Evaluation of cardiac toxicity related to capecitabine chemotherapy: single centre audit of local practice.

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Background:
Incidence of cardiotoxicity related to capecitabine chemotherapy is around 3-9%. There are no National or International guidelines on the use of capecitabine in patients at risk of developing cardiac side effects. Based on literature review, personal experience, and the New York Heart Association (NYHA) classification of cardiac disease1, we have developed a set of standards (see box) to guide its use with respect to cardiotoxicity, including dose modifications where a history of cardiac disease exists.

We report the results of an initial audit of practise against these standards.

Standards:

1. Cardiac history should be taken and documented for all patients being considered for treatment with capecitabine.
2. Where there is a positive cardiac history, the severity of symptoms should be recorded according to the NYHA classification.
3. All patients should be counselled regarding the risk of cardiac toxicity as part of an informed consent process.
4. Any patient developing possible cardiac symptoms during a course of capecitabine chemotherapy should have appropriate cardiac investigations including electrocardiogram (ECG) and cardiac enzymes. Results should be clearly documented in case notes.
5. Capecitabine dose should be electively modified according to cycle number and NYHA class (table 1).

Results:
9 patients (9%) had a prior history of cardiac disease. 7 patients developed probable cardiac symptoms whilst on capecitabine therapy. One of these patients had a prior history of cardiac disease, and one a history of atrial fibrillation and previous transient ischaemic attack. The remaining five patients experiencing symptoms had no cardiac history.

3 patients discontinued capecitabine because of cardiac side effects. One patient died suddenly at home within 30 days of receiving chemotherapy (cause unknown).

Were standards met?

1. and 2. Documentation of cardiac history: A cardiac history was taken in 95% patients but documentation of NYHA status was poor.

3. Counselling of cardiac risk: Information about cardiac risk is now printed on consent forms for capecitabine and 5-fluorouracil so this standard was not measured in this audit.

4. Appropriate investigations performed and results documented: Patients experiencing chest pain usually attend their local accident and emergency department so documentation of cardiac investigations was not always available in our case notes. Where results were available there were no cases of abnormal ECGs or raised cardiac enzymes.

Table 1. Recommended dose modifications according to cycle number and NYHA class:

<table>
<thead>
<tr>
<th>NYHA grade</th>
<th>Cycles 1 and 2</th>
<th>Cycle 3 onwards if no cardiac symptoms and tolerating treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>50-80%</td>
<td>100%</td>
</tr>
<tr>
<td>II</td>
<td>50%</td>
<td>80-100%</td>
</tr>
<tr>
<td>III</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>IV</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

Methods:
Case notes of 100 consecutive patients receiving capecitabine as adjuvant or metastatic treatment for colorectal and gastric cancers in 2008 were reviewed. Patient demographics were recorded, as well as regime and dose of capecitabine used, dose reductions and early termination of treatment. Toxicity was assessed using National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) version 3 and documentation of cardiac history and investigations (if appropriate) was noted.

Results were processed using SPSS software.

References:
1. www.hcoa.org/hcoacme/chf-cme/chf00070.htm