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RESEARCH ARTICLE

IMPACT OF DRUG USE ON QUALITY OF LIFE IN FOLLOW UP PATIENTS OF ACUTE CORONARY SYNDROME IN A TERTIARY CARE TEACHING HOSPITAL IN EASTERN INDIA

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ABSTRACT:

Introduction: Acute coronary syndrome (ACS) includes unstable angina, non-ST segment elevation myocardial infarction, and ST segment elevation myocardial infarction. Joint guidelines by American College of Cardiology (ACC) and American Heart Association (AHA) in 2007 suggest secondary drug prevention measures to be used in patients with ACS with aspirin, clopidogrel/prasugrel, ACE inhibitors/ ARBs, Statins, Beta blockers. This study is aimed to find out impact of drug use in quality of life of ACS patients during follow up period. **Materials and methods:** It was a prospective unicentric study done at the OPD of cardiology,R.G.Kar Medical college, Kolkata. All prescriptions issued to study subjects attending the cardiology clinic during 18 months period were intercepted after consultation. Pattern of drug use was noted. Patients were asked 21 questions of "Minnesota living with heart disease questionnaire" and scores were calculated in 3 visits of each patient. Impact of drug use was calculated. **Results:** 525 patients were included in study. aspirin was given in 100%, clopidogrel/prasugrel in 98.29%, ACEI/ARB in 87.43%, statins in 100%, beta blockers in 86.86%. Total 408 patients were given drugs from all 5 groups. There was overall significant satisfactory improvement with drug therapy. Prescription of all 5 drug groups had significant better outcome in quality of life score than prescription of less than 5 drug groups. **Conclusion:** Drugs from all these 5 groups should be given to all follow up patients of ACS, unless contraindicated as they significantly improve quality of life of the patients.

Key Words: Acute coronary syndrome, drug use pattern, Minnesota questionnaire, quality of life

**- ACE- angiotensin converting enzyme, ARB- angiotensin receptor blocker.*

INTRODUCTION

The term acute coronary syndrome refers to a range of acute myocardial ischaemic states. It encompasses unstable angina, non-ST segment elevation myocardial infarction (ST segment elevation generally absent), and ST segment elevation infarction (persistent ST segment elevation usually present).[1] An acute coronary syndrome may occasionally occur in the absence of electrocardiographic changes or elevations in biochemical markers, when the diagnosis is supported by the presence of prior documented coronary artery disease or subsequent confirmatory investigations.[2] In addition to primary prevention efforts, joint guidelines by the American College of Cardiology (ACC) and the American Heart Association (AHA) in 2007 suggest secondary drug prevention measures to be used in patients with ACS.[3,4] In conjunction with diet and lifestyle modifications, these guidelines suggest the use of statins, beta-blocker, and renin-angiotensin aldosterone system inhibitor drug therapies in ACS patients.[3,4] Several studies have shown survival benefit when these therapies were given to patients with ACS.

Anti-platelet therapy (aspirin) is the single most cost-effective adjunctive therapy for ACS treatment. It decreases mortality in treated patients by 23% (ISIS 2).[5] Multiple controlled trials have demonstrated that β-blocker therapy use for ACS patients decreases both early and late cardiovascular mortality and re-infarction rate, and increases survival by 20 to 40%.[6-10] The use of ACEI in treating ACS patients reduces mortality post-myocardial infarction by 7% in ISIS-4 trial[11] and by 12% in GISSI-3 trial.[12] The use of lipid-lowering therapy (statin) in ACS patients has revealed decreased rate of progression and modest regression of atheromatous disease in treated patients. It reduces all-cause mortality by 45%.[13] Several guidelines were established to improve care for ACS patients.[14,15] These guidelines emphasizes the importance of using these pharmacotherapies in managing patients with ACS for secondary prevention.

This study is aimed to show impact of drug utilization on quality of life of ACS patients, i.e., whether not using drugs from all these 5 groups in follow up patients of ACS due to contraindications or drug's side effects would differently affect the quality of life of patients, as measured by "Minnesota living with heart disease questionnaire"[16] as compared to the patients who received drugs from all 5 groups.

