Impacts of increasing statin dose on the ratio of atherogenic to protective lipid parameters: insights from the VOYAGER individual patient data meta-analysis

SJ Nicholls 1, P Lundman 2, G Brandrup-Wognsen 3, MK Palmer 4, PJ Barter 5

1 Cleveland Clinic Foundation, Cardiovascular Medicine, Cleveland, Ohio, USA; 2 Danderyd Hospital, Karolinska Institute, Stockholm, Sweden; 3 Åströmska, Malmö, Sweden; 4 Keel University, Keel, UK; 5 Heart Research Institute, Sydney, Australia

background

- There is increasing evidence that the ratios of atherogenic to protective lipid parameters are of major importance in predicting progression of atherosclerosis and cardiovascular event rates.

- In the INTERHEART case-control study, the apolipoprotein B/apolipoprotein A-I (ApoB/ApoA-I) ratio was the strongest of all potentially modifiable risk factors for predicting myocardial infarction (MI) in all geographic regions represented by the 52 countries studied. 1

- Furthermore, European guidelines for the prevention of cardiovascular disease identify the ApoB/ApoA-I ratio as one of the strongest risk markers. 2

- In a UK study of 3510 cases of acute MI and 9805 controls, the low-density lipoprotein cholesterol (LDL-C)/high-density lipoprotein cholesterol (HDL-C) ratio and particularly the ApoB/ApoA-I ratio were both more informative about risk than individual lipid fractions. 3

- In VOYAGER (an individual patient data meta-analysis of statin therapy in At/At risk Groups: Effects of Rosuvastatin, atorvastatin and simvastatin), it was shown that doubling the dose of rosuvastatin, atorvastatin or simvastatin resulted in greater reductions in LDL-C and ApoB (by increments of 5.7% and 4.6%, respectively). 4 A positive relationship between increases in HDL-C and dose of rosuvastatin, atorvastatin or simvastatin was also observed. 4 The percentage change in HDL-C was almost identical to that of ApoA-I at all doses of all three statins. 4

- To date, however, the impact of increasing statin dose on LDL-C/HDL-C and ApoB/ApoA-I ratios has not been elucidated.

purpose

- The aim of this study was to determine the impact of increasing statin dose on LDL-C/HDL-C and ApoB/ApoA-I ratios. Data from the VOYAGER database were used.

methods

- The VOYAGER database, which comprised 37 comparative studies with individual patient data, has been described previously. 4

- In the present analysis, the impact of increasing statin dose on LDL-C/HDL-C ratio (n=32 258) and ApoB/ApoA-I ratio (n=24 339) was investigated in patients treated with daily doses of rosuvastatin 5-40 mg, atorvastatin 10-80 mg and simvastatin 10-80 mg.

- Changes in ratios in lipids and lipoprotein ratios were compared using a single mixed effects model that employed fixed effects for trial/treatment periods and statin/doses, and a random effect for trial/period-by-treatment interaction. Changes in ratios were expressed as least-square mean (LSM) percent change.

- Differences in percentage change of ratios between each dose of rosuvastatin and each dose of either atorvastatin or simvastatin were calculated using only those trials that directly randomized the treatments being compared.

- Statistical analyses were carried out using SAS version 9.1.3.

results

- In the present analysis, there was a greater decrease from baseline with increasing statin dose for all three statins for both the LDL-C/HDL-C ratio (Figure 1) and the ApoB/ApoA-I ratio (Figure 2).

- Figures 3 and 4 show paired comparisons for percent change in LDL-C/HDL-C ratio and ApoB/ApoA-I ratio, respectively.

conclusions

- These results indicate that increasing the dose of rosuvastatin, atorvastatin and simvastatin has a beneficial incremental impact on the ratios of atherogenic to protective lipids for both the LDL-C/HDL-C ratio and ApoB/ApoA-I ratio.

- These findings support the need to use higher doses of effective statins in order to have a greater impact on cardiovascular risk.

disclosures

Development and analysis of the VOYAGER database was sponsored by AstraZeneca. PJ Barter has received research grants or support and/or honoraria from Merck, Pfizer, Roche and AstraZeneca and has been a consultant for AstraZeneca, CSL, Merck, Pfizer, Roche and Sanofi-Aventis. G Brandrup-Wognsen is an employee of AstraZeneca, Sweden. P Lundman has received honoraria from and served on national advisory boards for AstraZeneca, Merck and Pfizer. SJ Nicholls has received research grants and/or honoraria from AstraZeneca, Novartis, Reckitt, Eli Lilly and Amgen, and has been a consultant for Takeda and Roche. MK Palmer has received research support from AstraZeneca and Boehringer-Ingelheim and has been a consultant for Roche.

references


The study was sponsored by AstraZeneca. Medical writing support was provided by Prime Medica, Knutsford, Cheshire, UK and was funded by AstraZeneca. Presented at the European Society of Cardiology Congress, 28 August – 1 September 2010, Stockholm, Sweden.