Mad Margaret’s Loperamide Abuse/Misuse/Addiction and Cardiac Conduction Disturbances — Article Clearinghouse

[UPDATE 6 MAY 2015]

Posted on July 23, 2014 by madmargaret

Mad Margaret’s Loperamide Clearinghouse is here!

Enclosed herein are just some of the medical articles I’ve researched regarding loperamide. I will add more as they are published (or as I find them) so please stop back now and again.

So little scholarly information is easily or readily available to both the public at large and physicians trying to help their patients, I feel it’s incumbent upon me to provide pertinent data insomuch as I am able.

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Some definitions that will help comprehension for our non-medical personnel readers: QT/QTc, • Ventricular Tachycardia • Torsade de Pointes

Loperamide toxicokinetics: serum concentrations in the overdose setting.

Eggleston W1, Nacca N, Marraffa JM.

Clinical Toxicology

“We report a subsequent hospitalization and pharmacokinetic profile of one of the patients in the case series. A 30-year-old male presented to an outlying facility for a syncopal episode. The initial electrocardiogram (ECG) revealed a heart rate of 60 beats per minute, a QRS measurement of 192 ms, and a QT of 704 ms. He left against medical advice, only to be found pulseless and apneic by a family member hours later.”

Reply to: “Torsade de Pointes Associated with High–dose Loperamide Ingestion”

Jeanna M. Marraffa, PharmD, Dabat, Michael G Holland, MD, Michael J Hodgman, MD, Upstate Medical University, Syracuse, New York, NY
Accepted
March 16, 2015.
These reports underscore the need for further investigation of the cardiac effects of high-dose loperamide. Further research into the mechanism of both QRS widening and QTc prolongation is warranted. Clinicians need to consider loperamide abuse in otherwise healthy patients with syncope or ventricular arrhythmias, especially those with a history of drug abuse or opioid dependence.”

CASE REPORT: Loperamide dependence and abuse
Ryan MacDonald1, Jason Heiner2, Joshua Villarreal3, Jared Strote2
1 Department of Emergency Medicine, Madigan Army Medical Center, Tacoma, Washington, USA; 2 Division of Emergency Medicine, Department of Medicine, University of Washington, Seattle, Washington, USA; 3 Department of Pharmacy, University of Washington Medical Center, Seattle, Washington, USA
Published 2 May 2015
BMJ Case Reports 2015; doi:10.1136/bcr-2015-209705

“Summary: …. A 26-year-old man who was taking 800 mg of loperamide per day presented requesting detoxification referral. Loperamide has potential for euphoric effects and information on how to facilitate such effects is easily available. It is important for physicians to be aware of the potential for misuse of and dependence on loperamide, with symptoms mimicking opiate use.”

Ventricular Tachycardia Associated with High-Dose Chronic Loperamide Use
Hannah L. Spinner, 1,* Nick W. Lonardo, 1 Roja Mulamalla, 2 and Josef Stehlik 2
1 Department of Pharmacy, University of Utah Health Care, Salt Lake City, Utah; 2 Division of Cardiovascular Medicine, University of Utah Health Care, Salt Lake City, Utah

PHARMACOTHERAPY: Article first published online: 3 FEB 2015 DOI: 10.1002/phar.1540

“Conclusion: Our report concurs with two previous observations that patients exposed to high doses of loperamide may be at an increased risk of ventricular dysrhythmias. Further studies are needed to confirm a causal relationship, but clinicians should be aware of possible cardiac adverse effects related to the overuse of loperamide.”

BONUS: MPR Article regarding this case.

Torsade de Pointes Associated with High-dose Loperamide Ingestion
1 LUCAS N. MARZEC, MD, 1,2 DAVID F. KATZ, MD, 1,2 PAMELA N. PETERSON, MD, MSPH, 1 LAUREN E. THOMPSON, MD, 3 MARK C. HAGNEY, MD and 1,2 MORI J. KRANTZ, MD — 1 Cardiology Division, University of Colorado Hospital, Aurora, CO; 2
Cardiology Division, Denver Health Medical Center, Denver, CO; 3 Cardiology Division, Uniformed Services University, Bethesda, MD


“Conclusion: We report a case of markedly prolonged QTc and recurrent TdP in a patient who ingested large doses of loperamide coincident with cimetidine in an attempt to simulate the euphoric effects associated with opioid abuse. This is a sentinel case, as ingestion of large doses of loperamide for self-treatment of opioid withdrawal and as a drug of abuse appears to be increasing through internet dissemination. This may represent a growing public health danger and warrants further investigation.”

