ORIGINAL ARTICLE   **OPEN ACCESS**

Nitrates and Statins Prospective Comparative Study as Secondary Prevention in Patients with Post-Myocardial Infarction

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ABSTRACT
The goal of the study was to compare and evaluate the clinical efficacy of Glyceryl Trinitrate (GTN) and Isosorbide Dinitrate with Statin (Atorvastatin) in patients who had recently experienced a Myocardial Infarction, as well as to determine how well-being-related quality of life for these patients had improved as a result of education and counseling. A total 100 patients were enrolled and they were divided in 2 groups based on treatment viz. A and B to evaluate comparative efficacy of antiischemic agents in the study whereas Group A, Glyceryl trinitrate + Atorvastatin (n=50), versus Group B, Isosorbide dinitrate + Atorvastatin (n=50). The two groups' adverse effects and clinical effectiveness were contrasted. Both groups' illness symptoms were exacerbated. Self-reported questionnaires are a useful tool for evaluating and examining the psychological experience of heart disease patients. The original Mac-New and KAP questionnaires are diagnostic instruments that consist of multiple-choice questions. The findings of the current study show that education and counseling can help patients with myocardial infarction (MI) better understand their condition, their diet, the significance of lifestyle changes, and the need for self-management of their condition and its complications.
Keywords: Myocardial infarction, Mac-New and KAP questionnaire, Atorvastatin, Isosorbide dinitrate

INTRODUCTION
There are two types of acute myocardial infarction: ST-segment elevation MI and Non-ST-segment elevation MI (STEMI). NSTEMI and unstable angina are comparable. Over the past few decades, the prognosis for MI has steadily improved. Case fatality after MI has decreased, and long-term survival has increased. This improvement is most likely attributable to the introduction, increased availability, and utilization of acute non-invasive and invasive interventions along with the development of potent drugs for secondary prevention. Aspirin, beta-blockers, statins, nitrates, while angiotensin converting enzyme inhibitors have drawn the greatest interest among the drugs for long-term secondary intervention. Regardless of whether MI is linked to ST-elevation, practice guidelines advised the use of such drugs for prevention and treatment in patients with MI [1]. This proposed research work concentrates on the mainly two drug categories that are Nitrates and statins based on their therapeutic attributes in the treatment of post-MI patients. However, nitrates are now among the safest medications used to treat MI. It is commonly acknowledged that nitrates are therapeutically effective for the treatment of both acute and chronic MI. They effectively dilate the venous capacitance system and systemic resistance arteries, which lowers the ischemic ventricle's enlargement and improves blood flow to the ischemic sub-endocardial region [2]. Although the body needs cholesterol to function, too much low-density lipoprotein (LDL) can cause fatty deposits to build up in the arteries. The chance of developing illnesses including CHD, heart attacks, and stroke can rise as a result of these fatty deposits. Statins are medications that lower blood cholesterol levels by lowering the liver's production of cholesterol, which lowers the risk of heart disease [3]. To compare the therapeutic efficacy of nitrates and statins as secondary prophylaxis in post-MI patients is the goal of the proposed research. Due to a lack of awareness of the risk factors for coronary heart disease and a disregard for preventative guidelines, these diseases' mortality rates will rise in developing nations [4]. According to a German study, MI survivors had significantly lower health-related quality of life (HRQoL) than the general population [5]. Therefore, the goal of this proposed effort is to evaluate how counseling and education affect the health-related quality of life of MI patients in order to increase their life expectancy.

MATERIAL AND METHODS
Ethical clearance
The study protocol was prepared and submitted to Ethics Committee Appasaheb Birnale College of Pharmacy, Sangli. The study was initiated after obtaining the approval from the IEC.

Permission

A permission to use the patients for study was taken from at Kranti Cardiac Centre, Sangli

Place of study – The investigation was conducted at the Kranti Cardiac Center in Sangli. It contains 30 bedded, multispecialty, tertiary care hospital providing inpatients as well as outpatients healthcare services in and around Sangli district.

Study population

125 cases has been selected randomly, however 07 were loss to follow up, 15 did not meet inclusion and exclusion criteria, 03 were excluded due to insufficient information for analysis, leaving 100 eligible patients are taken our study.

Period of study- September 2018-Feb 2019.

Study design-Single centered observational, prospective, comparative clinical study.

Informed consent administration to the subject

Informed Consent Forms were developed in two different regional languages (English and Marathi) and were administered to the subject or their legally acceptable representatives in the language well understood. Subjects were explained about the study and asked for their willingness in being a part of the study. On obtaining verbal approval, ICF was provided to the subjects; as per the language feasibility. After obtaining the sign Informed consent form from the subjects they were enrolled for the present study according to inclusion criteria.

