



Oxybutynin Misuse

Purpose: To inform healthcare professionals in Saskatchewan about increases in oxybutynin misuse, to review appropriate prescribing practices of oxybutynin and to briefly describe the manifestations and management of oxybutynin toxicity.

Background: During the past few years, oxybutynin has been gaining popularity as a treatment for hyperhidrosis (excessive sweating). A randomized, placebo-controlled trial published in 2015 demonstrated that low-dose oxybutynin is effective in reducing symptoms of hyperhidrosis in generalized or localized forms,¹⁰ and several other observational studies have also determined that oxybutynin is effective in this application.¹¹⁻¹⁴ Hyperhidrosis is a common adverse effect experienced by patients using methadone as opioid replacement therapy; research has suggested the rate may be as high as 45%.^{15,16} Due to this adverse effect, a seemingly increasing number of methadone patients have been requesting oxybutynin as a treatment to combat hyperhidrosis. However, there has been growing concern among members of the medical community that because oxybutynin has the potential to be misused, some patients are requesting prescriptions when no clinical indications are actually present. This potential problem is compounded by reports that oxybutynin can now be sold on the street for as much as \$5 per tablet, making it an attractive source of revenue. In addition, at least one death is reported to have occurred as a result of a patient injecting crushed oxybutynin.¹⁷

Though no statistics are currently available, anecdotal reports suggest that oxybutynin misuse may be on the rise in Saskatchewan. Anticholinergic drugs are not commonly perceived as having misuse potential; however, there is a long history of such misuse which was first reported with frequency among psychiatric patients.¹ More potent anticholinergics such as trihexyphenidyl, procyclidine and benztropine were the typical agents of misuse among these patients,² but despite the relatively low anticholinergic effects of oxybutynin, its popularity as a drug of misuse has increased dramatically in recent years. Multiple case reports have been published regarding oxybutynin misuse or dependence,³⁻⁵ often originating from Turkey where it has been readily available without a prescription. Some patients reported taking as many as 80-100 tablets (400-500mg) per day.^{6,7} It has also been noted as a medication at high risk for diversion and abuse in correctional facilities.^{8,9} Reasons provided in reports for using oxybutynin include to overcome depression and social anxiety or to reduce withdrawal symptoms of alcohol and other substances.^{5,6}

Reducing Misuse Potential through Appropriate Prescribing

Evidence-Based Use of Oxybutynin¹⁸

- Overactive Bladder

- Immediate release: 5 mg BID-TID; maximum: 5 mg QID
- Extended release: Initial: 5 to 10 mg once daily, adjust dose in 5 mg increments at weekly intervals; maximum: 30 mg once daily
- Also available as topical gel and transdermal patch
- This medication is on the Beers list and should be avoided where possible for elderly patients.¹⁹ If prescribing for an elderly patient, it is suggested to initiate immediate release 2.5 mg BID to TID and to ↑ cautiously

Limited Evidence Use of Oxybutynin^{10,14}

- **Primary Hyperhidrosis:** off-label use - data from randomized, placebo-controlled trials with limited numbers of patients and of short duration suggest that oxybutynin may be beneficial for treatment of primary hyperhidrosis
 - Immediate release: Initial: 2.5 mg once daily; gradually titrate per effect and tolerance. Target doses of 7.5 to 10 mg/day in two divided doses have been studied

Tips for Prescribers and Pharmacists

- ✓ PIP all patients requesting a prescription or presenting a prescription for oxybutynin to identify multiple and/or recent fills
- ✓ For patients taking methadone or Suboxone®, only fill prescriptions for oxybutynin that have been written by an Opioid Substitution Therapy prescriber
- ✓ Watch for patients requesting new prescriptions of the drug by name, rather than requesting help with symptom management
- ✓ Monitor for behaviours of substance misuse disorder (e.g. CAGE-AID tool)
- ✓ Counsel patients to store securely
- ✓ Keep oral daily doses ≤ 20 mg for OAB, ≤ 10mg for hyperhidrosis; be wary of early refill requests
- ✓ Consider topical gel or transdermal patch options for OAB (though neither are currently on the Saskatchewan nor Non-Insured Health Benefits formularies)
- ✓ Start with lower doses in elderly patients (if no suitable alternative available)
- ✓ Maximum daily doses are lower for pediatric patients with overactive or neurogenic bladder