MATERIALS AND METHODS

The primary objective is to study the drug utilization pattern in post acute coronary syndrome patients in their follow up visits and secondary objective is to study how drug utilization pattern impacts health outcomes.

Ethical considerations-

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The study protocol, informed consent form (in Bengali, Hindi & English) and case report form (CRF) was submitted to the institutional ethics committee of R.G.Kar Medical College & Hospital, Kolkata for approval. Subject recruitment was commenced only after such approval is obtained.

Written informed consents were taken from each participant according to standard accepted norms. Illiterate individuals gave their fingerprint (left thumb impression) instead of signature in the presence of an appropriate witness.

Study duration- The study was completed within 18 months after commencement. It ran from January 2011 to June 2012.

Study population- Patients who have been recently suffered from acute coronary syndrome and are attending cardiology outdoor of R.G.Kar Medical College, Kolkata.

Subject selection criteria-

Inclusion criteria: Patient (age group 20 yrs to 70 yrs) who have suffered acute coronary syndrome (unstable angina, ST elevation and non- ST Elevation acute myocardial infarction, diagnosed by ECG and/or biochemical tests) in recent past.

Study methodology -

It is a longitudinal prospective unicentric study done at the out patient department of cardiology and at the department of pharmacology, R.G.Kar Medical college, Kolkata.

All prescriptions issued to study subjects attending the cardiology clinic during this whole study period were intercepted after consultation. Number of patients who received drugs from all 5 groups (aspirin, clopidogrel/prasugrel, beta blockers, ACE inhibitor/ARB, statin) were noted as well as patients who were not given drugs from all groups. Patients were asked 21 questions of "Minnesota living with heart disease questionnaire" and scores were calculated in 3 visits of each patient. 1st visit was 1 week after discharge from hospital, subsequent visits were at 1 months and 3 months following discharge.

For health outcome at different visits, Kruskalwallis test was done to measure effectiveness of therapy of different groups (according to number of essential drug groups prescribed to different patients) and unpaired t test was done to evaluate whether quality of life score reduction differed significantly between these groups.

RESULTS

Total 525 patients were included in this study.

Among them, 453 patients are male and 72 are female. Male: female ratio was 6.29:1.

Majority of the patients were above 40 years of age with mean age 56.83 years and standard deviation 8.83 years. (table 1).

Table 1: Demographic variables of study subjects

Age of patients	Mean- 56.63 years, Standard deviation- 8.83
Sex of patients	Male: female- 6.29:1
Body mass index of patients	Mean- 22.12, Standard deviation- 2.06
Monthly family income of patients (in rupees)	Mean- 11628.57, Standard deviation- 6522.5
Patients from Rural: urban background	1.10:1

Among 525 patients, number of ST elevation acute myocardial infarction (ICD Code- I 21.0, 21.1, 21.2, 21.3) were- 333(63.43%) , number of unstable angina patients (ICD Code- I 20.0)- 144 (27.43%), number of non ST elevation acute myocardial infarction (ICD code- I 21.4) patients 48 (9.14%).

Significant Co-morbidities:

Total 135 patients out of 525 (25.71%) acute coronary syndrome patients had concomitant diabetes mellitus, 290 patients (55.24%) had concomitant hypertension, 103 patients (19.62%) had smoking history. Only 4 patients (0.76%) had chronic kidney disease.

Pattern of drug use:

Antiplatelet agents:

Aspirin was prescribed to all patients (100%). Among them 120 patients (22.86%) were given 75 mg aspirin per day, 402 patients (76.57%) were given 150 mg aspirin per day, 3 patients were given 300 mg aspirin per day.

Clopidogrel was prescribed in 432 patients (82.29%). Among them 228 (52.78%) were given 75 mg/day and 204 (47.22%) were given 150 mg/day. Prasugrel was given to 84 patients (16%) in 10 mg/day dose.it has been seen that 9 patients out of 525 (1.71%) were not given clopidogrel/ prasugrel.

Beta blockers

Beta blockers were prescribed in 456 patients (86.86%), among them, metoprolol was given in 384 patients (84.21%), carvedilol in 48 (10.53%) and atenolol in 24 patients.(5.26%). (Figure 1)

Metoprolol was used in different dose from 12.5 mg/day to 100 mg/day. Most frequently (49.22%) prescribed dose of metoprolol was 50 mg/day.

