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ORIGINAL RESEARCH

Evaluation of the Role of Nitrates in the Management of Recurrent Angina Post-PCI in the Real-World setting

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ABSTRACT

Background: Nitrates are highly effective both in terminating acute attacks of angina pectoris and for the prophylaxis of symptomatic and asymptomatic ischemic heart disease. The present study aimed to gather insights from Indian physicians and cardiologists regarding the occurrence of angina post-intervention and the treatment approach in a real-world setting. **Methods:** An observational survey-based study conducted by cardiologists and physicians with clinical expertise in the management of ischemic heart disease. A structured questionnaire was prepared to solicit the opinion of the experts regarding their practice and preference of drugs for the management of angina post-intervention in the real-world setting. Data entry and statistical analysis were done for completed questionnaires. **Results:** A total of 51 cardiologists participated in this survey. The majority of respondents (56.9%) reported that the occurrence of angina post-intervention [percutaneous coronary intervention or coronary artery bypass grafting] falls between 20-40%. A total of 41.1% of respondents preferred using a combination of beta-blockers and nitrates. In cases of microvascular angina, most cardiologists preferred a combination of beta-blockers and nitrates (33.3%), with nitrates alone (15.6%) and beta blockers alone (3.9%) being less favored. **Conclusion:** The present survey concluded that nitrates remain the favored choice of anti-angina medication in real-world clinical practice in India.

Key words: Beta-blockers, coronary artery bypass grafting, ischemic heart disease, percutaneous coronary intervention

INTRODUCTION

Ischemic heart disease (IHD) is the leading cause of death and its prevalence increases with age. Angina pectoris is the common clinical manifestation of coronary heart disease [1]. Results from an imbalance between the myocardial oxygen supply through the coronary arteries and oxygen demand [1]. The most severe type of IHD is acute myocardial infarction (AMI), with ST-segment elevation myocardial infarction (STEMI) being the most common form of AMI [2].

Percutaneous Coronary Intervention (PCI) is the fastest and most effective clinical treatment for STEMI. PCI can rapidly help to restore blood flow in obstructed coronary arteries, relieve chest pain, reduce AMI-related mortality, and improve the quality of life of patients. Previous studies have shown that following intervention and revascularization procedures, a significant proportion of patients (30%) still experience recurrent angina despite treatment efforts [3,4].The recurrence of anginal symptoms post-PCI is an important risk factor for adverse cardiovascular events [5]. Recurrent angina limits physical activity and impaires the quality of life of patients [6]. Readmission of such patients post-PCI is a common occurrence. Nearly half of these readmissions (44%) are due to cardiac-related issues, underscoring the persistent challenges in managing cardiovascular health post-intervention [7].

Nitrates have been used to treat symptoms of chronic stable angina for more than 135 years [1]. Nitrates are highly effective both in terminating acute attacks of

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angina pectoris and for the prophylaxis of symptomatic and asymptomatic ischemic heart disease [8]. The present study aimedto solicit the opinion of Indian physicians and cardiologists regarding the occurrence of angina post-intervention and the treatment approach in the real-world setting.

METHODOLOGY

Study design

This was an observational survey-based study conducted in cardiologists and physicians with clinical expertise in the management of ischemic heart disease. A structured questionnaire was prepared to solicit the opinion of the experts regarding their practice and preference of drugs for the management of angina post-intervention in the real-world setting (Table 1).

The survey questionnaire consisted of five questions. The key questions covered in the survey include occurrence, treatment choices, and prevalence of angina, especially in the context of post-intervention [such as PCI and coronary artery bypass grafting (CABG)]. The study-related documents, including the survey questionnaire, were reviewed by experienced cardiologists.

Participants' recruitment

The survey questionnaire was given to clinicians and a duration was allocated for completing the survey questionnaire. Prior to participation, clinicians received an overview of the study's objectives and methodologies. It was emphasized that participation was entirely voluntary. This approach was adopted to minimize the potential risk of participation bias and guarantee the authenticity of individual perspectives. In order to uphold participant confidentiality, all collected data were anonymized. Access to the survey responses was restricted to only the research team, ensuring that individual responses remained confidential. All clinicians participated in the survey voluntarily.

Statistical analysis

Data entry and statistical analysis were performed for completed questionnaires. Data were presented as percentages for categorical measurements. Graphical representations of the data were presented for visual impression.

RESULTS

A total of 51 cardiologists participated in this survey. A total of 56.9% of respondents reported that the occurrence of angina post-intervention (PCI or CABG) falls between 20-40%, while 35.3% of respondents responded the prevalence is less than 20%, and a smaller percentage (7.8%) reported the prevalence to be >40% (Table 2).