An interventional study Patient enrollment- Based on the study's inclusion criteria, 100 patients in total were enrolled.

Inclusion criteria

i. Patients of either sex having age between 50-80 yrs. having Myocardial Infarction.

ii. Those are willing to give written informed consent

b) Exclusion criteria –

i. Patients had age below 50 more than 80yrs.

ii. Unwilling or unable to give informed consent.

iii. Pregnant and lactating women.

iv. Patients with other concomitant disease.

A) A total 100 patients were enrolled and the patients were divided in Group A and B to evaluate comparative efficacy between nitrates with statins.

Group A -received Glyceryl trinitrate 2.6mg by sublingual route and atorvastatin by oral route while Group B- received Isosorbide dinitrate by oral or sublingual route and atorvastatin by oral route. Group A- (50 patients)-Nitrate +Statin (Glyceryl trinitrate 2.6mg +Atorvastatin 10mg)

Group B -(50 patients) –Nitrate + Statin (Isosorbide dinitrate 20mg +Atorvastatin 10mg)

Quality of life (QOL) questionnaire

1) Above 100 enrolled patients were divided in 2 groups control and test for education And counseling to study QOL.

Control group

At initial treatment (n=100) without counseling and education to these patients Provided KAP questionnaires and data were filled up by asking the information to the patients.

Test group

At final treatment (n=100) Educate and counseled these patients and after counseling and education KAP questionnaires were filled up by asking information to patients.

Study material

The following study material was used to assess the heath related quality of Life of MI patients

i) KAP questionnaire

There are 28 questions in it that gauge patients' knowledge, attitudes, and practices around MI. Questions will be assessed with one point for accurate answers and zero for wrong ones. The patient's socio economic position was evaluated using the original demographic characteristics. The degree of understanding of coronary artery disease risk factors, symptoms, and indicators was evaluated using knowledge questions. The sociobehavioral prospective level of attitude questions was evaluated. Practice questions were used to identify preventative and health-seeking behaviours [6].

ii) Mac-New questionnaire

The Mac-New questionnaire contains 25 questions. It is a readily deployable and immediately useful neurobehavioral instrument. We can acquire valuable information from this self-reported questionnaire to improve the patient's therapy and way of life. There are multiple-choice questions in it. Each question on the questionnaire was assessed for how much it contributed to the physical, emotional, and social dimensions. Patients are not allowed to choose more than one response for each suggested question in order to get their final score. Instead, they are directed to check only one of the five checkboxes viable replies. The minimum score was 1 and the maximum score was 5 (excellent health-related quality of life) (poor health-related quality of life). The average responses to the 10 items that made up the emotional domain were used to

calculate the emotional score. The average responses to the 10 items that made up the physical domain were used to calculate the physical score. The average responses to the 5 items that made up the social domain were used to calculate the social score. The items inside the three domains were scored in accordance with best practices [7].

Method of study

a) Chart Review method: The Chart Review Method was used to gather the data for the current research.

b) Patient data collection Proforma:

On a patient information gathering Proforma, all required and pertinent baseline data was gathered. Before and after the interventional study, all recruited patients received all questionnaires, including the Mac-New and KAP questionnaires. The only valid response is "YES." The response does not know was only regarded as "No." Subjects were required to fill out the Proforma on their own, however for those who were illiterate; proforma was filled out by asking the subjects the questions aloud and documenting their responses.

Control group (Group A, B) n= 100

The control group didn't get any education and counseling during their First visitswith patients information leaflets regarding the diseases. All questionnaires i.e. the Mac-New questionnaire and KAP questionnaire were given to all patients at 1st visit for initial data and at final visit were collected.

Test group (Group A, B) n=100

To assess the impact of patient education and motivation on the study population, an intervention-based study was created. The patient received verbal and visual information about the disease, risk factors, treatment compliance, and lifestyle changes. Each patient receives oral counseling for a minimum of 45 minutes; however this time may be increased based on the patient's educational level and capacity for comprehension until they are pleased with the information given.

Further these patients were also informed to give next visit for the follow-up after 1 month. All questionnaires were provided to patients. Disease condition of each patient was evaluated by Form C and Knowledge, attitude and practice of patients were assessed and required data was collected by KAP questionnaire. The data has been collected and segregated.

KAP questionnaire

This will make it easier to design a health education programme that is specific to the requirements of the local community. All study participants were given a KAP questionnaire that had been properly developed and validated at the start and the end of the trial to gauge their knowledge of the condition and its treatment [6].

