Prevalence of SLCO1B1 single nucleotide variations and their association with hypercholesterolaemia in hypercholesterolemic patients in Gauteng, South Africa

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Introduction

Statins, the most widely prescribed and standard treatment for hypercholesterolemia, have been associated with a range of side effects, including muscle toxicity and fatigue.[1 - 2]

Genetic variations, such as single nucleotide variations (SNV), may affect the pharmacokinetics and hence plasma concentrations and total exposure to a drug. [4]

It is hypothesized that *SLCO1B1* (*rs4149056, rs2306283* and *rs4363657*) SNVs diminish statin uptake and metabolism and may thus be associated with statin intolerance. [3 - 5]

Aim

This study determined the prevalence of SLCO1B1 single nucleotide variations (SNVs) and possible associations between SLCO1B1 SNVs, statin intolerance and creatine kinase (CKM) in hypercholesterolemia.

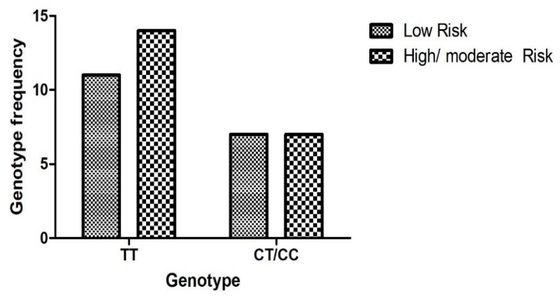
Methods

181 healthy controls and 100 hypercholesterolemic patients receiving either simvastatin (71%) or atorvastatin (29%) were recruited.

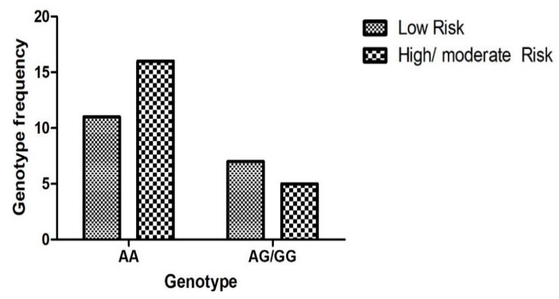
- A quantitative questionnaire was used to assess their risk of statin intolerance.
- Polymerase Chain Reaction - Restriction Fragment Length Polymorphism was used to identify the presence of SLCO1B1 SNVs (rs4149056, rs2306283 and rs4363657).
- Enzyme-linked immunosorbent assay was used to quantify serum CKM levels.

Results

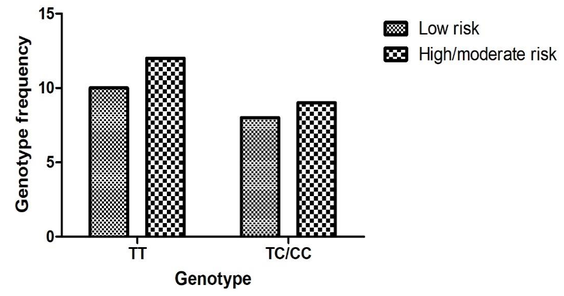
- Of the 100 hypercholesterolemic patients, 15% were at high risk, 49% at moderate risk and 36% at low risk of statin intolerance.
- The prevalence of the rs4149056 variant was 16% and 20% for the test and control groups, respectively. (OR=1.324; 95% CI=0.8430 to 2.078; p=0.2405).
- The rs2306283 variant was present in 31.5% of the control group compared to only 10.5% in the test group (OR=0.2552 95% CI=0.1542 to 0.4223, p< 0.0001).
- The prevalence of the rs4363657 variant was similar in each group. (OR=1.345, 95% CI=0.8492 to 2.129, p=0.2380).
- A comparison of genotype frequencies based on calculated statin intolerance risk showed no significant association between any of the SNVs,).



(1) rs4149056, OR=0.7857, 95% CI=0.2115 to 2.919, relative risk (RR)= 0.8800, 95% CI= 0.4433 to 1.747, p=0.7496

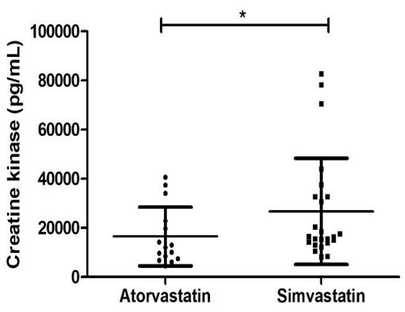


(2) rs2306283, OR=0.4911, 95% CI=0.1234 to 1.954, RR=0.9659, 95% CI= 0.4888 to 1.909, p=0.4877

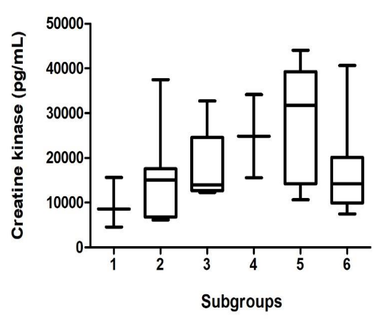


(3) rs4363657, OR= 0.9375, 95% CI= 0.2634 to 3.3337, RR=0.6984, 95% CI=0.3609 to 1.352, p=1.0000

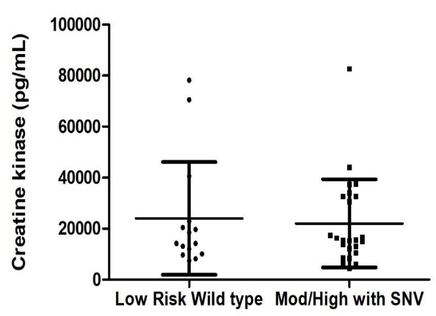
- CKM levels in patients on simvastatin were significantly higher compared to those on atorvastatin (p=0.0418).



Serum CK levels of patients within the simvastatin and atorvastatin treatment groups
*p= 0.0418, Indicates statistical significance with p<0.05



Serum CK levels of patients in subgroups.
Box whisker plot representing median, interquartile range and standard deviation



CK levels of patients within the Low-risk Wild type and moderate/high risk with one SNV subgroups

Conclusion

The prevalence of the SLCO1B1 SNVs in this population is novel data. No association between the presence of any one of the SNVs and the statin intolerance severity risk score or CK elevation was found. These findings may facilitate a more personalized approach to statin therapy, especially relevant within the diverse South African population.

References

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