

Summary

Worldwide, cardiovascular diseases are estimated to be the leading cause of death and disability. Although cardiovascular death rates have declined in several developed countries in past decades, rates of cardiovascular diseases have raised greatly in low income and middle income countries.

The present study was conducted to investigate and compare the effect of ivabradine and bisoprolol on experimentally induced ischemia-reperfusion in rats, to determine if their action will differ if the involved coronary artery changed and to determine their effects on incidence of ventricular arrhythmias.

In the present study, a new multi-vessel ligation method for 30 minutes followed by 90 minutes of reperfusion was used as a procedure to induce ischemia-reperfusion and to assess effects of ivabradine versus bisoprolol on myocardial infarction in rats.

All rats were subjected to continuous ECG tracing for 2 hours for: detection of arrhythmias and time of its onset and for measurement of changes in heart rate, QT and QTc intervals and ST segment deviation before, during ischemia and after reperfusion. Then, the heart tissue was subjected to real-time quantitative polymerase chain reaction (PCR) for detection of BAX gene expression (apoptotic factor).

In the present study, it was found that ivabradine and bisoprolol led to significant heart rate reduction compared to control but insignificant change compared to each other.

In addition, bisoprolol led to significant reduction in ischemia induced ST segment elevation on left main and left anterior descending coronary arteries ischemia compared to ivabradine but insignificant change on right coronary artery ischemia. Overall, there was insignificant change between bisoprolol and ivabradine on ischemia induced ST segment elevation.

Compared to ivabradine, bisoprolol led to differential change in QT and QT intervals as it led to insignificant change in these intervals on left main coronary artery ischemia-reperfusion, significant reduction in these intervals on

left anterior descending artery ischemia-reperfusion and significant prolongation of these intervals on right coronary artery ischemia-reperfusion. Overall, the effects of bisoprolol and ivabradine on QT and QTc intervals were insignificant

Furthermore, Bisoprolol also led to significant decrease in arrhythmia score on left main and left anterior descending arteries ischemia-reperfusion but insignificant change on right coronary artery ischemia-reperfusion compared to ivabradine. Overall, bisoprolol led to decrease in arrhythmia score compared to ivabradine. Changes in time of onset of arrhythmia and incidence of heart block were insignificant between bisoprolol and ivabradine on left main, left anterior descending and right coronary arteries ischemia-reperfusion.

Moreover, changes in BAX gene expression were insignificant between ivabradine and bisoprolol on left main and left anterior descending arteries ischemia-reperfusion but ivabradine produce significant reduction in BAX gene expression compared to bisoprolol on right coronary artery ischemia-reperfusion. Yet, the overall differences were insignificant.

There was a strong significant negative correlation between percentage heart rate reduction and BAX gene expression.

It was concluded that, the more the reduction in the heart rate, the less the myocardial cell damage. In addition, Actions of ivabradine and bisoprolol differ if the culprit artery changed, hence, the importance of multi-vessel ligation method in myocardial infarction assessment. Furthermore, ivabradine was superior to bisoprolol as a cardio-protective drug on myocardial infarction caused by right coronary artery occlusion and was non-inferior to bisoprolol on myocardial infarction caused by left main and left anterior descending arteries occlusion. Moreover, ivabradine was safer than bisoprolol on QT and QTc intervals changes on MI caused by RCA occlusion and was non-inferior to bisoprolol on these intervals on MI caused by left main and left anterior descending arteries occlusion. Finally, bisoprolol was superior to ivabradine as an anti-arrhythmic drug.