Good! Is it the best???

Sir,

We read with great enthusiasm, the original article on "comparison of efficacy and tolerability of ivabradine and ranolazine in patients with chronic stable angina" published in January to March issue of JPP.[1] As we had currently analyzed our completed study comparing ranolazine and trimetazidine in patients with chronic stable angina,[2] we would like to bring to your kind notice certain issues in the published study.

The published article comparing ranolazine 500 mg BD and ivabradine 5 mg BD over 8 weeks has shown a reduction in the number of angina attacks per week from baseline angina frequency of 1.8 ± 0.2/week to complete absence of angina with 0 attacks per week. These findings with complete absence of angina after 2 months of treatment is quite surprising as the previous published studies with ranolazine have shown only reduction in the frequency of angina and not complete cessation of angina. Combination assessment of ranolazine in stable angina trial, done with ranolazine demonstrated a reduction in the mean number of weekly anginal attacks to 2.5 and 2.1 after 12 weeks of treatment at a dose of 750 mg BD and 1000 mg BD respectively.[3] Likewise, efficacy of ranolazine in chronic angina trial, showed a decline in the mean angina attacks from 5.5/week at baseline to 2.8/week in the ranolazine group at the end of 6-week of treatment.[4] The TERISA trial done in 462 patients with chronic angina and diabetes mellitus, found the angina frequency had decreased from 6.6 (6.3-7, confidence interval) to 3.8 (3.6-4.1, confidence interval) per week in the ranolazine group (1000 mg BD for 8 weeks).[5] All the above mentioned studies also had shown a decrease in the use of sublingual nitrates per week in the presence of ranolazine. On the contrary, MARISA trial in 191 patients with angina, surprisingly found angina pectoris as an adverse event reported in 8 patients (5%) receiving ranolazine 500 mg BD.[6] Similarly in our study, which is yet to be published comparing ranolazine 500 mg BD and trimetazidine 35 mg BD given for 12 weeks in patients with chronic stable angina and diabetes mellitus, we came across patients developing angina resulting in either withdrawal from the study or increase in sublingual isosorbide di nitrate consumption per week. Hence we feel that in the present study, a mention about the change in adjuvant anti-anginal drugs including nitrate consumption per week at the end of 8 weeks in both ranolazine and ivabradine groups could have helped in interpreting the efficacy of ranolazine in a better way. Moreover, as both primary and secondary outcomes of this study are based on questionnaire, a mention of the validity of the pre-tested questionnaire or a table showing the questionnaire used by the author to assess the angina frequency would have been of use for others planning to conduct a study on the frequency of angina attacks per week with anti-anginal drugs.

We are amazed at the perfectly matched baseline characteristics obtained in a non- randomized, open label study conducted as part of student project with lots of exclusion criteria, in which the patients were already receiving either ranolazine or ivabradine for at least 1 month before the study. We are intrigued this study conducted as a student project for 3 months, with strict criteria excluding patients with systolic blood pressure >170 mmHg and <100 mmHg, diabetes mellitus, past history of myocardial infarction, renal impairment, hepatic impairment, cerebrovascular event, moderate to severe heart failure, bradycardia, second to third degree heart block, arrhythmias, history of drug intake namely diltiazem, verapamil, beta blockers, simvastatin, digoxin, amiodarone, phenytoin etc., could still manage to recruit a sizeable number of patients for such a short period. This study based on subjective assessment using a questionnaire could have taken additional measures to assess compliance. Last but not the least, though it is a student project, the young investigator could have been sensitized regarding the need for registering the trial in Clinical Trials Registry – India (CTRI) as trial registration in the CTRI has been made mandatory by the Drugs Controller General (India) since 15th June 2009.

Sandhiya Selvarajan, Steven Aibor Dkhar, Ajith Ananthakrishna Pillai[1]

Departments of Clinical Pharmacology, and [1]Cardiology, JIPMER, Puducherry, India

Address for correspondence:
S. Sandhiya, Senior Resident,
Division of Clinical Pharmacology, JIPMER, Puducherry - 605 006.
E-mail: sandhiyaselvarajan@gmail.com

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