The Institute for Safe Medication Practices Canada (ISMP Canada) is an independent national not-for-profit agency established for the collection and analysis of medication error reports and the development of recommendations for the enhancement of patient safety.

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Iodine Overdose with Lugol's Solution Demonstrates Need for Safeguards for Infrequently Used Medications in Urgent Situations

The Institute for Safe Medication Practices Canada (ISMP Canada) has received 3 incident reports involving incorrect oral dosing of Lugol's solution (also known as Strong Iodine Solution USP). Lugol's solution is an infrequently used product containing 5% iodine (5 grams in 100 mL) and 10% potassium iodide (10 grams in 100 mL).[1,2] Given orally, Lugol's solution can be used to treat thyroid storm (thyrotoxic crisis) or before thyroid surgery to decrease blood loss; it may also be used as a thyroid-protective agent before radioactive chemotherapy.[1,3,4] Applied topically, Lugol's solution is used as a tissue stain in diagnostic tests and surgical procedures. This bulletin describes the risk of iodine overdose with orally administered Lugol's solution and suggests strategies to prevent similar incidents (including incidents caused by other iodide and iodine solutions administered orally). Some of these strategies may also be applicable for other infrequently used medications.

Medication Incident Example

An adult patient with Graves' disease was admitted to hospital with a diagnosis of thyroid storm. The physician prescribed 4 drops• of Lugol's solution to be given orally every 8 hours. The patient was inadvertently given an entire 100 mL container of Lugol's solution in one dose—a total of 5 grams of free iodine. The patient's condition deteriorated and intervention was required to manage the iodine overdose.

A literature search identified a previous incident in which the death of an infant with hyperthyroidism was attributed to a fatal overdose of Lugol's solution.[5]

Background

Graves' disease, otherwise known as diffuse toxic goitre, is an autoimmune disorder that targets the receptor for thyroid-stimulating hormone. Antibodies bind to the receptor, leading to overstimulation of the thyroid gland and production of excess thyroid hormones. Graves' disease is the most common cause of hyperthyroidism.[6,7] If left untreated or if treated improperly, Graves' disease can lead to thyroid storm, a life-threatening hyperthyroid condition characterized by elevated body temperature, nausea, vomiting, tremors, congestive heart failure, hypotension, tachycardia, arrhythmias, agitation, and psychosis.[6,7]

Administration of oral iodide prevents the thyroid gland from releasing hormones and is one of several pharmacologic interventions that may be used in the initial management of thyroid storm.[6] The iodide preparation is given at least 1 hour *after* the administration of propylthiouracil or methimazole, both of which block synthesis of thyroid hormones.[6,7] Lugol's solution, which contains both iodine and iodide, is one type of iodide preparation used for this purpose.[3,6]

The acute toxicity of Lugol's solution is related to its iodine content.[8,9] As noted above, a 100 mL bottle of Lugol's solution contains 5 grams of free iodine, which is more than the mean lethal adult dose (2 to 4 grams of free iodine).[8,9] Acute iodine toxicity can result in metabolic acidosis, renal failure, hypotension, circulatory collapse, and death.[8]

Recommendations

The potential for errors leading to severe harm with oral administration of Lugol's solution, as exemplified by the incident described, suggests that this item requires proactive safeguards, such as the following:

Hospitals

- Ensure that information about managing acute hyperthyroidism is readily accessible (e.g., a treatment protocol for thyroid storm, including optimal treatment options and dosing information).
- Include recommended options for oral dosing of iodide therapy, such as Lugol's solution, in pharmacy and prescriber order entry systems. Incorporate a verification step when building new medication files for information systems. Make entering test orders a part of the verification process, to ensure that medication dosing information displays correctly on order entry screens and on labels printed in the pharmacy.
- Dispense Lugol's solution in a quantity appropriate for the intended and safe use of the medication. For oral treatment of an individual patient, dispense the smallest possible volume and provide an appropriate oral measuring device along with clear dosing instructions. Consider providing Lugol's solution in a unit-dose format.[5]

• Clinical references typically present information about the dosing of potassium iodide and iodine solutions in terms of "drops".

- Provide information about Lugol's solution (e.g., indications, usual and maximum doses, instructions for preparation and administration, potential adverse effects) for healthcare providers who may be prescribing, dispensing, or administering Lugol's solution orally. It is important to note that drug information for this product may not be readily available to practitioners. For example, Lugol's solution is not listed in the 2011 edition of the *Compendium of Pharmaceuticals and Specialties*[10], a drug reference that is commonly available in patient care areas. To ensure that critical information is readily available at the point of care, consider supplementary measures such as placing drug information with the product.

Community Pharmacies

- For patients who require Lugol's solution for oral use, provide a product that has been approved for oral use and that is labelled accordingly. Products approved for oral use come with important information, such as dosage and directions for administration, whereas other Lugol's solution products may have only a Workplace Hazardous Materials Information System (WHMIS) label and no directions for oral use.
- Oversight and counselling by a pharmacist are important components in facilitating the correct use of Lugol's solution whenever a community pharmacy provides this agent to a patient for oral use. Ideally dialogue would be supported by written information.

Manufacturers

- ISMP Canada strongly encourages manufacturers to make Lugol's solution available for purchase in smaller volumes that would contain less than a lethal dose of iodine.
- Provide an oral measuring device, such as a calibrated dropper, to facilitate measurement of Lugol's solution for oral administration.
- Add a warning to bottles of Lugol's solution containing a total dose of free iodine that could be lethal (e.g., 100 mL and 500 mL bottles).
- Consider providing consumer product information for Lugol's solution intended for oral use.

This bulletin is intended to serve as a cue to healthcare organizations, prompting them to review their current management of Lugol's and other iodide solutions, to identify potential vulnerabilities in existing processes, and to implement specific safeguards for this infrequently used medication. The strategies described above may also be applicable to other infrequently used medications. It is also hoped this bulletin will serve as an alert to manufacturers, prompting them to consider ways to improve the safe use of iodide and iodine products that are available for oral use.

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New USP Requirement for Drug Vial Caps and Ferrules

The United States Pharmacopeia (USP) has finalized a standard that allows only cautionary statements intended to prevent imminent life-threatening situations to be printed on the cap or ferrule (the metal band holding a stopper in place) of a drug vial. One example of such a cautionary statement is the warning that appears on caps and ferrules of neuromuscular blocking agents (e.g., ''Warning–Paralyzing Agent''). If the medication does not need a cautionary statement, this area of the vial must remain blank. These new requirements, which come into effect on December 1, 2013, are intended to make it more likely that doctors, nurses, pharmacists, and other healthcare practitioners will see and act on the labelling statements that appear on injectable products. Manufacturers using USP standards will need to provide a rationale if they want to include a cautionary statement in this location. Under the new requirements, other information will still be permitted elsewhere on the medication vial.

Additional information on this USP standard is available from: http://www.usp.org/USPNF/notices/ferrulesCapOverseals.html

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ISMP Canada is a national voluntary medication incident and 'near miss' reporting program founded for the purpose of sharing the learning experiences from medication errors. Implementation of preventative strategies and system safeguards to decrease the risk for error-induced injury and thereby promote medication safety in healthcare is our collaborative goal.

Medication Incidents (including near misses) can be reported to ISMP Canada:

(i) through the website: http://www.ismp-canada.org/err_report.htm or (ii) by phone: 416-733-3131 or toll free: 1-866-544-7672.

ISMP Canada can also be contacted by e-mail: cmirps@ismp-canada.org. ISMP Canada guarantees confidentiality and security of information received, and respects the wishes of the reporter as to the level of detail to be included in publications.

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