but in 8% of Group SL ($p = 0.03$, Fisher's exact test). There was no significant variation in heart rate and blood pressure during the procedure (see Table 2). There were no adverse events noted with the usage of nitroglycerin in this study.

The mean grade of change in palpability of pulse in Group NL was 2.7 ± 0.8 while that in Group SL was 1.7 ± 0.9.

Fig. 1 – Assessment of diameter of radial artery: ultrasonographic image shows assessment of diameter of radial artery at peak of R wave in electrocardiogram using 9 MHz vascular probe.

The median (50th percentile) number of punctures needed for successfully puncturing radial artery in Group NL was 1 (range: 1–4) while that in Group SL was 2 (range: 1–5). There was significant difference between Group NL and Group SL with respect to the grading of change in palpability of pulse ($p < 0.0001$, Student's unpaired t test) and the number of punctures of radial artery ($p < 0.0001$, Mann–Whitney U test). Similarly there was statistically significant difference between Group NL and Group SL with respect to the time needed for successful access of radial artery (162.8 ± 4.7 s vs. 207.2 ± 10.9 s, $p < 0.0001$; Student's unpaired t test).

Linear regression analysis was done and found that diameter of radial artery significantly predicted palpability of radial pulse ($R^2 = 0.06$, $p = 0.02$), number of punctures ($R^2 = 0.07$, $p = 0.006$) and time needed for successful access of radial artery ($R^2 = 0.07$, $p = 0.009$) in Group NL.

Table 2 – Alteration in hemodynamics with subcutaneous infiltration of nitroglycerin.

Parameter	Group NL Mean ± SD	Group SL Mean ± SD
Mean BP (mm Hg)		
Baseline	92.5 ± 10.7	93.8 ± 10.5
1 min post-injection	92.4 ± 10.1	93.7 ± 9.9
p Value	0.38*	0.82*
HR (bpm)		
Baseline	72.1 ± 10.3	73.7 ± 9.6
1 min post-injection	72.6 ± 9.7	74.1 ± 9.2
p Value	0.07*	0.15*

Note: BP: blood pressure; HR: heart rate; NL: nitroglycerin + lignocaine; SL: saline + lignocaine; SD: standard deviation; *Student's paired t test.

5. Discussion

In our study, it was objectively found that subcutaneous administration of nitroglycerin along with the routine local anesthetic preparation leads to significant increase in diameter of radial artery than that produced by lignocaine alone, as assessed by ultrasonography. This vasodilation of radial artery produced by subcutaneously administered nitroglycerin in turn leads to significant improvement in palpability of radial pulse, thereby reducing the number of punctures needed for accessing radial artery, decreasing the time needed for successful access and avoiding pre-cannulation spasm of radial artery.[7,15,16]

Ouadhour et al demonstrated that subcutaneous injection of dinitrate isosorbide along with lidocaine improved the accessibility of radial artery, but the endpoints were subjective and effect of nitroglycerin was not tested in this study.[15] Pancholy et al found that subcutaneous route compared with sublingual route of administration of nitroglycerin relieved radial artery spasm caused by failed attempts at cannulation.[7] This study had small sample size and subjective endpoints; moreover it was not randomized or placebo controlled. Study done by Candemir et al states that periradial infiltration of nitroglycerin along with prilocaine facilitated radial artery cannulation.[16] Though vasodilation of radial artery was objectively measured using ultrasonography by Candemir et al, this study also had relatively small sample size and lacked in randomization.[16] We had overcome these shortcomings in our study.

Subcutaneously administered nitroglycerin stays extravascular and acts locally for a longer duration to produce vasodilation.[7] The presence of functional endothelium is not essential for the vasodilatory action of nitroglycerin.[17] After entering the vascular smooth muscle, nitroglycerin undergoes rapid enzymatic bioconversion to nitric oxide.[17] The liberated nitric oxide activates intracellular soluble guanylate cyclase pathway, which in turn reduces cytoplasmic calcium level leading to smooth muscle relaxation and vasodilation.[17,18]

Although small in diameter (2.6 ± 0.4 mm),[19] radial artery has relatively thicker tunica media than many other muscular arteries. Hence, it is also more prone for vasospasm and this spasticity of radial artery has been attributed to greater alpha-1 innervation[6] and, higher endothelin-1 and angiotensin II receptor-mediated contractility.[20] Radial artery is more sensitive to nitroglycerin than other muscular arteries.[21]

Interestingly, in our study, not only nitroglycerin but also lignocaine, the local anesthetic infiltrated subcutaneously vasodilated radial artery. Inhibition of action potentials by blocking sodium channels in the sympathetic nerves and release of nitric oxide are the reasons for vasodilation of radial artery after infiltration of lignocaine.[22–25] Paradoxical vasoconstriction had also been reported with lignocaine injection, particularly at lower concentration.[13]

Similar to prior studies, no adverse event or hemodynamic alteration was encountered with subcutaneous infiltration of nitroglycerin in our study.[18]

5.1. *Limitations*

All patients of this study were taking standard anti-ischemic medications including nitrates. We did not study the confounding effect of vasodilation produced by these medications. Inter-observer and inter-operator variability was also not studied. We intend to address these issues in a subsequent study involving patients undergoing transradial percutaneous coronary intervention.

6. Conclusions

Subcutaneously infiltrated nitroglycerin significantly increases the diameter of radial artery. This vasodilation avoids pre-cannulation spasm of radial artery and enhances the palpability of the radial pulse. The number of punctures and the time needed for successful access of radial artery are substantially reduced. Thus, the puncture of radial artery becomes easier. Hence nitroglycerin can be added to the routine local anesthetic preparation and subcutaneously administered for enabling access of radial artery during transradial coronary angiography.

Conflicts of interest

All authors have none to declare.

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