PROMETHAZINE INJECTION SBAR

PROMETHAZINE (PHENERGAN) INJECTION SAFETY

SITUATION:

Trinity Health needed to align to a single mechanism to address issues related to risks associated with promethazine administration.

Promethazine (Phenergan) administration was presented at Trinity Medication Cycle Improvement Team (MCIT) in 2016 and the discussion and conclusions were listed below.

- Institute for Safe Medication Practices (ISMP) recommends because of the frequency of serious, tragic, local injuries after infiltration or inadvertent intra-arterial injection that the FDA re-examine the product labeling and consider eliminating the intravenous (IV) route of administration of promethazine.
- Team agreed that relying on order comments for nurses to read and further dilute promethazine places patients at risk for an adverse reaction.
- Due to a previous claim, AA switched to using promethazine by IM route only, and has not had an incident since. It is used effectively in OB and in the ED as a second line agent behind IV Zofran.
- Based on what is best and safest for our patients, MCIT voted and unanimously approved promethazine being used IM, oral and rectal only, and will remove all IV administration routes. Will need to provide warnings in the comments or in Pyxis that promethazine should not be administered IV.
- Severity = Dangerous/Destructive; Priority = High; Development / Deployment = Reasonable.
- If possible, the picture or the promethazine induced gangrenous hand should be included in the education and in Pyxis/PowerChart.

Recently, ISMP published 2018-2019 Targeted Medication Safety Best Practices for Hospitals and recommended:

**BEST PRACTICE 13: Eliminate injectable promethazine from the hospital.**

- Remove injectable promethazine from all areas of the hospital including the pharmacy.
- Classify injectable promethazine as a non-stocked, non-formulary medication
- Implement a medical staff-approved automatic therapeutic substitution policy to convert all injectable promethazine orders to another antiemetic.
- Remove injectable promethazine from all computerized medication order screens, and from all order sets and protocols

This publication prompted a subsequent evaluation of the current state to understand the safe administration of promethazine (Phenergan) injection at Trinity Health.

BACKGROUND & ASSESSMENT

In 2006, ISMP published an article recommending "due to the frequency of severe, tragic, local injuries after infiltration or inadvertent intra-arterial injection, ISMP recommends that the FDA reexamine the product labeling and consider eliminating the IV route of administration." The article went on to suggest
that if IV is not eliminated as an option, to take steps to prevent or minimize tissue damage. Similarly, FDA should carefully investigate adverse events with this drug to determine if labeling changes are warranted, including removal of approval for IV administration.13

In 2000, Diana Levine, a professional musician living in Vermont suffered an arm amputation after receiving an injection of Phenergan, the branded version of promethazine. In the case litigation, 20 cases of amputations resulting in promethazine amputation were cited in court documents. The Supreme Court ruled in favor of the plaintiff with a 6.7 million dollar settlement.

Since the court decision, numerous episodes of serious injury from promethazine have been reported in FDA Adverse Event Report database and various medical and non-medical publications, but the FDA has not published the number in the database.6-11

There is an FDA boxed warning that states that parenteral promethazine should not be administered by subcutaneous or arterial route. More recently, the package insert was revised to state that the preferred route for parenteral administration of promethazine is via Intramuscular route. The package insert limits the dosage and speed of intravenous administration, but does not disallow parenteral administration.1

Adverse events at the site of injection mentioned in promethazine label include "severe chemical irritation and damage to tissues, regardless of the route of administration. Irritation and damage can also result from perivascular extravasation, unintentional intra-arterial injection, and intraneuronal or perineuronal infiltration. Adverse event reports include burning, pain, erythema, swelling, sensory loss, palsies, paralysis, severe spasm of distal vessels, thrombophlebitis, venous thrombosis, phlebitis, abscesses, tissue necrosis, and gangrene. In some cases surgical intervention, including fasciotomy, skin graft, and/or amputation have been required."1 Essentially, the label states the injury can occur even if the recommended precautions for IV administration are closely observed.

An analysis of the Trinity Health medication errors (similar to those reported in ISMP) using Voice and Midas data is presented in table 1 below.

