3 (6%) patients, 6.25 mg in 1 (2%) patient, 10 mg in 1 (2%) patient, and 20 mg in 1 (2%) patients. Among Group-A patients who underwent combination therapy (ivabradine + beta-blockers) were 4 and who shifted from beta-blocker to ivabradine were 8. Among 100 patients, males were 71%, females were 29%. Age categorization of total study population was done in 100 patients, aged between 35 and 44 years was 13 (13%), aged between 45 and 54 years was 30 (30%), aged between 55 and 64 years was 32 (32%), aged between 65 and 74 years was 21 (21%), and >75 years was 4 (4%) were found. The maximum number of patients 32 (32%) was present in the age group between 55 and 64 and the minimum number of patients 4 (4%) was present in the age group >75 years. The majority of the patients were in the age group between 55 and 64 (32%) years of age, which are highly affected by ACS. The prevalence of ACS was high in rural (56%). Diabetic mellitus (53%) and hypertension (51%) were found to be the leading risk factor for the development of ACS followed by smoking (15%) and alcohol consumption (8%). Among the 100 patients, surgical procedure was performed in 58 patients, coronary artery bypass grafting (CABG) (29%), and percutaneous transluminal coronary angioplasty (PTCA) (28%). Coronary angiography showed single vessel disease is 30% in Group-A and 21% in Group-B, double vessel is 14% in Group-A and 11% in Group-B, and triple vessel is 23% in Group-A and 18% in Group-B. In Group-A, patients with severe EF was 14 (14%) and with moderate 36 (36%) and in Group-B, patients with severe EF was 4 (4%) and with moderate 46 (46%). Contraindications for beta-blockers to select ivabradine include pulmonary edema 22 (44%) patients, persistent tachycardia 21 (42%) patients, cardiogenic shock 4 (8%) patients, lower respiratory tract infection 2 (4%) patients, and severe airway obstruction 5 (10%) patients. Predisposing factors in ivabradine were done in 50 patients. Pulmonary edema was 22 (44%), persistent tachycardia was 21 (42%), cardiogenic shock was 4 (8%), lower respiratory tract infection was 2 (4%), and severe airway obstruction was 5 (10%). Pulmonary edema was more when compared with other factors. According to NYHA classification, Class-I (no limitation of physical activity; according to physical activity does not cause undue fatigue, palpitation, dyspnea) which includes 6 patients. Class-II (Slight limitation of physical activity. Comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea) which includes 14 patients. Class–III (Marked limitation of physical activity. Comfortable at rest. Less than ordinary activity causes fatigue, palpitation, or dyspnea) which includes 15 patients and Class –IV (unable to carry on any physical activity without discomfort. Symptoms of heart failure at rest. If any physical activity is undertaken, discomfort increases) which includes 15 patients. The NYHA classification was seen in 50 patients treated with ivabradine and in Grade I 6 (12%), Grade II 14 (28%), Grade III 15 (30%), and Grade IV 15 (30%) were found. Hence, maximum patients were found in Grades III and IV. Minimum patients were in Grade I, which are given in Table 1. Ivabradine decreased the mean heart rate from 112.98±23.90 to 89.97±10.27 (Group-A) beats/min and beta-blockers decreased the mean heart rate from 99.6±20.44 to 86.76±13.14 (Group-B) beats/min. p-value is analyzed by unpaired two-tailed t-test (p=0.24) (Table 2). Both drugs decreased the mean heart rate to 89.97±10.27 (Group-A) versus 86.76±13.14 (Group-B) beats/min. After performing statistical tests, ivabradine is equally effective as beta-blockers. p>0.05 says that the study accepts the null hypothesis. This analysis suggests that ivabradine is equally effective as beta-blockers (Table 2).

