Objective

Oral capecitabine is increasingly used to replace intravenously (IV) administered fluorouracil (5FU) in systemic oncology treatment protocols at the BC Cancer Agency (BCCA). However, the level of patient adherence with oral capecitabine is unknown and may potentially compromise treatment outcomes. This study was undertaken to determine the accuracy and efficiency of using prescription refill data to evaluate adherence to capecitabine compared to other methods of assessing adherence to oral prescription drugs from published literature.

Background / Purpose

Other methods of evaluating adherence to oral medications in the literature have included:

- Patient self-reporting
- Pill counts
- Micro-electronic monitoring of prescription vial opening

Literature reports indicate none of these methods fully identifies actual patient adherence. The purpose of this study is to evaluate whether a computer algorithm applied to prescription refill data could effectively and accurately evaluate adherence to oral capecitabine in cancer patients.

Methods

Two years of capecitabine refill data from Jan 1, 2009 to Dec 31, 2010 were extracted from the BCCA Pharmacy Data Warehouse for prescriptions dispensed at the regional centres of the BC Cancer Agency using a custom Java-based software tool. Patients on concurrent chemoradiation or clinical trial protocols were excluded.

Extracted data included:

- BCCA patient registration number
- Dispense dates
- Dosage strength(s), quantity, & dosing instructions
- Treatment protocol code
- Blister packaging or standard prescription vial

Review by computer algorithm

Based on cycle length of the specified protocol cycle, the computer algorithm estimated a predicted next dispense date and calculated the difference between the predicted vs actual next dispense dates. Differences less than or greater than zero were identified as potential Altered Treatment Date Incidents (ATDI) by the computer.

Potential ATDIs were further reviewed to exclude:

- Refills within +/- 1 day counts because BCCA allows scheduling chemotherapy appointments within +/- 1 day of the treatment cycle
- Refills with actual refill dates exactly -7 days from predicted date (or -6 days if treatment interval included a statutory holiday) because they were associated with valid clinical reasons for delay. In these cases, patients would still have capecitabine dispensed while at the cancer clinic on the day of their physician appointment. Future appointments were already pre-scheduled resulting in appointments for reassessment a week in advance of their next treatment cycle.

Manual review of electronic medical charts

This was performed by a single investigator (LK) for all eligible patients to identify reasons for delays:

1. Clinical delay
2. Patient scheduling issues
3. Patient choice to delay treatment
4. No reason identifiable
5. Patient non-adherence
6. Chemotherapy restarted after intended treatment break (for cumulative toxicity or post-operatively)

Analysis

Data were presented in Microsoft Excel® format for analysis. Comparison was made of the prevalence of ATDIs as identified by the computer algorithm before vs. after exclusion of the +/-1, -6 and -7 day counts. In addition, based on manual chart review, modified predicted refill dates were assigned to ATDIs identified by computer algorithm. ATDIs were excluded if:

1. Delays were due to clinical issues (reason 1) or treatment break (reason 6)
2. Delays were due to scheduling issues (reason 2) if the difference between the modified predicted vs actual dispense dates was +/-1, -6, or -7 days.

Results

A total of 894 patients (36.4% male, median age 66 y) were identified (gastrointestinal 62.5%, breast 37.5%). A total of 6,880 prescriptions representing 4412 refill dates were reviewed, with 1995 (45.2%) having different computer predicted vs actual refill dates. This was reduced to 807 (18.3%) after manual chart review to adjust for valid reasons for delay.

During the chart review, 192 (21.4%) patients were excluded because they had only one cycle of capecitabine dispensed. The patients were labeled as being “not applicable” (NA). No treatment delays were found for 79 (3.3%) patients. For the remaining 623 (69.7%) patients, the median, mean and range of incidences of ATDIs were determined as follows:

<table>
<thead>
<tr>
<th>Incidence of ATDIs per patient</th>
<th>According to computer algorithm before adjustments</th>
<th>According to computer algorithm after adjustments</th>
<th>According to manual chart review after adjustments</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEDIAN</td>
<td>2.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>MEAN</td>
<td>2.8</td>
<td>1.8</td>
<td>1.1</td>
</tr>
<tr>
<td>RANGE</td>
<td>0-2</td>
<td>0-2</td>
<td>0-11</td>
</tr>
</tbody>
</table>

Incidence of actual patient non-adherence was only 0.9% of the ATDIs. Other reasons for ATDIs, as determined by the chart review, are shown below:

Discussion

- Significant reductions in the numbers of ATDIs occurred as a result exclusion of the +/- 1 day counts both before and after the chart review. Manual workload could have been reduced by creating auto-exclusions for these as well as for the -6 & -7 day counts within the algorithm.
- The manual chart review significantly reduced the number of ATDIs but was very labour intensive to perform. The BCCA’s order entry system, WOR®, has space available for Pharmacy notes at the time of dispensing and could be utilized to reduce this workload.
- The manual chart review was limited by lack of apparent documentation of reasons for ATDIs (39.3%). Had the reasons for these ATDIs been identified the apparent incidence of non-adherence to capecitabine could have been quite different than these results show.
- The incidence of actual cases of patient non-adherence was extremely low (0.9%). These incidences included those times when patients did not follow dosing instructions or did not complete the treatment cycle for non-clinical reasons. If the times that patients make the choice to delay treatments (ie. for vacations or family events) that otherwise clinically could have occurred on time, the incidence of non-adherence would have totaled 5.0%.

Conclusion

With modifications the computer algorithm used may provide trends in adherence to oral capecitabine with some efficiency. However, without manual chart review to verify results the algorithm cannot be used in isolation of actual clinical data for this purpose.

References


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