Possible Alternative to Treat Methadone-Induced Hyperhidrosis

One case report from the United Kingdom proposed that a non-sedating antihistamine may control methadone-induced hyperhidrosis, owing to the capacity of opioids to act

as potent stimulators of mast cell degranulation and thereby trigger a diaphoretic effect. The authors treated two methadone maintenance patients who were suffering from excessive sweating with desloratadine 5mg per day; both patients reported that the excessive sweating ceased within 1 day of treatment initiation.²⁰ Though this is very poor-quality evidence, it offers a potential treatment alternative with no recognized misuse potential.

Oxybutynin Toxicity

Mild to Moderate Toxicity²¹

Characteristic symptoms are somnolence, mydriasis, flushing, fever, dry mouth, decreased bowel sounds and tachycardia. Mild hypertension, nausea and vomiting may occur. Moderate poisoning may result in agitation, confusion and hallucinations.

Severe Toxicity²¹

Manifestations may include agitated delirium, psychosis, hallucinations, seizures, hyperthermia and coma.

Overdose

Information regarding oxybutynin overdose is scarce, but a few case reports on the topic have been published. One report described a patient as, after ingesting 100mg of oxybutynin, experiencing “anticholinergic effects, including stupor, followed by disorientation and agitation on awakening, dilated pupils, dry skin and retention of urine. She had a sinus tachycardia which resolved 3 h after admission, and in addition ventricular ectopics and bigeminy which continued for a further 30 h.”²² Another report described a patient who had been ingesting as much as 350mg per day as experiencing symptoms including “psychosis, constipation, fainting, severe palpitations and dry mouth.”²³ These reports are in accordance with expected responses to oxybutynin toxicity as noted above.

Management^{21,24}

Symptomatic / Supportive

- **Airway management**; protect airway early in patients with severe intoxication (i.e. seizures, severe delirium or hyperthermia), may require orotracheal intubation
- Treat **seizures** with intravenous benzodiazepines; add propofol or barbiturates if seizures persist or recur
- Treat **agitation** and/or **delirium** with benzodiazepines as necessary; large doses may be required
- For **hyperthermia**, initiate aggressive external cooling measures (i.e., remove patient's clothing, cover with a damp sheet or spray skin with water and direct fan at the patient's skin to enhance evaporation)

Decontamination

- **Activated charcoal** may be administered if recent, substantial ingestion has occurred and airway is protected
- Gastric lavage is not necessary after small-to-moderate ingestions if activated charcoal can be given promptly. Because of slowed GI motility, gut decontamination procedures may be helpful, even in late-presenting patients

For more information, as well as for support in the management of individual patient cases, please consult PADIS 1-866-454-1212

Prepared by Clarke Cousins, Pharmacy Intern
Reviewed by Karen Jensen BSP, MSc and Carmen Bell BSP
medSask, April 2018

References:

1. Buhrich N, Weller A, Kevans P. Misuse of anticholinergic drugs by people with serious mental illness. *Psychiatr Serv.* 2000; 51(7): 928-9.
2. Marken P, Stoner S, Bunker M. Anticholinergic drug abuse and misuse: epidemiology and therapeutic implications. *CNS Drugs.* 1996;5(3):190-199.
3. Guloksuz S, Eren K, Gurol DT. A case of oxybutynin dependency. *Gen Hosp Psychiatry.* 2010;32(4): e5-e6.
4. Kinik M, Donder F, Duymaz M, et al. Addiction of oxybutynin: an adolescent case report. *J Addict Res Ther.* 2015; 6(2):228.
5. Oxybutynin abuse: Multisystem disorders: case report. *Reactions Weekly.* 2016;1601(1):189.
6. Oxybutynin abuse/overdose/withdrawal: Various toxicities: 2 case reports. *Reactions Weekly.* 2016;1619(1):144.
7. Oxybutynin abuse. *Reactions Weekly.* 2012;1399(1):24.
8. Keller J. Medications at high risk for diversion and abuse in correctional facilities [Internet]. *Jail Medicine.* 2017 [cited 16 Apr 2018]. Available from: <http://www.jailmedicine.com/medications-at-high-risk-for-diversion-and-abuse-in-correctional-facilities/>
9. Keller J. Is this inmate gaming me? [Internet]. *Jail Medicine.* 2012 [cited 16 Apr 2018]. Available from: <http://www.jailmedicine.com/is-this-inmate-gaming-me/>
10. Schollhammer M, Brenaut E, Menard-Andivot N, et al. Oxybutynin as a treatment for generalized hyperhidrosis: a randomized, placebo-controlled trial. *Br J Dermatol.* 2015 Nov;173(5):1163-8.
11. Millán-Cayetano J, Boz, J, Rivas-Ruiz F et al. Oral oxybutynin for the treatment of hyperhidrosis: outcomes after one-year follow-up. *Australasian Journal of Dermatology,* 58(2), E31-E35. *Australas J Dermatol.* 2017 May;58(2):e31-e35.
12. Hong J, Lee J, Totouom-Tangho H, et al. Methadone-induced hyperhidrosis treated with oxybutynin. *J Addict Med.* 2017 May/Jun;11(3):237-238.
13. Campanati A, Gregoriou S, Kontochristopoulos G, et al. Oxybutynin for the treatment of primary hyperhidrosis: current state of the art. *Skin Appendage Disord.* 2015 Mar;1(1):6-13.
14. Wolosker N, Teivelis M, Krutman M, et al. Long-term results of oxybutynin use in treating facial hyperhidrosis. *An Bras Dermatol.* 2014 Nov-Dec;89(6):912-6.
15. Gahr M, Eller J, Cabanis M, et al. Drug safety and adverse drug reaction reporting behavior related to outpatient opioid replacement therapy: Results from a survey among physicians. *J Subst Abuse Treat.* 2017 Mar;74:7-15.
16. Yaffe GJ, Strelinger RW, Parwatikar S. Physical symptom complaints of patients on methadone maintenance. *Proc Natl Conf Methadone Treat.* 1973;1:507-14.
17. Verbal communication with Dr. Morris Markentin, M.D., C.C.F.P., F.C.F.P., Apr 2018.
18. Oxybutynin. In: Lexi-Comp Online Database [database on the Internet]. Hudson, Ohio: Lexi-Comp, Inc.; 2018; [cited 16 Apr 2018]. Available from: <http://online.lexi.com>
19. American Geriatrics Society 2015 Beers Criteria Update Expert Panel. American Geriatrics Society 2015 updated Beers criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc.* 2015 Nov;63(11):2227-46.
20. Al-Adwani A, Basu N. Methadone and excessive sweating. *Addiction.* 2004 Feb;99(2):259.
21. Oxybutynin Toxicology. In DRUGDEX® System (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. Available at: <http://www.micromedexsolutions.com> (cited: 16 Apr 2018)
22. Banerjee S, Routledge PA, Pugh S, et al. Poisoning with oxybutynin. *Hum Exp Toxicol.* 1991 May;10(3):225-6.
23. Oxybutynin overdose/abuse/addiction. *Reactions Weekly.* 2016;1630(1):193.
24. Manning B. Anticholinergics. In: Olson KR, Anderson IB, Benowitz NL, et al, eds. *Poisoning and drug overdose.* 7th ed. New York, NY: McGraw-Hill; 2017. Available at: <http://accessmedicine.mhmedical.com/content.aspx?bookid=2284§ionid=177337924>. Accessed 16 Apr 2018.