Cardiac conduction disturbance after loperamide abuse

J. M. Marraffa, M. G. Holland, R. W. Sullivan, B. W. Morgan, J. A. Oakes, T. J. Wiegand, and M. J. Hodgman. 1 Department of Emergency Medicine, Upstate Medical University, Syracuse NY, USA. 2 Department of Emergency Medicine, School of Medicine, Emory University, Atlanta, GA, USA. 3 Department of Emergency Medicine, URMC and Strong Memorial Hospital, Rochester NY, USA. 4 URMC and Strong Memorial Hospital, Ruth A. Lawrence Poison and Drug Information Center, Rochester, NY, USA

CLINICAL TOXICOLOGY: November 2014, Vol. 52, No. 9 , Pages 952-957

“Conclusion: This case series describes several patients with cardiac conduction abnormalities and life-threatening ventricular arrhythmias temporally related to loperamide abuse. With the recent efforts to restrict the diversion of prescription opioids, increasing abuse of loperamide as an opioid substitute may be seen. Toxicologists should be aware of these risks and we urge all clinicians to report such cases to FDA Medwatch®”

Cardiac Conduction Disturbances Secondary to Chronic Abuse of Loperamide: An Initial Case Report

Audi J,1 Layher J,2 Morgan B.11 Georgia Poison Center and Emory University Department of Emergency Medicine. Atlanta, GA;2 Athens Regional Medical Center. Department of Cardiology. Athens, GA

Journal of Toxicology. CLINICAL TOXICOLOGY, Vol. 42, No. 5, pp. 713–826, 2004

“Conclusion: This is the first case report of an adult with cardiac conduction disturbances following chronic high-dose loperamide use. Negative toxicologic screens, cardiac studies and normal electrolytes, and resolution of cardiac abnormalities after loperamide cessation leaves no other plausible explanation for this presentation.”
Syncope and Recurrent Polymorphic Ventricular Tachycardia Following Loperamide Misuse

Jeanna M Marraffa, Michael G Holland, Ross W Sullivan, Robert Seabury, Michael J Hodgman; Upstate Medical University, Syracuse NY USA

From “2013 Annual Meeting of the North American Congress of Clinical Toxicology”

“Conclusion: Massive loperamide abuse may result in QTc prolongation and subsequent recurrent ventricular arrhythmias."

1274: Loperamide: The Unexpected Culprit

Pokhrel, Kiran; Rajbhandary, Arunima; Thapa, Jhapat

Critical Care Medicine: December 2013 – Volume 41 – Issue 12 doi:10.1097/01.ccm.0000440506.29056.c1
Poster Session: Case Reports

“Discussion and Conclusion: Loperamide is not known to cause QTc prolongation but methadone, also an opioid, dose cause QTc prolongation. Loperamide is also structurally similar to Haloperidol which has potential to prolong QTc. To our knowledge there is no known cases of Loperamide induced VT-storm. A case series (n=216) of Loperamide overdose failed to reveal any cardiac toxicity but the maximum ingested dose was 0.94mg/kg which is much less than in our patient. Internet search reveals that Loperamide is popular among substance abusers to prevent opioid withdrawals and to produce euphoric effects. Hence, Loperamide needs to be further evaluated for cardiac toxicity at super high doses.”

1204: Ventricular Tachycardia Storm – Can It Be A Side Effect From Over the Counter Anti-Diarrheal?

Boppana, V Subbarao; Kahlon, Arundeep; Bhatta, Luna

Critical Care Medicine: December 2012 doi: 10.1097/01.ccm.0000425416.95852.ed
Poster: ABSTRACT Only

“The spectrum of side effects from high doses of loperamide is still unknown. Abrupt resolution of the VT, normalization of QT and lack of the need for an anti-arrhythmic after discontinuation of loperamide in our patient makes us believe a causal relationship, but the pathogenesis remains unclear.”
1.2 Loperamide Intoxication in the Pursuit of Opioid Effects: Report of Two Fatalities

J. Denton1, A. Youmans 1, V. Arangelovich 2
1 McLean County Coroner’s Office, Bloomington, IL; 2 Will County Coroners Office, Joliet, IL

National Association of Medical Examiners
Abstracts of the 2013 Annual Meeting
October 12-15, 2013

“We present two deaths from loperamide intoxication from excess ingestion of loperamide pills, likely related to attempts at attaining euphoria. Thorough death investigation, autopsy, and additional toxicology testing studies were required to establish the cause of death.”