For managing angina following the intervention, 41.1% of respondents preferred using a combination of beta-blockers and nitrates. Additionally, 27% of cardiologists prescribed beta-blockers alone, 25.4% opted for nitrates alone, and 5.8% recommended other anti-anginal medications.In cases of microvascular angina, the most favored treatment was a combination of beta-blockers and nitrates (33.3%), followed by nitrates alone (15.6%), beta-blockers alone (3.9%), and other drugs (47.1%).

The prevalence of angina among patients with diabetes was reported to be high by most of the respondents.

Table 1: Questionnaire for In Practice Survey program for recurrent angina post intervention

Questionnaire	
1.	What is the occurrence of angina post intervention (PCI/CABG)?
2.	What is the treatment choice in angina post intervention?
3.	What is the treatment choice in microvascular angina?
4.	What is the prevalence of angina among diabetics?
5.	What is the treatment choice in diabetes with angina equivalent symptoms?

Table 2: Occurrence of angina post intervention

Questionnaire	
1.	What is the occurrence of angina post intervention (PCI/CABG)?
2.	What is the treatment choice in angina post intervention?
3.	What is the treatment choice in microvascular angina?
4.	What is the prevalence of angina among diabetics?
5.	What is the treatment choice in diabetes with angina equivalent symptoms?

DISCUSSION

Recurrent angina has been reported in patients undergoing PCI. In the study by Huqi A.,et al, recurrent angina was reported post-PCI in about 29% of patients after 1 month while 31% of patients reported recurrent angina after 6 months [9].

A meta-analysis of studies and registries in post-PCI patients indicated that within 1 year after successful PCI, the recurrence of angina ranges between 20% and 30% [10]and, within 3 years, angina persisted or reoccurred in up to 40% of cases [11]. A real-world analysis [10] found that due to post-primary PCI angina recurrence, the total healthcare costs in the first year after the index PCI were 1.8 times greater for those with angina or chest pain compared to angina-free patients [10]. Among the 30% who reported angina

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within 6 weeks after the procedure, 68% continued to be treated with beta-blockers as anti-angina drugs and did not receive a second anti-anginal drug [12].

A combination of anti-angina drugs may be a treatment approach in patients with angina post-PCI. The STable Coronary Artery Diseases RegisTry (START) study, a prospective, observational, nationwide study was conducted to evaluate the presentation, management, treatment, and quality of life of patients with stable CAD. The results indicated that treatment is still suboptimal in patients with angina [13].

Another subset of patients who suffer from recurrent angina include patients who undergo de-escalation of antianginal medications after PCI. This is particularly observed in patients with incomplete revascularization [14].

Nitrates have been used to treat symptoms of chronic stable angina for more than 135 years [1].Nitrates are highly effective both in terminating acute attacks of angina pectoris and for the prophylaxis of symptomatic and asymptomatic ischemic heart disease [8]. Nitrates activate the endogenous NO-cGMP signaling pathways reduce the intracellular free Ca^{2+} and cause desensitization of vascular smooth muscle cell vasoconstrictor elements to Ca2+, and this results in vasorelaxation. The action of nitrates may compensate for deranged endothelial function [1].Akin to other anti-anginal drugs, long-acting nitrates improve exercise tolerance, time to symptom onset and time to ST-segment depression during exercise testing in patients with stable effort-induced angina. In a meta-analysis of 51 clinical trials (*n*= 3,595 patients), nitrate therapy decreased the number of angina episodes by about 2.45 episodes per week [1].

In the current option survey, 54.9% of respondents reported that less than 10% of their patients have recurrent angina post-PCI/CABG while 25.4% of respondents opined that the prevalence of angina is 25-30% post-intervention. Combination therapy of beta blockers and Nitrates was preferred by 41% of the respondents. Combination therapy was preferred by 33.3% of respondents in their patients with microvascular angina. Monotherapy with Nitrates was preferred by 15.6% of respondents while beta-blockers were prescribed by 3.9% of respondents in their patients with microvascular angina.

Currently, practice guideline recommendations regarding the management of patients with angina post-PCI are unclear. The limitations of the current survey is the subjective nature of the opinions of the respondents in the survey which is based on their in-clinic experience in the real world setting. Corroboration of these observations is required in a phase IV setting.

CONCLUSION

Persistence or recurrence of angina after a percutaneous coronary intervention (PCI) has been reported in about 20-40% of patients during short-medium-term follow-up. Suboptimal treatment of recurrent angina must be addressed effectively. Healthcare costs may double among patients with persistent or recurrent angina post-PCI. Nitrates continue to be effective anti-anginal drugs in the real-world setting in India. Combination therapy of nitrates with beta-blockers is currently practiced by more than one-third of practitioners. Addressing the gaps in evidence in the effective management of recurrent angina post-PCI is required and more research is warranted.

Conflict of interest: Amit Gupta and Neeta Keertane are employees of USV Pvt. Ltd. All other authors have nothing to declare.

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