DABIGATRAN AND MYOCARDIAL INFARCTION, DRUG OR CLASS EFFECT. META-ANALYSIS OF RANDOMIZED TRIALS WITH ORAL DIRECT THROMBIN INHIBITORS

ACC Oral Contributions
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Background: The recent trial on dabigatran versus warfarin in Atrial Fibrillation (RE-LY) demonstrated dabigatran 150 mg twice daily was associated with small but statistically significant increased number of Myocardial Infarction (MI) as compared to warfarin. The purpose of this study was to investigate whether this finding was due to Drug or Class effect.

Methods: We systematically searched MEDLINE using key words, oral, direct thrombin inhibitors and randomized trials. Studies were included in Meta-Analysis if comparison between an oral direct thrombin inhibitor and warfarin was made for any indication and if data on Myocardial Infarction after randomization was available. Fixed and Random effect models were applied when appropriate.

Results: Five trials fulfilled the inclusion criteria with total of 30470 patients. RE-LY and RECOVER using dabigatran, THRIVE, SPORTIF III&V using ximelagatran. Meta-Analysis of the 2 trials with dabigatran revealed significantly higher rates of MI as compared to warfarin, 179/13364 vs 65/7288, Odds Ratio (OR) 1.40 (95% CI 1.05-1.86) p = 0.005, Cochrane Q = 0.16, Degree of Freedom (DF) = 1 and P = 0.68 for heterogeneity. In the 3 trials with ximelagatran, MI occurred in 60/4904 in the ximelagatran arm and 51/4914 in the warfarin arm. OR 1.65 (95% CI 0.55-4.93), p NS. Q=10, DF=2, P = 0.007 for heterogeneity. Overall the oral direct thrombin inhibitors were associated with significantly higher rates of Myocardial infarction as compared to warfarin, 239/18268 vs 116/12202, OR 1.32 (95% CI 1.053-1.66), p= 0.005 Q = 6.02, DF= 3, P= 0.11 for heterogeneity using Fixed effect model.

Conclusions: 1) Our findings suggest an overall trend toward increased rate of myocardial infarction for patients treated with oral direct thrombin inhibitors and dabigatran in particular as compared to warfarin. This trend is statistically significant and may be suggestive of a class effect based on Fixed effect model Meta-Analysis. 2) Clinicians involved in the care of patients with coronary artery disease may need to exercise caution in the use of these agents. 3) Further research is needed to address these concerns.