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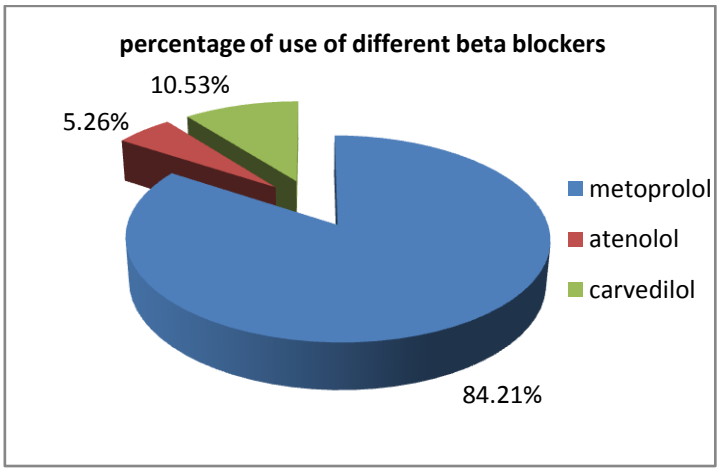

Figure 1: Percentage of use of different beta blockers

Angiotensin converting enzyme inhibitors(ACEI)/ angiotensin receptor blockers (ARB)

Angiotensin converting enzyme inhibitors/ angiotensin receptor blockers were given in 459 patients (87.43%). Among them ramipril was given in 270 patients (58.62%), enalapril in 69 patients (15.03%), perindopril in 9 patients (1.96%), losartan in 57 patients (12.42%), telmisartan in 48 patients (10.46%), olmesartan in 6 patients (1.31%). (figure 2). Among ramipril users, 120 patients (44.44%) were given 2.5 mg/day and 123 (45.56%) were given 5 mg/day dose. 6 patients received 1.25 mg/day and 21 patients received 10 mg/day dose.

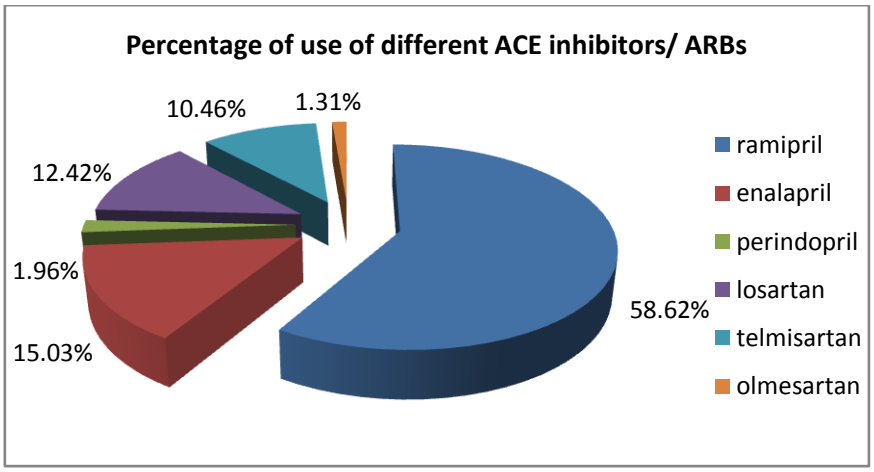

Figure 2: Percentage of use of different ACE inhibitors/ARBs

HMG-Co A reductase inhibitors

Atorvastatin was given to 100% of patients and among them, 72 (13.71%) were given 20 mg/day dose, 276 (52.57%) were given 40 mg/day dose and 177 (33.71%) were given 80 mg/day dose.

Other drugs-

Proton pump inhibitors in 411 patients (78.29%),

Anxiolytics in 207 patients(39.43%),

Nitrates in 165 patients(31.43%),

Calcium channel blockers in 93 patients (17.71%),

Spironolactone in 90 patients (17.14%),

Diuretics in 84 patients(16%, thiazide and loop diuretics),

H2 receptor blockers in 84 patients (16%),

Cilostazole was used in 51 patients(9.71%),

Nicorandil was used in 36 patients (6.86%).

