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# **ORIGINAL RESEARCH**

# Use of topical nitroglycerin and lidocaine in locally vasodilating the radial artery

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#### Abstract

**Introduction:** In medical facilities all throughout the world, many specialists adopt the radial method for coronary angioplasty. In comparison to conventional femoral access, using radial access is linked to less vascular problems and the same success rate. Spasm of the radial artery is one of the key issues with this approach. The radial artery's short size and high density of alpha-1 adrenergic receptors in this artery can cause the spasm to progress more quickly. The purpose of this study was to determine whether radial artery dilation and decreased patient pain and sympathetic response may occur during radial puncture using a topical gel formulation of lidocaine, verapamil, and nitroglycerin.

**Methods:** In a single-center, double-blind research, patients receiving elective trans-radial angioplasty were randomly assigned to the placebo or therapeutic gel groups. 1 cm near the radial styloid process, a placebo or therapeutic gel is placed. Ultrasound was used to gauge the size of the radial artery. Visual analogue scale (VAS) was used to measure radial pain, and changes in systolic (SBP), diastolic (DBP), and heart rate were used to measure the sympathetic response (HR). The radial artery spasm score was used to determine the incidence of spasm.

**Results:** This study involved 60 patients, with 30 patients in each group. When compared to the placebo group, the group receiving the therapeutic gel showed a substantial increase in radial artery size (mean diameter, mm:  $2.95 \pm 0.48$  vs.  $2.54 \pm 0.43$ , p = 0.001; area, cm2: 0.07 vs. 0.05, p = 0.001). Patients receiving therapeutic gel experienced considerably less radial discomfort during radial puncture (4 (1-5) vs. 2 (1-2), p = 0.003. There were no radial artery spasms in any of the groups.

**Conclusion:** According to our findings, giving patients having trans-radial angioplasty a topical gel combination of verapamil, nitroglycerin, and lidocaine before to the procedure greatly expands the size of the radial artery and significantly lessens radial pain during radial puncture.

**Keywords:** Radial artery; Catheterization; Invasive monitoring; Coronary angiography; Vasodilation

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#### Introduction

In the emergency room, intensive care unit, and operating room, radial artery cannulation is a routine operation used for arterial blood gas analysis, invasive blood pressure monitoring, and as continuous access for frequent blood samples. Additionally, the use of radial artery cannulation for percutaneous intervention (PCI) and diagnostic coronary angiography is expanding quickly. [1]

Small arterial size is frequently the cause of radial artery cannulation failure in clinical practise, and repeated attempts to cannulate the artery can lead to haemorrhage, radial artery dissection, vasospasm, pseudoaneurysm development, discomfort, and vascular thrombosis [2-4]. The modified Allen test and/or Barbeau test to determine the arterial's patency have been used as methods for enhancing radial artery cannulation [5], as well as direct visualisation of the vessel using ultrasonography at the moment of cannulation and the use of a wire guided cannula [6-8].

The vasodilator nitroglycerin (NTG) has been demonstrated to be beneficial in treating radial artery spasm when delivered from within the artery for radial artery catheterization during coronary angiography [9]. Others have successfully treated radial artery spasm with subcutaneous injections of NTG [10]. It has been demonstrated that subcutaneous injections of dinitrate isosorbide and lidocaine increase the success rates of radial artery cannulation [11]. The use of transdermal NTG prior to cannulation has also been discussed [12], although to our knowledge, the efficacy of this method has not been examined. It is unknown if NTG applied transdermally can raise radial artery diameter (RAD) and avoid spasm prior to cannulation, or if NTG combined with lidocaine will lessen this effect.

In light of this, we created the current study to investigate the claims that topical NTG will act locally and directly on the radial artery to cause vasodilation and that topical lidocaine combined with topical NTG will cause significantly more radial artery dilatation than topical lidocaine alone.

#### Materials and methods

Single-center, randomised, double-blind, placebo-controlled design characterised the trial. All subjects gave written informed permission, and the study received approval from the institutional review board of AIIMS. Healthy volunteers over the age of 18 were sought out. A systolic blood pressure of less than 90 mm Hg, a history of radial artery catheterization within the previous year, the presence of liver, cardiovascular, rheumatologic, or renal disease, current treatment with any vasodilator therapy, and the absence of radial artery blood flow in one or both arms are all exclusion criteria.

The topical gel was made by dissolving the gelling agent, hydroxylpropyl methylcellulose (HPMC), in water while stirring continuously. The correct amounts of verapamil (15%), lidocaine (5%), and nitroglycerin (2%) were added to the aqueous phase to create the therapeutic gel. The placebo gel was tasteless and colourless and had the same appearance as the therapeutic gel.