Systems Pharmacology of Arrhythmias

Seth I. Berger, Avi Ma’ayan, and Ravi Iyengar* Department of Pharmacology and Systems Therapeutics and Systems Biology Center New York, Mount Sinai School of Medicine, One Gustave L. Levy Place, Box 1215, New York, NY 10029, USA

Science Signaling; 3(118): ra30. doi:10.1126/scisignal.2000723

From P.10: “The identification of such potential signaling pathways provides initial insights. For example, two drugs, dasatinib and loperamide, used to treat different pathophysiologies, cancer and severe diarrhea can have QT prolongation as an adverse event and can be connected to the LQTS disease genes through the LQTS neighborhood (Fig. 5C). The paths can be short; for example, loperamide can be connected to KCNH2 through CALM1 (one step), and dasatinib can be connected to KCNQ1 through PRKACA and SRC (two steps), or more convoluted. Such a tracking exercise provides hypotheses about how these drugs might affect the QT interval and increase TdP risk, which can be used to design experiments in animal models or combined with whole genome information to identify “at-risk” patients.”

Tissue distribution of loperamide and N-desmethylloperamide following a fatal overdose.

Sklerov J, Levine B, Moore KA, Allan C, Fowler D., Division of Forensic Toxicology, Office of the Armed Forces Medical Examiner, 1413 Research Blvd., Rockville, Maryland 20850, USA.


“Abstract: We report a case involving a fatal intoxication with loperamide (Imodium).”

Loperamide Induced Brugada Syndrome
Sheyman, D.O. | Robert Crake, D.O.; Ohio Valley Medical Center, Wheeling WV; Feb 2014

February 2014 — Poster Presentation

“Conclusion:
Although rare, there have been reported cases of antihistamine, cocaine, and psychotropic drug induced Brugada Syndrome. Loperamide is another agent that could induce this syndrome. At present, there are no reported case studies that involve loperamide and Brugada Syndrome, however, because of the patients lack of family or personal history of cardiac problems we believe this may be the first case of loperamide induced Brugada Syndrome.”

A Web-based Study of Extra-medical Use of Loperamide: “I just wanted to tell you that loperamide WILL WORK”:

Raminta Daniulaitytea, Robert Carlsona, Russel Falcka, Delroy Cameromb, Sujan Pererab, Lu Chenb, Amit Shethb; a Center for Interventions, Treatment, and Addictions Research (CITAR), Department of Community Health, Boonshoft School of Medicine, Wright State University, United States; b Ohio Center of Excellence in Knowledge-Enabled Computing (Kno.e.sis), Wright State University, United States1

Drug and Alcohol Dependence: [LINK1]: Poster session — [LINK2]: Published Paper
Accepted 3 November 2012. Available online 30 November 2012

“Conclusions: This study suggests that loperamide is being used extra-medically to self-treat opioid withdrawal symptoms. There is a growing demand among people who are opioid dependent for drugs to control withdrawal symptoms, and loperamide appears to fit that role. The study also highlights the potential of the Web as a “leading edge” data source in identifying emerging drug use practices.”

Characterizing the abuse potential of loperamide via physiologically-based pharmacokinetic/pharmacodynamic modeling and simulation

Garrett Ainslie 1,2, Evan Kharasch 3, Gary Pollack 2, and Mary Paine 1,2

1 Curriculum in Toxicology University of North Carolina Chapel Hill NC United States
2 College of Pharmacy Washington State University Spokane WA United States
3 Dept of Anesthesiology Washington University St Louis MO United States

April 2014 The FASEB Journal vol. 28 no. 1 Supplement 1053.6

“From the Abstract: Increased restrictions on opioid prescribing may fuel alternate means of abuse. Anecdotal reports suggest abuse of the over-the-counter opioid loperamide when taken at supratherapeutic doses with CYP3A/P-gp inhibitors.”
Loperamide overdose-induced catatonia: potential role of brain opioid system and P-glycoprotein

Enrica Di Rosa a1 and Antonio E. Di Rosa a2

a1 Department of Clinical and Experimental Medicine, University of Messina, via Consolare Valeria, 1, 98125, Messina, Italy
a2 Department of Neurosciences, University of Messina, via Consolare Valeria, 1, 98125, Messina, Italy

Acta Neuropsychiatrica / Volume 26 / Issue 01 / February 2014, pp 58-60

“From the Abstract: We describe the case of a 20-year-old man who presented with severe catatonia following excessive intake of loperamide…”

Editing note: I decided, out of respect to the authors, to not include content without permission aside from a notable quote that summarizes the article. But if you follow the links, I assure you, you’ll find what you’re looking for. Originally published 03 Apr 14.