EVALUATION OF OXALIPLATIN-SPECIFIC NEUROTOXICITY BASED ON TOTAL CUMULATIVE DOSE

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Background

Oxaliplatin is an effective drug for adjuvant or metastatic treatment of patients with colorectal cancer (CRC). Common side effects include acute cold-induced as well as chronic neurotoxicity resulting in dose reduction or even complete oxaliplatin discontinuation and treatment modification. For patients receiving high cumulative doses of oxaliplatin (780-850 mg/m²), the incidence of grade 2 or 3 neurotoxicity has been shown to be 12-18% (1).

Purpose

The aim of our study was to investigate both the incidence and significance of neurotoxicity in patients receiving cumulative oxaliplatin doses of 1000 mg/m² or higher. We could then determine whether a pre-emptive intervention of a clinical pharmacist is justified.

Materials and methods

In the period from January 2016 to July 2017 484 patients diagnosed with CRC received oxaliplatin as part of their treatment regimen. Among them, 40 patients who had received cumulative doses 1000 mg/m² or higher were selected based on automatic alerts generated by the software used for prescribing and preparation of cytotoxic drugs. For patients which the predetermined cumulative dose limit has been exceeded, therapy is validated for preparation by the pharmacist only after additional confirmation by the prescribing physician.

Materials and methods

An oxaliplatin specific scale (NCI-CTC 2.0) was used to assess the level of neurotoxicity (2).

Table 1. Classification systems for Oxaliplatin-induced neurotoxicity.

<table>
<thead>
<tr>
<th>Grade</th>
<th>NCI-CTC 2.0</th>
<th>Oxaliplatin-Specific Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>1</td>
<td>Loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function</td>
<td>Sensory symptoms of short duration</td>
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<tr>
<td>2</td>
<td>Objective sensory loss or paresthesia (including tingling), interfering with function, but not with activities of daily living</td>
<td>Sensory symptoms persisting between cycles</td>
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<tr>
<td>3</td>
<td>Sensory loss or paresthesia interfering with activities of daily living</td>
<td>Sensory symptoms causing functional impairment</td>
</tr>
<tr>
<td>4</td>
<td>Permanent sensory loss that interferes with function</td>
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</tbody>
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Abbreviation: NCI-CTC, National Cancer Institute common toxicity criteria.

Results

Symptoms presented as moderate paraesthesia (grade 1) occurred in 11 patients (28%), while 6 patients (15%) reported of mild or moderate objective sensory loss (grade 2). Dose-limiting neurotoxicity (grade 2 and 3) was observed in 9 patients (22.5%) with a complete oxaliplatin discontinuation being required in 3 patients (7.5%) due to sensory loss, polynuropathy and pain (grade 3). 11 patients (27.5%) remained asymptomatic according to the NCI-CTC scale.

Figure 2. Number of patients with oxaliplatin-specific symptoms of neurotoxicity.

Conclusion

The results of our study are in agreement with published data. Based on the findings that over one-fifth of patients receiving high cumulative doses of oxaliplatin experience significant neurotoxicity (grade 2 and 3), a clinical pharmacist’s intervention in the form of a consultation with the physician is thereby warranted in order to re-evaluate the benefit of chemotherapy treatment versus the impact on a patient’s quality of life.

References