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Effect of moderate sedation in reducing spasm during transradial coronary angioplasty: An observational study

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Abstract

Introduction: Traditional transfemoral route versus the recent transradial approach for percutaneous coronary interventions (PCI) has been the area of interest for all cardiologist and Cath lab anaesthesiologist. With better patient compliance with transradial approach significant research is being done to try reducing the only hindering complication responsible for femoral cross-over, i.e. radial artery spasm. We propose to observe the effect of prior moderate sedation in reducing radial artery spasm during the transradial coronary angioplasty.

Methodology: All patients who underwent angioplasty by transradial route during May 2018 to May 2019 were included in the study. Patients were categorized into two groups as those who received sedation using Inj. Midazolam 0.01mg/kg and Inj. Fentanyl 1 µg/kg maximum up to 2µ/kg(Group A) repeat dose if required in the event of spasm and those without sedation(Group B). Demographic data, procedural parameters, pre, intra and post-operative haemodynamic parameters were noted. Visual analogue Scale (VAS) was monitored for pain, sedation score for sedation and radial artery spasm was monitored by observatory (clinical) and definitive parameters. 30 day follow up was monitored for infection, pain, haematoma at the site.

Results: There was no significant difference in the demographic data and comorbidity pattern of both the groups. No significant change was seen in haemodynamic stability and procedural parameters in both the groups also. Patients who received sedation were calmer at the end of 30 mins compared to control group. The incidence of radial artery spasm in group A was 25% as compared to 39% in the control group, a

higher number of access cross cover to femoral in control group was noted.

Conclusion: The study proves via statistical analysis that the incidence of radial artery spasm during coronary angioplasty was significantly lower in patients who received moderate sedation as compared to those who received none. However, there was no significant difference in the incidence of haematoma, infection, pain at the site in patients of both the groups at the end of 30 days.

Keywords: Haematoma, Haemodynamic Visual Analogue Scale.

Introduction

The Trans femoral method has traditionally been used for coronary artery interventions like angiography, angioplasty, and cardiac catheterization. However, since the last decade trans radial approach has been increasingly used worldwide for diagnostic and therapeutic percutaneous cardiac interventions. The evidence through various research papers of this access being associated with lesser vascular complications, shorter duration of hospital stay and better patient compliance has popularized this approach over femoral.[1, 2]

However, the radial artery being a thick-walled vessel, has a marked muscular component, and together with the high density of alpha-1 receptors, makes this vessel especially susceptible to spasm.[3] Once in spasm, the advantages of this approach are nullified, as it leads to access site cross-over. Access site cross-over increases the complexity of the procedure, prolongs the duration of hospitalization and also has an impact on major vascular complications thereafter. Incidence of radial artery spasm is 15% to 30% of the procedures, even in experienced hands.[4]

Fear, anxiety, and pain can be factors triggering radial artery spasm (RAS). Conscious sedation using sedative anxiolytic combined with analgesic may alleviate these symptoms to an extent, reducing the incidence of spasm.[4]

There is no definitive standard protocol for preventing spasm using optimal vasodilatory cocktail with or without sedation; though there are many studies suggesting use of nikorandil, nitroglycerine, verapamil etc.[5-8] There are two randomized controlled trials so far regarding usage of conscious sedation one which showed significant reduction in spasm and access site cross-over, while the other showed no such difference.

Our study was aimed at retrospective observation and analysis of the effect of moderate sedation in reducing radial arterial spasm during transradial coronary angioplasty. Secondary objective is to find out the incidence of pain, infection, haematoma at the site of radial approach at the end of 30 days. It analyses the angioplasty cases done by transradial route in a single center by single operator over one year.

Methods

This is an observational study. All patients who underwent angioplasty by transradial route during May 2018 to May 2019 were included in the study. Patients were categorized into two groups as those who received sedation using Inj. Midazolam 0.01mg/kg and Inj. Fentanyl 1 µg/kg maximum up to 2µ/kg(Group A) repeat dose if required in the event of spasm and those without sedation(Group B).

Exclusion criteria: All those in cardiogenic shock requiring inotropic or ventilator support, end stage renal disease, chronic substance abuse, complicated triple vessel disease were excluded.

This was single operator, single center study minimizing operator bias.

Both the groups were compared for demographic data, comorbidities, medications prior procedure. The operator chose radial artery, either left or right after performing modified Allen's test and rechecking the pulse quality.