For health outcomes, we measured the score of "Minnesota living with heart disease questionnaire" on 3 visits of each study subjects, at the initial visit after discharge from hospital, 1 month after that and 3 months after that. There are 21 questions having score range 0 to 5 for each question. Mean score at 1st visit,2nd and 3rd visit were 45.36, 24.29 and 12.94. Comparison between scores at different visits were done by Kruskalwallis test and Dunn's multiple comparison test (as post hoc test) and it showed very significant reduction in score ($p<0.0001$) while comparing between each two sets, i.e., between score at 1st visit and score after 1 month, between score at 1st visit and score after 3 months and between score after 1 month and score after 3 months. It indicates satisfactory improvement in quality of life due to drug therapy.

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But there were some patients who were not given beta blockers (69 patients) nor ACE inhibitors/ Angiotensin receptor blockers (66 patients) or both due to some contraindications or adverse effects or other reasons. Total number of such patients was 117. Total 408 patients were given all the drugs for main indication, i.e., aspirin-clopidogrel, beta blockers, statins, ACE inhibitors/ angiotensin receptor blockers. We compared scores of "Minnesota living with heart disease questionnaire" on 3 visits in these 2 groups by unpaired t test. (table 2)

Table 2: evaluation of health outcome by improvement in quality of life

visit	Minnesota score in groups receiving 5 major drug groups	Minnesota score in groups not receiving 5 major drug groups	Test applied	P value
1st	Mean score- 47.18 95% CI*- 45.22 to 49.14	Mean score- 44.78 95% CI- 43.56 to 46.00	Unpaired t test.	0.0522
2nd (after 1 month)	Mean score- 29.23 95% CI- 27.00 to 31.46	Mean score- 22.57 95% CI- 21.40 to 23.74	Unpaired t test.	<0.0001
3rd (after 3 months)	Mean score- 16.95 95% CI- 15.40 to 18.49	Mean score- 11.86 95% CI- 11.10 to 12.63	Unpaired t test.	<0.0001

**CI- Confidence interval*

This table showed that in patients who were given all the 5 drugs for main indication fared significantly better than those who were not given all drugs.

DISCUSSION

From our study it is clear that incidence of ACS increases with age with a strong trend to peak over 60 years. There is also a very high male:female ratio amongst ACS patients in this study, which is similar to other studies involving patients of acute coronary syndrome.[17,18]

All the prescriptions were intercepted after consultation by a senior consultant cardiologist, thus reducing the impact of prescriber's variables like age, sex, qualifications etc. on prescribing pattern.

There was a high incidence of comorbid conditions like diabetes mellitus, hypertension and smoking among study subjects establishing their role in pathogenesis of ACS.

The number of patients who were prescribed these drugs was high (87%) compared to similar other studies. The studies in Hyderabad, Saudi Arabia and Spain showed use of ACE inhibitors only in 45.71%, 59%, 32% respectively. A strong correlation was found regarding prescription of this group of drugs and presence of diabetes mellitus.

Number of subjects prescribed beta blockers is quite satisfactory (86.86%) compared to other similar studies. The studies in Hyderabad[19], Saudi Arabia[20] and Spain[21] showed use of beta blockers in only 60%, 69% and 50.2% patients respectively.

And while comparing the score of "Minnesota living with heart disease questionnaire" on 3 visits of each study subjects, it has been found though there is overall significant satisfactory improvement with drug therapy. But while comparing the improvement over time between 2 groups (patients who were not prescribed drugs from all the 5 groups for main indication and patients who were given all the 5 drug groups), it was found that improvement over time is very significant in the latter group. It indicates that drugs from all these 5 groups must be given to all follow up patients of ACS, unless contraindicated as they significantly improve quality of life of the patients with heart disease and this beneficial effect is additive with each drug group.

CONCLUSIONS

The quality of prescriptions among this important group of patients was very good compared to similar other studies, done in India or abroad.

There is overall significant satisfactory improvement with drug therapy.

Prescription of all 5 drug groups (as per AHA/ACC 2007 guidelines) has significant better outcome in quality of life score than prescription of less than 5 drug groups.

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Conflict of interest- Nil

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