The "KAP Questionnaire," which assessed KAPs in relation to myocardial infarction, covered three domains. KAP The KAP questionnaire with myocardial infarction has a total of 28 items, including 9 questions about myocardial infarction knowledge, 9 questions to gauge patients' attitudes toward the disease, including 10 questions about behaviours. Comparably, the myocardial infarction questionnaire comprised 28 questions (knowledge-9, attitude-9, and practice-10 questions), which were answered during a face-to-face interview with the patients in an effort to increase their understanding through education and counseling. The maximum possible score was determined by awarding 1 point for each accurate response and 0 points for a hesitant or wrong response during scoring.

Analysis of the KAP survey questionnaires was done in order to create a suitable counseling programme. Over the course of six months, counseling sessions in the local language were conducted at intervals of one month for 15-20 minutes per time. The concerns surrounding myocardial infarction that were discussed included its pathophysiology, causes, and both short- and long-term effects. Electrocardiogram, dietary advice, and suggestions for suitable lifestyle modifications (such as exercising, quitting smoking, etc.).

After the first counseling session, all group patients were provided printed handouts inthe local language (Marathi) containing information on and myocardial infarction desirable dietary and lifestyle changes. The patients in the all group received counseling and patient information leaflets only at the end of the study.

Mac-New questionnaire

The Mac-New questionnaire contains 25 questions. It is a readily deployable and immediately useful neurobehavioral instrument. We can acquire valuable information from this self-reported questionnaire to improve the patient's therapy and way of life. Self-reported questionnaires are a useful tool for evaluating and examining the psychological experience of heart disease patients. A diagnostic tool, the original Mac-New questionnaire consists of multiple-choice questions. Patients are not allowed to choose more than one response for each proposed question in order to get their final score. Instead, they are directed to check only one of the five check boxed viable replies. In three subscales measuring physical, emotional, and social functions, the Italian version of the Mac-New consists of 25 questions, including seven about symptoms. A global health-related quality of life (HRQL) score is generated from all scored items.

The Mac New contains 26 items with a global HRQL score, physical limitation (10 items), emotional (10 items), and social function (6 items) subscales with a 2-week timeframe, with 12 items falling into more than one domain. It is intended to measure patients' perceptions of how ischemic heart disease affects daily functioning. The following is an example of a subscale item: "How frequently throughout the last two

weeks have you experienced chest pain while doing your normal daily activities?" How frequently in the past two weeks have you felt unworthy or inadequate? (emotional function) and "How frequently in the previous two weeks have you felt that your heart condition prevents you from socializing?" (Social purpose). Apple New questions and subscales are graded on a scale of 1 to 5 (low HRQL to high HRQL) [8].

Statistical analysis

After collection, each piece of data was examined. After that, data were entered into a computer, and Microsoft Excel was used to calculate the results. Column charts were used to display the results. Using the graph pad prism software, the Student-t test will be used to get the P-value for the purpose of comparing the findings. P values below 0.05 were considered significant.

RESULT

Table 1. Distribution of group a post-MI patients having emotional score at baseline and final visit

Sr. No	Mac New Questionnaire	Group A(at baseline)					Group A(at final)				
		Never	1-2 times	3-4 times	5-10 times	Always	Never	1-2 times	3-4 times	5-10 times	Always
		1	2	3	4	5	1	2	3	4	5
1.	Frustrated, impatient or angry?	0	25	18	0	0	0	1	4	38	8
2.	Worthless or inadequate?	15	23	12	0	0	0	0	4	38	8
3.	Very confident and sure?	0	7	12	31	0	39	5	4	0	0
4.	Discouraged or down in the dumps?	12	16	14	8	0	0	0	4	38	8
5.	Feel relaxed and free of tension?	1	13	31	5	0	34	13	3	0	0
6.	Happy, satisfied, or pleased?	0	6	15	26	3	15	24	11	0	0
7.	Tearful or like crying?	40	4	6	0	0	0	3	15	30	2
8.	Less confident?	15	24	8	3	0	0	0	17	26	7
9.	Unsure of yourself or lacking in self-confidence?	24	15	10	1	0	0	3	12	29	6
10.	Apprehensive or frightened?	20	18	12	2	0	0	7	17	15	11
11	Worn out or low in energy?	0	14	20	4	0	0	0	27	14	9
12	Restless, or as if you were having difficultytrying to calm down?	10	20	18	2	0	0	0	24	26	9
13	Shortness of breath while doing your day-to-day physical activities?	25	16	8	1	0	0	0	24	26	9
14	More dependent?	12	30	5	4	0	0	6	12	23	9
15	Chest pain while doing your day-to-dayactivities?	23	18	8	1	0	0	9	15	19	7
16	Bothered by aching or tired legs?	8	26	10	6	0	0	2	11	25	12
17	Limited in doing sports or exercise as a resultof your heart problem?	6	22	17	5	0	0	4	12	28	6
18	Dizzy or lightheaded?	6	20	15	9	0	0	8	23	10	9
19	Restricted or limited as a result of your heart problem?	7	20	11	6	6	0	8	9	15	18
20	Burden to others?	15	14	9	7	5	0	2	15	26	7
21	Unable to do your usual social activities?	17	15	10	8	0	0	3	26	19	2
22	Over-protective?	8	18	10	8	6	0	2	9	19	20
23	Excluded from doing things with otherpeople?	18	20	6	4	2	0	2	17	22	9
24	Unable to socialize?	16	20	5	6	3	0	3	19	20	4
25	Socially restricted or limited?	15	24	3	5	3	0	8	15	23	4