Group A patients received intravenous injection midazolam 0.01mg/kg and injection fentanyl 1µg/kg 15 minutes prior procedure. Group B comprised of patients who didn't receive any sedation.

In Cath-lab all patients were given local anesthesia 1ml using 2% lignocaine plain. Radial artery puncture was done using 20G intravenous catheter, hydrophylic Terumo sheath (either 5 Fr-grey or 6 Fr-green, length7.5cm) secured. Spasmolytic cocktail injection nitroglycerine 50 microgram, injection diltazem 5 miligram diluted to 10cc 0.9% NS given slowly. Injection heparin 100U/kg was given intravenously.

The diameter and type of guiding used was decided by the operator, based on the patient and procedure requirement. The number of guiding catheters changed, duration of procedure and access site cross over due to radial artery spasm and or difficult manipulation was noted.

All patients were given tight radial bandage for next 12 hours, and evaluated at frequent intervals for discoloration, pain and haematoma.

Evaluation of radial artery spasm

The radial artery spasm (RAS) was defined on two parameters observatory and confirmatory

Observatory

- Persistent forearm pain complained by the patient on basis of VAS (Visual Analogue Scale)
- Pain on introduction and manipulation of the guiding (operator based)
- Requirement of additional dose of sedation or spasmolytic agent.
- Access site cross over to femoral artery.

Confirmatory

- Documented radial artery spasm on contrast shoot.

The contrast shoot was taken with 2 or more of observatory parameters of RAS being positive and repeat shoot was taken 5 minutes after administering additional aliquots of sedative dose. Radial angiography enabled us to detect the anatomic anomalies of this vessel. All these findings were systematically collected.

The severity of RAS was assessed by the operator and graded as:

- Mild: Catheter manipulation causing operator discomfort, patient tolerating; VAS <3
- Moderate: Catheter manipulation causing operator and patient discomfort requiring additional aliquot of sedation VAS >3
- Severe: Catheter manipulation causing operator and patient discomfort to an extent to cause access site cross over

These patients were asked to keep a follow-up and return after one month or prior if any of the following were noted:

- Persistent pain, tingling numbness, motor deficit
- Hematoma, digital discoloration

The Primary end point of this study was incidence of RAS as documented by radial angiography, requiring access site cross-over to femoral artery. The secondary end point being 30 day morbidity related to incidence of persistent forearm pain, hematoma and limb disability.

Statistical analysis

The data collected was analyzed statistically by using SPSS software, version 10.0 for Windows. Continuous variables were expressed as the mean, plus or minus the

standard deviation, and categorical data as percentages. For statistical comparison between two groups (A and B), continuous data was compared using Students T test while for categorical data CHI test was applied.

Results

Of the 385 patients that underwent transradial angioplasty, 346 were eligible, while 39 were excluded due to above mentioned reasons. Out of the 346 patients, 175 received sedation included in group A, while group B had 171 patients.

The clinical variables are given in **Table 1.** There is no significant difference in the demographic pattern of both the groups.

Table 1: Add headings

	Group A (n=175)	Group B (n=171)	
Demographic data			
Age	61.4 ± 6	63.7±8	Not Significant
Females, n (%)	62 (35.4)	55 (32.1)	Not Significant
Body Mass Index	27.5 ± 3.4	28.2±5.1	Not Significant
Hypertension, n (%)	106 (60.5)	98 (57.3)	Not Significant
Diabetes, n (%)	56 (32)	47 (27.7)	Not Significant
Smoking, tobacco chewing, misri n (%)	88 (50.2)	79 (46.1)	Not Significant
Peripheral Vascular Disease, n(%)	21 (12)	19 (11.1)	Not Significant
Dyslipidemia, n (%)	95 (54.2)	102 (59.6)	Not Significant
Procedural parameters			
No. of catheters used	2.45±0.9	2.48±0.9	Not Significant
Contrast volume (ml)	93±30.5	91±28.7	Not Significant
Procedure duration (min)	38 ± 7.3	42 ± 6.7	Not Significant

Not Significant: p>0.05 *Mean mentioned in ( ); SD as ±

Table 2: Procedure related parameters

Procedural parameters			
No. of catheters used	2.45±0.9	2.48±0.9	Not Significant
Contrast volume (ml)	93±30.5	91±28.7	Not Significant
Procedure duration (min)	38±7.3	42±6.7	Not Significant

Not Significant: p>0.05

There was no significant difference in either group where demographic data was concerned. Also the procedure related parameters did not vary significantly.