Patients were divided into the intervention and placebo groups after randomization. A high frequency (13 MHz) linear array transducer was used to assess both groups' baseline right radial artery diameter. The radial styloid process was 1 cm apart from the location of all ultrasonography measurements. 30 minutes to 3 hours prior to arterial puncture, the right wrist was wrapped with a clear bandage and either the therapeutic gel (2 g) or the placebo (2 g) was put over the radial pulse. The topical gel was removed after the patient was admitted to the catheterization lab, and the radial artery diameter was once more evaluated by ultrasound using the same technique as at the baseline. All of the patients received subcutaneous 1% lidocaine for local anaesthetic and intravenous midazolam for mild sedation

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prior to cannulation. Following sheath insertion into the artery, 100 micrograms of nitroglycerin and 50–70 units/kg of unfractionated heparin were given.

Each patient's level of pain was assessed using the visual analogue scale when the introducer sheath was put into the radial artery (VAS). A 10 cm line with descriptive descriptions at either end makes up the VAS. By selecting a position on the line, the patient gauges the intensity of the pain [13]. Before lidocaine infiltration, sympathetic tone, including systolic, diastolic, and heart rate (HR), was assessed as a baseline value using noninvasive blood pressure and digital pulse oximeter monitoring. Following sheath insertion, these parameters were once more measured.

The median and interquartile range were used to convey qualitative variables, whereas the mean and standard deviation were used to express quantitative variables. The percentages used to represent the categorical data. These categorical variables were compared using the v2 test. With the help of SPSS software, version 26, statistical analyses were carried out. The results were compared using the Mann-Whitney U test for nonparametric variables and the unpaired t-test for regularly distributed variables. Statistical significance was defined as a P value 0.05.

# Results

A final analysis was performed on 30 patients in the placebo group and 30 patients in the treatment group out of a total of 113 individuals. 103 patients were randomised in a doubleblind method. Tables 1 and 2 show the clinical traits and medications of the patients in the two groups. Age, gender, medical history, smoking, previous interventions, access to care, and medication use were evenly distributed between the two groups. In the gel therapy group, the body mass index was higher than in the placebo group ( $27.6 \pm 4.7 \text{ vs. } 24.5 \pm 4.1$ ; P = 0.009). The radial artery was successfully accessed at the first puncture for every patient in both groups, and the sheath was successfully inserted on the first try. The right radial artery was used for all trans-radial angioplasties. Although the therapeutic gel group's procedure took longer than the placebo group's (50 min. vs. 35.5 min), this difference was not statistically significant (P = 0.07).

Variables	Placebo gel	Therapeutic gel	P value
Age (y) [mean $\pm$ SD]	$64.2\pm8.996$	$59.967 \pm 8.467$	0.66
Gender (male) [N (%)]	22 (73.3%)	21 (70%)	0.774
Body mass index (kg/m2) [mean ±	$24.537 \pm 4.112$	$27.617 \pm 4.736$	0.009
SD]			
Diabetes (Yes) [N (%)]	4 (13.3%)	6 (20%)	0.488
Hypertension (Yes) [N (%)]	10 (33.3%)	9 (30%)	0.781
Prior myocardial infarction (Yes)	1 (3.3%)	5 (16.7%)	0.195
[N (%)]			
Smoking (Yes) [N (%)]	1 (3.3%)	4 (13.3%)	0.353
Prior intervention (Yes) [N (%)]	23 (76.7%)	20 (66.7%)	0.39
Access (femoral) [N (%)]	14 (46.7%)	14 (46.7%)	0.569
Procedural duration (median	35.50(20-50)	50.00(35-70)	0.076
[IQR])			

#### **Table 1 Patient characteristics**

#### Table 2 Drugs before Procedure

Drugs before procedure	Placebo gel	Therapeutic gel	P value
Aspirin (Yes) [N (%)]	73.34	66.67	0.573

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Clopidogrel (Yes) [N (%)]	20	30	0.371
Nitrates (Yes) [N (%)]	50	46.67	0.796
Calcium Channel Blockers	23.34	13.34	0.317
(Yes) [N (%)]			
Beta blockers (Yes) [N (%)]	90	76.67	0.166

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In this study, the average diameter (mm) and area of the radial artery were reported (cm2). The treatment group experienced a significant increase in the radial artery's diameter and area (mean diameter, mm:  $2.95 \pm 0.48$  vs.  $2.54 \pm 0.43$ , p = 0.001; area, cm2: 0.07 vs. 0.05, p = 0.001). (Table 3). There was no discernible difference between the groups in terms of sympathetic tone, including SBP, DBP, and HR (Table 4). The group receiving the therapeutic gel experienced considerably less radial discomfort during radial puncture (4 [1-5] vs. 2 [1-2]; P = 0.003). (Table 5).