**Table 1: Analysis of the Medication Event Reports for Trinity Health since 2011**

<table>
<thead>
<tr>
<th>Event</th>
<th>Number of events reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrong route – promethazine was ordered to be administered IM and was administered IV instead</td>
<td>17</td>
</tr>
<tr>
<td>Harm to patient – IM administration</td>
<td>3</td>
</tr>
<tr>
<td>Harm to patient – IV administration (i.e. damage to vein, phlebitis, etc)</td>
<td>22</td>
</tr>
</tbody>
</table>

Further, evaluating Trinity Health claims data for occurrence dates between 2011 and present, there have been 10 cases related to parenteral promethazine administration.

- Two patients suffered damage from Intramuscular (IM) administration resulting in development of abscess.
- Eight patients suffered damage from intravascular (IV) administration resulting in thromboembolism or permanent damage to patient.

Last year, in Trinity Health, there were 66,500 doses of promethazine injection vials/amps purchased.
Based on an analysis of Cerner data from 2017, (approximately)
25% doses – administered in ER
50% doses – administered on inpatient floors
10% doses – administered in surgery
15% doses – administered other locations (L&D, oncology locations, etc)

Table 2: Currently available antiemetics and associated costs\textsuperscript{16,17}

<table>
<thead>
<tr>
<th></th>
<th>GPO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexamethasone 4mg/1 mg vial</td>
<td>$0.71</td>
</tr>
<tr>
<td>Droperidol 2.5 mg/2ml vial</td>
<td>*Not available</td>
</tr>
<tr>
<td>Diphenhydramine 50 mg/1 ml</td>
<td>$0.55</td>
</tr>
<tr>
<td>Haloperidol 5 mg/ml</td>
<td>$0.56</td>
</tr>
<tr>
<td>Metoclopramine 10 mg tablet</td>
<td>$0.03</td>
</tr>
<tr>
<td>Metoclopramide 10mg/2ml vial</td>
<td>$0.97</td>
</tr>
<tr>
<td>Ondansetron 4 mg ODT</td>
<td>$0.29</td>
</tr>
<tr>
<td>Ondansetron 4 mg/2ml vial</td>
<td>$0.38</td>
</tr>
<tr>
<td>Prochlorperazine 5 mg tablet</td>
<td>$0.04</td>
</tr>
<tr>
<td>Prochlorperazine 10 mg tablet</td>
<td>$0.05</td>
</tr>
<tr>
<td>Prochlorperazine 10mg/2ml vial</td>
<td>$9.20</td>
</tr>
<tr>
<td>Promethazine 12.5 mg tablet</td>
<td>$0.12</td>
</tr>
<tr>
<td>Promethazine 25 mg tablet</td>
<td>$0.03</td>
</tr>
<tr>
<td>Promethazine 25 mg/ml vial</td>
<td>$0.92</td>
</tr>
<tr>
<td>Promethazine 12.5 mg suppository</td>
<td>$5.52</td>
</tr>
<tr>
<td>Promethazine 25 mg suppository</td>
<td>$5.52</td>
</tr>
<tr>
<td>Scopolamine 1.5 mg patch</td>
<td>$15.73</td>
</tr>
</tbody>
</table>

Ohio Health has successfully removed injectable promethazine from formulary. They shifted utilization of promethazine injection to either: promethazine tablets, haloperidol injection (low dose), or prochlorperazine injection.
If ministries in Trinity Health directly shifted purchases from promethazine injection to prochlorperazine injection, the impact would be approximately a $580,000 annual increase in medication cost. If the utilization of promethazine were converted to promethazine tablets or haloperidol injection low dose, there would not be an increase in purchase cost for Trinity Health. Patient characteristics would determine best alternatives to promethazine injection.

**RECOMMENDATION/CONCLUSIONS**

Promethazine injection utilization is across many patient populations in Trinity Health. ISMP has identified as a best practice that promethazine injection should be removed from formulary for several reasons:

1. There are alternatives available
2. There are significant safety risks associated with administration of IV promethazine
3. Promethazine injection if designated as IM only could still be given IV

An analysis of medication error data for Trinity Health as well as lawsuits identified that there has been patient injury associated with both IV and IM promethazine, and that even if promethazine has been designated as IM only – it has been given IV in error. The consensus guidelines for management of postoperative nausea and vomiting identify some alternative agents for management of nausea and vomiting.

Recommend to:

1. Remove promethazine injection from formulary
2. Work with service line experts to identify appropriate alternatives to promethazine injection for various indications.

**REFERENCES:**