DISCUSSION

The study was on considerations and comparative efficacy between ivabradine and beta-blocker in patients with the ACS. CAD is affecting Indians 5–10 years earlier than other communities. In some studies, below 4–5 years suffering from acute myocardial infarction is reported to be high in 25–40% [1]. Therefore, existing guidelines for STEMI have given Class-I recommendation to oral beta-blockers therapy administration promptly to patients without contraindications. Beta-blockers have the propensity to cause AV block and there is a 19% incidence of high degree heart block complicating acute inferior infarction [16]. However, the use of beta-blockers is restricted in some patient's subgroups with severe LV dysfunction and acute bronchospasm or having cardiac conduction abnormalities. In this case, ivabradine can be a best possible alternative. Ivabradine is a pure heart rate lowering agent in patients with sinus rhythm [15]. The greater part of studies stated that beta-blockers were equally effective with ivabradine in reducing the heart rate. In our study, we have found that in non-surgical patients both drugs showed equal effects but during the surgical intervention in the patients who underwent surgery with CABG and PTCA, there was post-operative persistent tachycardia with heart rate (>120 bpm). Ivabradine is a safe alternative to lessen heart rate in post-cardiac surgery patients; it allows to reduce the heart rate, which is the target in the immediate post-operative phase and that cannot be obtained in all patients by increasing the beta-blockers dose. Ivabradine particularly inhibits the I_f of cardiac pacemakers without disturbing other cardiac ionic currents and has no effect on cardiac contractility, repolarization, (or) AV conduction [15]. Beta-blockers are the most regularly used first-line therapy. The use of β-blockers is complex and controversial in patients with conduction abnormalities, severe LV dysfunction and active bronchospasm, severe airway obstruction, chronic fatigue, cardiogenic shock, hypersensitive to β-blockers, severe hypertension, peripheral vascular disease, patient on ventilator, persistent tachycardia, and post-operative persistent tachycardia [16]. Ivabradine quite the reverse to beta-blockers has been shown better myocardial perfusion. Ivabradine showed improvement in clinical outcomes in treating heart rate in ACS patients [15]. Both drugs decreased the mean heart rate to 89.97±10.27 (Group-A) versus 86.76±13.14 (Group-B) beats/min (p=0.24). We found that beta-blockers were equally effective as ivabradine in ACS patients for lowering the heart rate. The result obtained was clinically significant and statistically not significant at p>0.05. Hence, it was proved that ivabradine and beta-blockers both effective in view of efficacy. Clinically, ivabradine showed a significant reduction in heart rate than beta-blockers. Studies in patients with ischemic heart disease have revealed that a combination of ivabradine and beta-blockers is more effective than beta-blockers alone in improving exercise tolerance [8]. In our study, we were unable to reach the equal number of gender distribution in both groups and unintimidated discharge of a few patients. Follow-

Table 1: Patients basic information

Patient information	Number of patients (%)
Age distribution in total study	
35–44	13 (13)
45–54	30 (30)
55–64	32 (32)
65–74	21 (21)
>75	4 (4)
Total	100 (100)
Predisposing factors percentage in ivabradine	
Pulmonary edema	22 (44)
Persistent tachycardia	21 (42)
Cardiogenic shock	4 (8)
Lower respiratory tract infection	2 (4)
Severe airway obstruction	5 (10)
New York Heart Association classification in ivabradine	
Grade I	6 (12)
Grade II	14 (28)
Grade III	15 (30)
Grade IV	15 (30)

Table 2: Mean heart rate before and after treatment in ivabradine and beta-blockers

Ivabradine mean heart rate		Beta-blockers mean heart rate	
Before	After	Before	After
112.98±23.90	89.97±10.27	99.6±20.44	86.76±13.14

p=0.243783962

up was only up to the hospital stay. The sample size was limited only up to 100 patients. The study period of 6 months was short to evaluate the complete health status after the treatment. We were unable to assess the serious adverse drug reactions on drug administration during a hospital stay. However, rational drug prescribing and patient safety are important things; polypharmacy and misuse of drugs are also the most important things; physicians and clinical pharmacists must focus to avoid all, which cause non-adherence to patients [23-25].

CONCLUSION

Our study highlights the predisposing factors for selecting ivabradine, also tolerability, and efficacy between ivabradine and beta-blockers. The final conclusion suggests that ivabradine is equally effective as beta-blockers.

AUTHORS' CONTRIBUTIONS

All authors have equally contributed to make this research to be successful.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest regarding the content of this article.