Table 3: Add heading.

VAS	Group A (n=175)	Group B (n=171)	
at 0 minutes or radial prick	1.27 ± 0.45	1.93 ± 0.69	P< 0.0001
at 30 minutes	1.83 ± 0.38	2.73 ± 0.83	P< 0.0001
at 60 minutes	1.93 ± 0.25	2.93 ± 1.11	P< 0.0001
at 120 minutes	2.80 ± 1.00	2.10 ± 1.03	P<0.001
Sedation Score			
at 0 minutes or radial prick	1.20 ± 0.41	1.17 ± 0.38	P>0.05
at 30 minutes	2.93 ±	2.10 ±	P< 0.0001

	0.25	0.31	
at 60 minutes	1.80 ± 0.41	1.53 ± 0.51	P<0.05
at 120 minutes	1.00 ± 0.00	1.00 ± 0.00	P>0.05

The VAS scoring shows significant difference in pain component from onset of radial prick upto one hour post procedure, indicating that group A patients complained of less pain and had better compliance throughout. The Sedation Score didn't have significant variation at 0, 60 and 120 minutes. However, at 30 minutes, Group A patients were considerably sedated than Group B.

	Group A (n=175)	Group B (n=171)	
Radial Artery Spasm, n (%)	45 (25.7)	67 (39.1)	P<0.0001
Severity: n, (%) mild moderate severe	39 (86.66) 06 (13.33) 00	48 (71.6) 14 (20.8) 05 (07.4)	P< 0.0001
Access: right radial artery left radial artery	174 (99.4) 01 (0.6)	171 (99.9) -----	Not Significant
Previous radial artery catheterization	172 (98.2)	169 (98.8)	Not Significant
Access site cross over, n (%)	5 (2.8)	17 (9.9)	P<0.0001

Not Significant: p>0.05

There was radial artery spasm in around 25% patients who received prior sedation and anxiolysis compared to ~39% in control group. This denotes a significant difference. Almost 98% patients in both groups underwent prior radial artery catheterization (angiography). Also, the severity of spasm requiring access site cross over to femoral was noted in 5 patients implicating positive outcome of hypothesis.

Table 4: Add heading

Complications / 30 day morbidity

	Group A (n=175)	Group B (n=171)	
Follow up patients: n (%)	163 (93.1)	158 (92.3)	Not Significant
Avg duration of follow up visit (days)	24±11	27± 9	Not Significant
Pain : n, (%) mild % moderate % severe %	147(84) 81.4 10.6 08	129(81) 78.9 13.6 07.5	Not significant
Haematoma:	4	5	

According to table 3, almost 92-93 % patients came for follow up examinations between durations which were also comparable in both the groups.

Incidence of pain in group A patients was 84% while that in group B was around 81%. In both the groups there were maximum patients with mild discomfort.

Haematoma was present in 4 of the group A cases evaluated and 5 from group B, but yet comparable.

There was no significant difference noted in the parameters assessed for 30 day morbidity in both the groups.

Discussion

Radial artery versus femoral artery approach for percutaneous transluminal coronary angioplasty has been proved to be the choice of treatment modality through various documented RCTs.[1] However each approach has its own merits and demerits. As noted in various studies radial artery spasm still remains the main challenge in radial artery approach, which then leads to

access site cross-over. Fewer bleeding and access site complications, higher patient comfort level, earlier patient mobilization, and early discharge from hospital are some of the advantages of the transradial approach. The reported incidence of RAS during transradial cardiac catheterization ranges from 4 to 20 % in the literature.[2]

The reasons for radial artery spasm have been attributed to various factors like anatomical i.e muscularity, relative lumen size, course of the artery; technical i.e size of sheath, size and type of catheter used, no. of catheters used, times manipulation was done for engagement of catheter; patient related i.e female sex, acute or chronic stable disease, diabetic, hypertensive, PVD, hypertriglyceridemia which influence the lumen size and atherosclerotic deposits, anxiety, type A personality and so on.[4, 5]

To prevent the spasm, various vasodilator drugs have been tried alone or in combination like nitroglycerine, verapamil, preservative free lignocaine and heparin. Studies have proven variable effect of combination drugs leading to fixed protocol or guidelines to suggest the choice and dose of drug. Another effective way of reducing incidence of spasm is handling of hardware, using hydrophilic hydrophilic coated sheath.[6-9]

Another way of reducing radial artery spasm is minimizing the anxiety. Procedure related stress and anxiety is a proven risk factor causing vasoconstriction. Studies have proven that fentanyl and midazolam apart from sedation, analgesia and anxiolysis have a vasorelaxant effect on radial artery musculature.[10] This infact can potentiate the effect of vasodialatory drugs otherwise used after the radial artery puncture.