Patients in the treatment and placebo groups did not report any procedure-related pain that grew greater as the catheter or sheath moved, and neither group experienced any problems advancing the catheter or removing the sheath. In neither group was the vasodilator combination re-administered. Patients in the treatment group or the placebo group did not exhibit RAS in relation to the RAS score.

<b>Table 3 Radial Artery</b>	Size at Baseline and after the To	pical Gel Application.
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Variables	Placebo gel	Therapeutic gel	P value
Baseline Diameter Mean	$2.445\pm0.432$	$2.472\pm0.537$	0.833
$(mm) [mean \pm SD]$			
Final Diameter Mean (mm)	$2.54\pm0.43$	$2.95\pm0.48$	0.001
[mean $\pm$ SD]			
Baseline Area (cm2)	0.04 (0.04–0.05)	0.05 (0.04-0.06)	0.643
[median (IQR)]			
Final Area (cm2) [median	0.05 (0.04-0.06)	0.07 (0.05-0.09)	0.001
(IQR)]			

#### Table 4 Sympathetic System Response at Baseline and after the Sheath Insertion

Variables	Placebo gel	Therapeutic gel	P value
Baseline SBP[mean ± SD]	$131.533 \pm 16.408$	$131.20 \pm 15.904$	0.937
Final SBP [mean ± SD]	$107.87\pm25.9$	$111.93 \pm 15.97$	0.467
Baseline DBP [mean ± SD]	$77.933 \pm 9.645$	$79.2\pm9.59$	0.612
Final DBP [mean ± SD]	$65.2\pm10.55$	$66.93 \pm 13.58$	0.583
Baseline HR [mean ± SD]	$72.7\pm9.12$	$71.5\pm5.918$	0.548
Final HR [mean ± SD]	$73.5\pm9.47$	$74.03 \pm 8.33$	0.818

#### Table 5 Radial pain score during the procedure

Variables	Placebo gel	Therapeutic gel	P value
Patient pain (Median[IQR])	4 (1–5)	2 (1–2)	0.003

# Discussion

Even while trans-radial catheterization is becoming more and more common and has a low rate of access site complications, there are still issues with this technique that could cause the treatment to fail [14]. One of the biggest issues with this method is the possibility of spasms, which can make the process take longer, cause the patient more pain and anguish, and potentially trigger a crossover to femoral access [15,16].

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There is growing evidence that radial artery catheterization is a safe and effective alternative to femoral artery catheterization for diagnostic coronary angiography and PCI, in addition to the usual indications for radial artery cannulation [17]. Radial artery catheterization can be carried out successfully in anticoagulated patients[3] and has been linked to lower incidence of access site complications[17] and lower procedure-associated costs[18]. Because it is smaller than the femoral artery and more prone to spasm, the radial artery is more likely to experience arterial blockage in severe situations (20–30% of the time) [19,20].

Alternative access points, like the femoral artery, are required in these circumstances. Second, access through the radial artery induces vessel trauma, and in 2.2% to 4.5% of cases, a proliferative or restenotic response to trauma might result in vessel occlusion[20]. Due to this, just 1.3% of cardiac catheterizations in the US are carried out using the radial method; instead, most US operators prefer to use the femoral artery [1].

Our innovative method of vasodilating the radial artery before radial artery cannulation may make catheterization easier, less likely to result in unfavourable results, and more appealing to practitioners as a substitute for femoral artery catheterization. We did not assess which combination, if any, of topical lidocaine and NTG was more effective at raising RAD due to lack of power given the study's small sample size. Additionally, we did not examine whether topical NTG increases the rate of radial artery cannulation and lowers adverse events; these questions should be investigated in future prospective trials. The fact that this study was conducted on healthy young volunteers rather than critically ill patients must be emphasised. Future research will examine if topical NTG may be used safely in critically unwell, hypotensive patients in the intensive care unit.

#### Conclusion

Preprocedural treatment of a topical gel containing verapamil, nitroglycerin, and lidocaine dramatically enhanced the size of the radial artery and considerably decreased patient radial discomfort during radial puncture in our randomised, double-blind, and placebo-controlled trial.

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