

Oral Clonidine Suspension: 1000-Fold Compounding Errors Cause Harm to Children

ISMP Canada has received 3 reports of children experiencing harm because of errors during preparation of oral clonidine suspension from clonidine powder. This bulletin provides information about the incidents, describes the dangers associated with clonidine overdose, and suggests strategies to prevent recurrence of this type of error.

Incident Reports

In each of the 3 incidents, a pharmacist working in a community pharmacy used clonidine powder (provided in containers labelled by weight, in grams) to prepare a suspension for pediatric use. The prescribed doses for clonidine ranged from 25 mcg (0.025 mg) to 125 mcg (0.125 mg). In each case, there was a mix-up during the conversions among grams, milligrams, and micrograms, and the concentration of the suspensions dispensed was 1000 times greater than intended.

Each child required emergency treatment and admission to hospital. Two of the children were admitted to the intensive care unit, and one of these required treatment of severe hypotension.

Background

Clonidine is a centrally acting α_2 -adrenergic agonist approved for use in Canada for the treatment of hypertension (e.g., Catapres and generic agents; available as 0.1 mg and 0.2 mg tablets).¹ In addition to its use in treating hypertension, clonidine (Dixarit and generic agents; available as 0.025 mg tablet) has also been approved for the relief of menopausal flushing in patients for whom hormone replacement therapy is unsuitable.² With the availability of newer and better-studied anti-hypertensives, however, the use of clonidine has waned over the past couple of decades. With this less frequent use of clonidine has come reduced familiarity with the drug and its dosing.

Clonidine is also used for off-label treatment of several conditions in the pediatric population.³ In particular, it is often used as a first-line treatment option for pediatric patients with tics.⁴ The use of clonidine in combination with stimulant medications has been supported by various

expert organizations that address ADHD and its comorbidities.^{5,6} Clonidine is often dosed in micrograms for pediatric use, whereas for adults, the dosing is typically expressed in milligrams.

The therapeutic window for children is narrower than that for adults, and compounding errors can lead to significant harm. Among children, ingestion of 10 mcg per kilogram body weight can result in severe overdose.⁷ In the 3 incidents described earlier, the children experienced symptoms consistent with clonidine overdose, including shallow breathing, sweating, and hypotension.

The most common signs of clonidine toxicity include profound hypotension, bradycardia, and central nervous system depression.⁸ Signs and symptoms similar to those exhibited with narcotic overdose may also occur, including respiratory depression (which may progress to apnea), miosis (i.e., constriction of the pupils), muscle flaccidity, and hyporeflexia.⁹ Although uncommon, early hypertension may also occur in cases of severe clonidine overdose because of activation of the peripheral α -adrenergic receptors.⁹ Symptoms of overdose generally arise within 30 minutes to 2 hours after ingestion, with hypotensive effects peaking in 2 to 4 hours.⁸

Recommendations

Clonidine suspension is not commercially available, and suspensions must be compounded individually. The following strategies are suggested to prevent compounding errors with clonidine:

- Use a standard formula and worksheet to prepare oral liquid clonidine, preferably one based on commercially available tablets, such as the clonidine compounding formulation available from The Hospital for Sick Children in Toronto.¹⁰ This formulation does not necessitate weighing of powder; instead, it uses a specified number of tablets in a dose readily available from manufacturers. The tablets are labelled in terms of milligrams, which reduces the complexity of converting a powder weighed in grams to a dose prescribed in micrograms.
- Ensure that effective, *independent* double-checks¹¹ are performed for critical steps in the process (identified on

the worksheet) to increase the chance that errors are identified.

- In cases where practitioners must work alone, explore options for independent double-checks. For example, pharmacists who work alone can consult drug information centres or collaborate with pharmacists in other pharmacies for a check on calculations.
- Encourage parents to bring to the pharmacist's attention

any refill prescription that seems to differ, in terms of appearance, taste, or instructions, from the previous prescription.^{7,12,13}

Other cases of clonidine overdose in children because of compounding errors have been reported.^{7,12,13} It is hoped that the sharing of information through this bulletin will help to inform practitioners and reduce the potential for recurrence of such incidents.

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References – please refer to page 3.

Community Pharmacy Incident Reporting Program

ISMP Canada, with support from the Ontario Ministry of Health and Long-Term Care, developed the Community Pharmacy Incident Reporting (CPhIR) Program (www.cphir.ca) to allow community pharmacies to document and analyze factors contributing to errors in the medication-use system. Input from the Nova Scotia SafetyNET-Rx project, and implementation across the province of Nova Scotia, has also facilitated quality improvements to the program.

CPhIR assists community pharmacy teams to develop and implement system-based strategies for improving the quality of medication use in the community and for preventing medication-related incidents.

The program is designed to benefit provincial and national patient safety initiatives and contribute to the Canadian Medication Incident Reporting and Prevention System (CMIRPS) (www.ismp-canada.org/cmirps.htm).

If you would like more information about the CPhIR Program, please contact ISMP Canada by email: cphir@ismp-canada.org or by telephone: 1-866-544-7672.

Risk Assessment Program for Medication System Safety in Community Pharmacy

The [Medication Safety Self-Assessment \(MSSA\) for Community/Ambulatory Pharmacy](#) was developed to assist and guide individual community pharmacies in identifying opportunities to improve their medication-use systems. The program's self-assessment criteria are related to potential system improvements that have been identified through analysis of medication incidents. Completion of this MSSA can be an important element of a community pharmacy's quality improvement initiatives.

The program's web-based interface allows individual community pharmacies to compare their own results over time, thereby tracking the impact of any changes made, as well as to compare their results with the aggregate results of other participants in the program, both regionally and nationally. Several Canadian provinces have supported the use of this program as a component of quality improvement. The program is also available at a reasonable cost to individual community pharmacies.

For more information about the MSSA program for community pharmacy, please contact ISMP Canada by email: mssa@ismp-canada.org or by telephone: 1-866-544-7672.

Evaluation of Services Provided by ISMP Canada through the Canadian Medication Incident Reporting and Prevention System (CMIRPS)

In 2010, ISMP Canada engaged Prairie Research Associates (PRA) Inc. to conduct an evaluation of the work that ISMP Canada has delivered through the CMIRPS program. The evaluation (available from: www.ismp-canada.org/download/cmiprs/rptISMPC_CMIRPS_Final_Report.pdf) focuses on the impact of the products and services offered by ISMP Canada, and the extent to which the work has resulted in changes to the healthcare system across Canada. The evaluation identified several potential enhancements to services, which are being incorporated into the organization's future work plans.

ISMP Canada sincerely appreciates the time taken by the many Canadian practitioners who provided feedback and participated in the evaluation.

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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.

A Key Partner in the Canadian Medication Incident Reporting and Prevention System