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PHARMACOGENETIC TESTING FOR PERSONALISATION OF STATIN THERAPY

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INTRODUCTION

The *SLCO1B1* protein facilitates the hepatic uptake of simvastatin. The *SLCO1B1* c.521T>C genetic polymorphism (rs4149056) decreases the function of *SLCO1B1* and is a predictor of simvastatin-induced myopathy.[1] *SLCO1B1* pharmacogenetic testing and pharmacist interpretation of test results are a step forward to personalise statin therapy.

AIMS

- To classify a cohort of cardiac patients on simvastatin according to *SLCO1B1* c.521T>C genotype and function
- To investigate the correlation of *SLCO1B1* genotype and function to myopathy risk

Setting

Cardiac Catheterisation Suite, Mater Dei Hospital, Malta

METHOD

1. Patient recruitment (on simvastatin, ≥18 years, no severe renal or hepatic impairment)
2. Compiling patient data and collection of EDTA-blood sample
3. Genomic DNA extraction with QIAamp® DNA Mini kit *(Qiagen®)*
4. Real-time PCR *SLCO1B1* rs4149056 c.521T>C genotyping with Sacace® Biotechnology kits using the Rotor-Gene™ 6000/Q *(Corbett Research, Qiagen)*
5. Patient classification according to *SLCO1B1* genotype, function and myopathy risk. Follow-up for muscle symptoms after 6 months

Ethics approval was obtained

RESULTS

- A total of 110 Caucasian patients (mean age 65.44 ±10.73 years, 81.8% male) were genotyped.
- Twenty-four patients (21.8%) were genotyped as heterozygous TC and homozygous variant CC, corresponding to intermediate and low *SLCO1B1* function respectively (Table 1).
- 15 of the 24 patients genotyped as TC or CC were on simvastatin 40mg daily, which is higher than 20mg daily dose recommended by the Clinical Pharmacogenetics Implementation Consortium guideline.[2]
- 15 of the 110 patients had documented muscle symptoms at follow-up; stiffness (n=6; 5 TT, 1 TC), cramps (n=4; TT), pain (n=4; 3 TT, 1 CC) and weakness (n=1; TC).

Table 1. Patients classified according to SLCO1B1 genotype and function (N=110)

SLCO1B1 genotype	Percentage of patients % (n)	*SLCO1B1* function
TT	78.2 (86)	Normal
TC	20.0 (22)	Intermediate
CC	1.8 (2)	Low

CONCLUSION

Patients genotyped as TC and CC (21.8%) have mild and high myopathy risk respectively compared to TT patients. One out of the 2 CC patients had documented muscle pain which may be an important signal however the sample was too small for statistical analysis. Participation of hospital pharmacists in the clinical implementation of *SLCO1B1* pharmacogenetic testing for statin therapy may improve patient safety with respect to myopathy.

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