This observational study gives us the principal finding as reduction in the incidence of radial artery spasm by administration of opioid analgesia combined with midazolam sedation in a patient undergoing percutaneous transradial coronary angioplasty.

A randomized control trial by M.A. Astarcioglu et al.[11] proved that nitroglycerine in combination with midazolam can effectively reduce radial artery spasm compared to using nitroglycerine alone. However, this study had shortcomings as only angiographies were involved and as appropriate dose of midazolam required for preventing radial artery spasm is yet not prescribed anywhere, larger doses could be used.

Spyridon Deftereos et al.[12] also in a randomised control trial proved that routine administration of relatively low doses of an opioid/benzodiazepine combination during transradial interventional procedures is associated with a substantial reduction in the rate of spasm, the need for access site crossover, and the procedure-related level of patient discomfort. Limitations would include involvement of three different centres with different operators. Although spasm definition was categorised objectively on basis of angiogram, operator bias could still preclude the findings.

Our study was based on single centre and single operator findings. Also the combination drug used was not fixed but titrated according to the requirement of the patient sealed to a maximum of 2μ/kg for fentanyl and 0.04mg/kg for midazolam. This took care of the physiological variations for the drug requirement in particular patient.

The sedative-analgesic relieves anxiety and procedure related stress which precipitates spasm. Gursoy et al.[(10)]. studied the vasodilatory effect of opioids on the isolated radial artery concluding that they produce concentration-dependent and endothelium independent relaxation. The in-vitro studies on human vein have demonstrated the

vasodilatory effects of fentanyl. Benzodiazepine-induced vasodilation is documented by Colussi et al[13]. in their study which showed that low concentrations of midazolam induce vasodilation via an endothelium-dependent mechanism whereas high concentrations of midazolam induce vasodilation via an endothelium independent mechanism.

We chose the Visual Analogue Scale as a guide to assess the pain component and Ramsay score to assess the level of sedation before, during, after procedure and also at the end of 30 days. Pain score assessment cannot be utilized to quantify the intensity of radial artery spasm as it is subjective and entirely based on patient's perception. A check radial angiogram prior and after procedure confirmed radial artery spasm in patients having a higher VAS score reducing the bias. However, it can under diagnose spasm in patients with higher threshold for pain or over diagnose in those with lower threshold for pain. Sedation score monitoring helped titrating the doses so as to provide conscious sedation allowing the patient to pick up any sharp pain during the procedure suggesting dissection of the coronary and to follow commands.

In the nut shell, there cannot be an alternate to the use of vasodilator, single or as cocktail to reduce radial artery spasm in patient undergoing transradial coronary procedure. However, addition of opioid and benzodiazepine definitely helps reducing the spasm by allaying anxiety and minimizing pain which are documented factors causing RAS. The results indicate that spasm occurred in 25.7% in those who received sedation and 39.1% with no sedation. The relative risk reduction was 68.7% which statistically signifies the outcome of the study. The access site cross-over rate was 34% lower in the treatment group: 9.9% versus 15.0% thus preventing further morbidity of femoral approach and reducing hospital stay.

However, there was no significant difference in the incidence of pain, haematoma or localised inflammatory reaction at the end of 30 days in both the groups. This proves that there is no significant difference in the 30 day morbidity (as analysed parameters suggest) in both the groups.

Pitfalls and shortcomings

This was an observational study and definitely requires a strong RCT to recommend sedation in each and every case of radial angioplasty. Being a single centre, single operator study design, reduced the chances of bias during the study. However, in not so skilled or freshly started apprentices' the requirement for sedation during procedure may increase due to various reasons like increased operating time, more handling, frequent change of hardware. Hence, multicentric trial is advocated.

Conclusion

The study proves via statistical analysis that the incidence of radial artery spasm during coronary angioplasty was significantly lower in patients who received moderate sedation as compared to those who received none. However, there was no significant difference in the incidence of haematoma, infection, pain at the site in patients of both the groups at the end of 30 days.

List of abbreviations

NS	Normal saline
PCI	Percutaneous coronary intervention
RAS	Radial artery spasm
VAS	Visual analogue Scale

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