Reporting the Incidence of Platinum-Induced Ototoxicity: A Review of Prevailing Ototoxicity Criteria

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Abstract

The chemotherapeutic agents carboplatin and cisplatin are widely used and are highly effective against a variety of cancers; however, their use is limited by side effects such as ototoxicity, leading to devastating consequences on the quality of life of cancer survivors. Defining and grading of ototoxicity is essential for clinicians and researchers. Yet, there is a paucity of reliable and validated literature regarding accurate comparisons among different criteria.

A review was performed in order to evaluate the commonly used ototoxicity criteria, develop a method for establishing comparisons, and use this method to evaluate the effects of individual and treatment factors on the reported ototoxicity incidence. The paucity of reliable and validated literatureRegarding the Incidence of Platinum-Induced Ototoxicity: A Review of Prevailing Ototoxicity Criteria

Introduction

Early detection and improved cancer treatments have contributed to an increased number of cancer survivors. Five-year survival rates for all cancer patients have risen to 62% and 82% in Canadian adults and children, respectively. As a result, there is increasing concern in the medical community regarding the long-term consequences of oncology regimens. The platinum compounds carboplatin and cisplatin are widely used against a variety of malignancies. Despite their effectiveness, however, treatment with platinum compounds may lead to serious side effects such as nephrotoxicity, neurotoxicity and ototoxicity.

Ototoxicity manifests with tinnitus and/or a permanent, bilateral and progressive sensorineural hearing loss. Defining and grading the severity of hearing loss following chemotherapy is essential and critical to the decision-making and for determining appropriate clinical interventions. Furthermore, the definition of ototoxicity can affect the rate and degree of hearing loss among studies.

A review of the literature was performed with the following objectives: (1) use an identification method to develop a method for establishing comparisons among studies. (2) Use the method to evaluate the effects of individual & treatment factors on the incidence of ototoxicity.

1 - Prevailing Ototoxicity Criteria

A review of recently-published studies led to the identification of 10 different methods for defining platinum-induced ototoxicity, including the National Cancer Institute Classification system, the World Health Organization (WHO) hearing threshold changes, American Speech-Language Hearing Association (ASHA) self-assessment of hearing loss, Pediatric Oncology Group (POG) criteria, Child Oncology Group (COG) criteria, Musteran classification and Functional Hearing Loss (FHL) scale among others (Figure 1).

Table 1 - Five criteria used in the literature for defining platinum-induced ototoxicity

<table>
<thead>
<tr>
<th>Classification</th>
<th>Authors</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>POG-Chemo WHO</td>
<td>Li Y et al</td>
<td>60 dB or more above normal at all frequencies</td>
</tr>
<tr>
<td>POG-Chemo WHO</td>
<td>Li Y et al</td>
<td>60 dB or more above normal in at least one frequency</td>
</tr>
<tr>
<td>POG-Chemo WHO</td>
<td>Li Y et al</td>
<td>Prophylactic hearing testing at each chemotherapy dose level</td>
</tr>
<tr>
<td>POG-Chemo WHO</td>
<td>Li Y et al</td>
<td>70% or more of audiograms expected to be abnormal</td>
</tr>
<tr>
<td>POG-Chemo WHO</td>
<td>Li Y et al</td>
<td>Hearing screening every 3 months; if abnormal, repeat every 6 months</td>
</tr>
</tbody>
</table>

2 - Comparing Among Different Criteria

The incidence of ototoxicity is highly variable among studies, varying from 0 to 100%. The variability can be due to treatment and individual differences & use of different definitions of ototoxicity. In order to decrease variability due to different definitions, grades within each system were classified as either “mild-to-moderate”, or “severe” ototoxicity, with the former represented in the literature representing hearing loss likely to have significant functional consequences or require intervention (Table 1).

3 - Factors Affecting Incidence of Ototoxicity

Adult vs. Paediatric Patients

A total incidence of ototoxicity of 20% was detected (n=879/4,861), with severe ototoxicity occurring in 11% of patients. In children, the incidence of ototoxicity was highest among those receiving cisplatin only (n=70/1,686), with severe ototoxicity being seen in 30% of patients. Yet, in the paediatric (A) and adult (B) population.

Treatment and Assessment Factors

Chemotherapy & Radiotherapy: The effect of the chemotherapy agents used, patients were classified into those receiving carboplatin only, cisplatin only, or both. Cisplatin was used to cause greater hearing loss as compared to carboplatin. This was the case in this review. Due to the low ototoxicity in the carboplatin-only group, the POG-Chemo WHO, POG-Chemo ASHA criteria, was used for defining platinum-induced ototoxicity.

Table 2: Factors that affect the incidence of ototoxicity

<table>
<thead>
<tr>
<th>Factors</th>
<th>Adults</th>
<th>Paediatric</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin only</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Cisplatin only</td>
<td>25%</td>
<td>50%</td>
</tr>
<tr>
<td>Both</td>
<td>50%</td>
<td>25%</td>
</tr>
</tbody>
</table>

Conclusion

A variety of criteria are now available to grade the severity of platinum-induced ototoxicity. Variation among the criteria as well as the incompatibility reporting in the literature leads to discrepancies in conclusions. Hence, further work is required in order to establish a gold standard protocol for hearing loss detection and grading.

Acknowledgements

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References


Figure 1: Distribution of ototoxicity criteria within studies on platinum-induced ototoxicity.