PHARMACOGENETIC TESTING FOR PERSONALISATION OF STATIN THERAPY

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INTRODUCTION

The SLC01B1 protein facilitates the hepatic uptake of simvastatin. The SLC01B1 c.521T>C genetic polymorphism (rs4149056) decreases the function of SLC01B1 and is a predictor of simvastatin-induced myopathy.1 SLC01B1 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 SLC01B1 c.521T>C genotype and function
• To investigate the correlation of SLC01B1 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 QuAmp® DNA Mini kit (Qiagen®)
4. Real-time PCR SLC01B1 rs4149056 c.521T>C genotyping with Sacace® Biotechnology kits using the Rotor-Gene™ 6000/Q (Corbett Research, Qiagen)
5. Patient classification according to SLC01B1 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 SLC01B1 function respectively (Table 1).

<table>
<thead>
<tr>
<th>SLC01B1 genotype</th>
<th>Percentage of patients (% (n))</th>
<th>SLC01B1 function</th>
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<tbody>
<tr>
<td>TT</td>
<td>78.2 (86)</td>
<td>Normal</td>
</tr>
<tr>
<td>TC</td>
<td>20.0 (22)</td>
<td>Intermediate</td>
</tr>
<tr>
<td>CC</td>
<td>1.8 (2)</td>
<td>Low</td>
</tr>
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</table>

• 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 SLC01B1 genotype and function (N=110)

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 SLC01B1 pharmacogenetic testing for statin therapy may improve patient safety with respect to myopathy.

Funding: University of Malta Research Grant PHHRP12-17

REFERENCES