Table 2. Distribution of Group B post-MI patients having emotional score at baseline and final visit

Sr. No.	Mac New Questionnaire	Group B (at baseline)					Group B (at final)				
		Never	**1-2 times**	**3-4 times**	**5-10 times**	**Always**	**Never**	**1-2 times**	**3-4 times**	**5-10 times**	**Always**
		1	**2**	**3**	**4**	**5**	**1**	**2**	**3**	**4**	**5**
1	Frustrated, impatient or angry?	9	27	14	0	0	0	1	4	38	8
2	Worthless or inadequate?	19	25	6	0	0	0	0	4	38	8
3	Very confident and sure?	0	4	10	36	0	39	5	4	0	0
4	Discouraged or down in the dumps?	19	18	10	3	0	0	0	4	38	8
5	Feel relaxed and free of tension?	0	2	12	32	2	34	13	3	0	0
6	Happy, satisfied, or pleased?	0	2	12	32	2	15	24	11	0	0
7	Tearful or like crying?	39	5	6	0	0	0	3	15	30	2
8	Less confident?	19	25	6	0	0	0	0	17	26	7
9	Unsure of yourself or lacking in self-confidence?	27	15	8	0	0	0	3	12	29	6
10	Apprehensive or frightened?	19	15	8	8	0	0	7	17	15	11
11	Worn out or low in energy?	14	12	22	2	0	0	0	27	14	9
12	Restless, or as if you were having difficultytrying to calm down?	12	20	16	2	0	0	0	24	26	9
13	Shortness of breath while doing your day-to-day physical activities?	30	14	6	0	0	0	0	24	26	9
14	More dependent?	9	32	9	0	0	0	6	12	23	9
15	Chest pain while doing your day-to-dayactivities?	26	15	9	0	0	0	9	15	19	7
16	Bothered by aching or tired legs?	8	28	9	5	0	0	2	11	25	12
17	Limited in doing sports or exercise as a resultof your heart problem?	8	23	9	2	0	0	4	12	28	6
18	Dizzy or lightheaded?	22	18	10	0	0	0	8	23	10	9
19	Restricted or limited as a result of your heartproblem?	8	23	13	6	5	0	8	9	15	18
20	Burden to others?	8	23	13	6	5	0	2	15	26	7
21	Unable to do your usual social activities?	19	15	8	8	0	0	3	26	19	2
22	Over-protective?	8	23	13	6	5	0	2	9	19	20
23	Excluded from doing things with otherpeople?	18	17	6	5	4	0	2	17	22	9
24	Unable to socialize?	19	22	4	3	2	0	3	19	20	4
25	Socially restricted or limited?	19	19	5	4	3	0	8	15	23	4

Patients distribution according to emotional, physical and emotional status post MI patients after 2 monthfollow-up from baseline

Study outcomes of mac new is represented as score 1, 2, 3 is low improvement in HRQOL and score 4, 5 is high improvement in HRQOL.

