MONITORING THIOPURINE METHYLTRANSFERASE (TPMT) ACTIVITY IN INFLAMMATORY BOWEL DISEASE: IS IT WORTH IT?

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Introduction Azathioprine and 6-mercaptopurine are immunosuppressants used to treat inflammatory bowel disease (IBD). Marrow toxicity occurs in 3% of patients receiving these drugs. Some practitioners propose that checking Thiopurine methyltransferase (TPMT) activity can predict this myelosuppression and improve patient safety. Currently such practice is not widespread.

Methods The aim was to review our current practice and determine if knowledge of TPMT activity prior to starting thiopurines leads to fewer myelosuppressive events and therapy adjustments.

Data from IBD patients taking thiopurines between 2007 and 2010 were reviewed for measurement of TPMT activity, incidence of leucopenia (white cell count <4.0) and dosage changes as a result of leucopenia.

Results 229 patients received a thiopurine between 2007 and 2010. Of these, 82 (35.8%) had a TPMT result available. No patients were deficient in TPMT (<10 μ/l). There were 68 patients (82.9%) identified with low levels of TPMT (10–67 μ/l) and 14 patients (17.1%) had normal TPMT levels (68–150 μ/l). No patients in our cohort had high levels of activity (>150 μ/l).

Overall, leucopenia was identified in 45 patients (19.7%). The majority, 35 patients (78%), had a mild transient leucopenia needing no dose adjustment. 7 patients developed leucopenia which did not resolve and required dose reduction and 3 patients had therapy stopped. Of those patients with low TPMT activity, 18/68 developed leucopenia (26.5%), 1 had therapy stopped and 2 reduced. Two patients (14.3%) with normal TPMT activity developed leucopenia, of which only one had therapy stopped. In patients with no TPMT result, 25 (16.9%) developed leucopenia of which 1 patient had therapy stopped and 5 had therapy reduced. There were no serious adverse events relating to immunosuppression during the study period.

Conclusion Although there were no patients deficient in TPMT, there was a higher than expected number with low levels. Such low TPMT activity levels were associated with a higher incidence of mild transient leucopenia. However, the incidence of clinically significant leucopenia requiring dosage change was the same in all study groups although absolute numbers are small. Although measurement of TPMT activity may have a role in identifying the 1 in 300 patients who are deficient and at risk of developing severe myelosuppression, initiating thiopurine use in IBD without measuring TPMT activity appears to be safe with standard blood monitoring.

Competing interests None.

Keywords Inflammatory Bowel Disease, TPMT.

REFERENCE

Table 1

<table>
<thead>
<tr>
<th>TPMT phenotype</th>
<th>No of patients</th>
<th>Transient leucopenia (%)</th>
<th>Leucopenia requiring dose change (%)</th>
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</thead>
<tbody>
<tr>
<td>Not checked</td>
<td>147</td>
<td>25/147 (17)</td>
<td>6/147 (4.1)</td>
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<tr>
<td>Low</td>
<td>68</td>
<td>18/68 (26)</td>
<td>3/68 (4.4)</td>
</tr>
<tr>
<td>Normal</td>
<td>14</td>
<td>2/14 (14)</td>
<td>1/14 (7)</td>
</tr>
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