REFERENCES

1. Clinical Management Guideline for Coronary Artery Disease for National Programme for Prevention and Control of Diabetes, Cardiovascular Disease and Stroke. Available from: ???. [Last accessed on 2018 Oct 25].
2. Fox K, Ford I, Steg PG, Tendera M, Robertson M, Ferrari R, *et al*. Relationship between ivabradine treatment and cardiovascular outcomes in patients with stable coronary artery disease and left ventricular systolic dysfunction with limiting angina: A subgroup analysis of the randomized, controlled BEAUTIFUL trial. Eur Heart J 2009;30:2337-45.
3. Hidalgo FJ, Anguita M, Castillo JC, Rodríguez S, Pardo L, Durán E, *et al*. Effect of early treatment with ivabradine combined with beta-blockers versus beta-blockers alone in patients hospitalised with heart failure and reduced left ventricular ejection fraction (ETHIC-AHF): A randomised study. Int J Cardiol 2016;217:7-11.
4. Fiuzat M, Wojdyla D, Pina I, Adams K, Whellan D, O'Connor CM. Heart rate or beta-blocker dose? Association with outcomes in ambulatory heart failure patients with systolic dysfunction: Results from the HF-ACTION trial. JACC Heart Fail 2016;4:109-15.
5. Dyer AR, Persky V, Stamler J, Paul O, Shekelle RB, Berkson DM, *et al*. Heart rate as a prognostic factor for coronary heart disease and mortality: Findings in three Chicago epidemiologic studies. Am J Epidemiol 1980;112:736-49.
6. Kannel WB, Kannel C, Paffenbarger RS Jr., Cupples LA. Heart rate and cardiovascular mortality: The Framingham study. Am Heart J 1987;113:1489-94.
7. Volterrani M, Cice G, Caminiti G, Vitale C, D'Isa S, Perrone Filardi P, *et al*. Effect of carvedilol, ivabradine or their combination on exercise capacity in patients with heart failure (the CARVIVA HF trial). Int J Cardiol 2011;151:218-24.
8. Tardif JC, Ponikowski P, Kahan T, ASSOCIATE Study Investigators. Efficacy of the I(f) current inhibitor ivabradine in patients with chronic stable angina receiving beta-blocker therapy: A 4-month, randomized, placebo-controlled trial. Eur Heart J 2009;30:540-8.
9. DiFrancesco D, Tortora P. Direct activation of cardiac pacemaker channels by intracellular cyclic AMP. Nature 1991;351:145-7.
10. Volterrani M, Iellamo F. Complementary and synergic role of combined beta-blockers and ivabradine in patients with chronic heart failure and depressed systolic function: A new therapeutic option? Card Fail Rev 2016;2:130-6.
11. Ludwig A, Zong X, Jeglitsch M, Hofmann F, Biel M. A family of hyperpolarization-activated mammalian cation channels. Nature 1998;393:587-91.
12. DiFrancesco D. Funny channels in the control of cardiac rhythm and mode of action of selective blockers. Pharmacol Res 2006;53:399-406.
13. DiFrancesco D. The contribution of the "pacemaker" current (if) to generation of spontaneous activity in rabbit sino-atrial node myocytes. J Physiol 1991;434:23-40.
14. Schulz R, Rose J, Skyschally A, Heusch G. Bradycardic agent UL-FS 49 attenuates ischemic regional myocardial dysfunction and reduces infarct size in swine: Comparison with the beta-blocker atenolol. J Cardiovasc Pharmacol 1995;25:216-28.
15. Chatterjee K, Topol EJ. Cardiac Drugs. 2nd ed. New Delhi: Jaypee Brothers Medical Publishers; 2015. p. 280-2, 385-6, 467.
16. Priti K, Ranwa BL, Gokhroo RK, Kishore K, Bisht DS, Gupta S. Ivabradine vs metoprolol in patients with acute inferior wall myocardial infarction-"expanding arena for ivabradine". Cardiovasc Ther 2017;35:1-6.
17. Ptaszynski P, Kaczmarek K, Ruta J, Klingenheben T, Wranicz JK. Metoprolol succinate vs. ivabradine in the treatment of inappropriate sinus tachycardia in patients unresponsive to previous pharmacological therapy. Europace 2013;15:116-21.
18. Urbanek I, Kaczmarek K, Cygankiewicz I, Ptaszynski P. Risk-benefit assessment of ivabradine in the treatment of chronic heart failure. Drug, Healthc Patient Saf 2014;6:47-54.
19. Iliuta L, Rac-Albu M. Ivabradine versus beta-blockers in patients with conduction abnormalities or left ventricular dysfunction undergoing cardiac surgery. Cardiol Ther 2014;3:13-26.
20. Sulfi S, Timmis AD. Ivabradine--the first selective sinus node I(f) channel inhibitor in the treatment of stable angina. Int J Clin Pract 2006;60:222-8.
21. Yue-Chun L, Teng Z, Na-Dan Z, Li-Sha G, Qin L, Xue-Qiang G, *et al*. Comparison of effects of ivabradine versus carvedilol in murine model with the Coxsackievirus B3-induced viral myocarditis. PLoS One 2012;7:e39394.
22. Swedberg K, Komajda M, Böhm M, Borer JS, Ford I, Tavazzi L. Rationale and design of a randomized, double-blind, placebo-controlled outcome trial of ivabradine in chronic heart failure: The systolic heart failure treatment with the I(f) inhibitor ivabradine trial (SHIFT). Eur J Heart Fail 2010;12:75-81.
23. Borer JS, Böhm M, Ford I, Robertson M, Komajda M, Tavazzi L, *et al*. Efficacy and safety of ivabradine in patients with severe chronic systolic heart failure (from the SHIFT study). Am J Cardiol 2014;113:497-503.
24. Mukesh K, Dahiya V, Mishra S, Sharma D, Mishra N, Lahkar M. Cardiovascular disease prevalence and drug utilization patients at a tertiary care hospital in Northeastern India. Int J Pharm Pharm Sci 2016;8:116-9.
25. Altaf M, Rasheed A, Mujtaba A, Mohammed S. Drug utilization evaluation of antihypertensives in geriatric patients in a tertiary care hospital. Int J Pharm Pharm Sci 2014;6:261-4.

AQ3

Author Queries???

AQ1:Please review the sentence as it seems to be incomplete.

AQ2:Kindly review the text as it creates racism. Please provide modified word for the same.

AQ3:Kindly provide web link

AQ4:Please review the sentence as it seems to be too long.