Emotional Score Evaluation

Table 3: Emotional Score Evaluation

Mac Newscore	Group A		p-value	Group B		p-value
	At baseline	**At final**		**At baseline**	**At final**	
1	10.78±8.197	0	0.0043**	15.10±12.89	8.800±15.38	0.0067**
2	20.67±4.899	4.11±3.756	<0.0001****	13.80±9.987	5.600±7.633	0.0128*
3	12.44±5.223	17.44±6.948	0.0420*	9.20±9.100	9.100±5.896	0.0456
4	4.22±2.635	20.67±6.403	0.0003	11.10±15.58	21.40±16.31	<0.0001****
5	0.667±2.0	9.778±3.492	<0.0001****	7.600±15.38	0.400±8.433	0.0229*

Physical Score Evaluation

Table 4: Physical Score Evaluation

Mac Newscore	Group A		p-value	Group B		p-value
	At baseline	At final		At baseline	At final	
1	11.20±7.843	0	0.0015***	14.50±8.396	0	0.0004***
2	20.00±5.077	3.900±3.604	<0.0001****	20.80±6.303	3.900±3.604	<0.0001****
3	12.10±5.043	17.20±6.596	0.0224*	11.60±4.624	17.20±6.596	0.0190*
4	4.500±2.635	21.20±26.268	0.0001****	2.30±2.497	21.20±26.268	0.0001****
5	1.100±2.331	9.50±3.408	<0.0001****	1.0±2.108	9.50±8.403	<0.0001****

Social Score Evaluation

Table 5: Social score evaluation

Mac New score	Group A(mean±SD)		p-value	Group B(mean±SD)		p-value
	At baseline	At final		At baseline	At final	
1	14.80±3.962	0	<0.0001****	16.60±4.827	0	0.0004***
2	19.40±3.286	3.600±2.510	<0.0001****	19.20±3.347	3.600±2.510	<0.0001****
3	6.800±3.114	17.20±6.181	0.0250*	7.200±3.364	17.20±6.181	0.0190*
4	6.200±1.789	20.60±1.187	0.0008***	5.200±1.924	21.61±1.817	0.0001****
5	2.800±2.168	7.800±7.294	<0.8348*	2.800±1.924	7.800±7.294	0.0396*

Summary of Emotional score

Table 6: Summary of Emotional score

Mac New score	Group A(mean±SD)		p-value	Group B(mean±SD)		p-value
	At baseline	At final		At baseline	At final	
Low HRQL	7.730±6.376	3.93±13.83	0.0148	12.69±5.605	6.390±5.894	0.0247
%	15.46	7.86		25.38	12.78	
High HRQL	3.950±5.965	13.20±9.707	0.0077	3.750±8.094	13.20±9.707	0.0077
%	7.9	26.4		7.5	26.4	

(p-value <0.0001 is significant) (Low HRQL= score1, 2and3) (High HRQL= score 4 and 5)

Summary of Physical score

Table 7: Summary of Physical score

Mac New score	Group A(mean±SD)		p-value	Group B(mean±SD)		p-value
	At baseline	At final		At baseline	At final	
Low HRQL	14.43±1.765	7.031±1.903	<0.0001****	15.63±1.159	7.331±1.649	<0.0001****
%	28.86	14.06		31.26	14.66	
High HRQL	2.800±2.071	15.35±2.973	<0.0001****	1.650±2.174	15.40±1.649	<0.0001****
%	5.6	30.07		3.3	30.08	

(p-value <0.0001 is significant) (Low HRQL= score1, 2and3) (High HRQL= score 4 and 5)

Summary of Social score

Table 8: Summary of Social score

Mac Newscore	Group A(mean±SD)		p-value	Group B(mean±SD)		p-value
	At baseline	At final		At baseline	At final	
Low HRQL	13.66±0.998	6.928±2.191	0.0002**	14.33±0.5287	7.328±2.450	0.0033**
%	27.32	13.85		28.66	14.65	
High HRQL	4.500±1.500	14.20±3.493	0.0005***	4.00±1.118	14.20±3.493	0.0011**
%	9	28.4		8	28.4	

(p-value <0.0001 is significant) (Low HRQL= score1, 2and3) (High HRQL= score 4 and 5)

In present investigation comparative efficacy of nitrates with statin was studied. Results reported that more improvement in ECG and lipid profile in isosorbide dinitrate with Atorvastatin (group B) compared to glyceryl trinitrate with Atorvastatin (group A). Hence it is concluded that isosorbide dinitrate with atorvastatin is more effective than glyceryl trinitrate with atorvastatin. Hence isosorbide dinitrate with atorvastatin is most significant effective as secondary prevention in post-MI patients. Our study also discovered that, prior to counseling, the majority of patients had a lower quality of life and a worsening of their diseases because of their ignorance of diseases, risk factors, and preventive actions. The findings of the current study show that education and counseling can help patients with myocardial infarction (MI) better understand their condition, their diet, the significance of lifestyle changes, and the need for self-management of their condition and its complications. Thus high HRQL plays major role in improving

adherence to therapy by increasing interaction with post-MI patients, which would help in improving long term outcome of the disease.

Source of Funding: None.

Conflict of Interest: None

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