Background

• The National Institute of Occupational Safety and Health (NIOSH) is a US federal agency responsible for making recommendations to prevent work related exposure, injury, and illness.

• To minimize exposure to toxic agents, NIOSH publishes and updates a list of hazardous drugs (HD) with guidelines for appropriate handling.

• NIOSH classifies drugs as hazardous if they exhibit one or more of the following characteristics: carcinogenicity, teratogenicity or other developmental toxicity, reproductive toxicity, organ toxicity at low doses, or genotoxicity. New Drugs with structure and toxicity profiles that mimic existing drugs are also deemed hazardous by the above criteria.

• NIOSH then separates their HD into three groups:
  • Group 1: Antineoplastic agents.
  • Group 2: Non-antineoplastic agents that meet one or more of the NIOSH criteria for a hazardous drug.
  • Group 3: Drugs that pose potential risks to men and women trying to conceive and to women who are pregnant or breastfeeding.

Placement of a drug to the hospital’s hazardous drug list will cost ~$0.50 per tablet or capsule due to increased labor, packaging material and personal protective equipment (PPE) required.

• Therefore, classifying an agent as a “hazardous drug” represents a significant financial impact on the institution.

Description

The objective of this project was to evaluate the evidence for classification of NIOSH listed HD before adding them to the hospital’s HD list.

• There are a total of 184 agents on the NIOSH 2014 list: 97 in Group 1, 47 in Group 2, and 40 in Group 3

• Product monographs and available literature were reviewed for evidence of occupational risk, allowing for the development of an algorithm that systematically sorts and classifies drugs as a “Hazardous Drug” (drugs that pose a risk to all health care personnel handling the drug), a “Pregnancy or Reproductive Risk Drug” (drugs that pose a risk to pregnant or breastfeeding women, or men and women who are actively trying to conceive), or “Non-Hazardous”.

Evaluation

Figure 1: Algorithm for evaluating and classifying NIOSH-listed drugs.

Evaluation and Classification of Hazardous Drugs

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Table 1: Example of Product Monograph and literature review used to assess risk for Risperidone.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Risperidone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black Box</td>
<td>N/A</td>
</tr>
<tr>
<td>Pregnancy Risk</td>
<td>C</td>
</tr>
<tr>
<td>Notes</td>
<td>Evidence of tumors at low doses in laboratory studies, may be protracted</td>
</tr>
</tbody>
</table>

Recommended Classification: Hazardous Drug

Summary of Evidence

Risperidone was found to be associated with pituitary tumors in both humans and animal models. Risperidone is a second generation antipsychotic agent that is associated with a high frequency of hyperprolactinemia which can be associated with the development of pituitary tumors.

The first report of pituitary tumors associated with risperidone was published in 1997. Risperidone treated patients are more likely to undergo prolactin assessment, and MRI/CT. Therefore, increased workup in risperidone users, might account for the increased identification and reporting of pituitary adenomas. However, pituitary tumors are slow growing and frequently asymptomatic. Therefore, there is still a possibility that risperidone has a causal relationship to development or progression of prolactinomas.

References and Note


- Pituitary adenomas are common, frequently asymptomatic, and slow growing tumors with mass effect. Rispetrino treatment may be associated with increased reports of prolactinomas.
- Several studies have found that risperidone has a causal relationship to development or acceleration of pre-existing pituitary tumors.


- The recommended daily dose (RDD) of risperidone is 1-6 mg/day, but the maximum risk is seen with 12 mg/day.

- In rats, 12 mg/kg/day of risperidone was associated with increased prolactin levels, but not with tumor formation.

- In humans, the reported incidence of prolactinomas with risperidone is between 0.5% and 5%

- In a meta-analysis of 11 randomized, double-blind, placebo-controlled trials, risperidone was associated with a 2.2-fold increase in the risk of prolactinoma.

- In a meta-analysis of 12 case-control studies, risperidone was associated with a 4.3-fold increase in the risk of prolactinoma.

- In a meta-analysis of 32 case-control studies, risperidone was associated with a 5.7-fold increase in the risk of prolactinoma.

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