Wong Anselm (Orcid ID: 0000-0002-6817-7289)

Title Page: A case of liraglutide toxicity presenting to the emergency department and literature review.

Joe Anthony Rotella (1,2), Anselm Wong (1,3,4)

Affiliations:

1. **Victorian Poisons Information Centre, Austin Toxicology Unit and Emergency Department, Austin Health, Victoria, Australia.**
2. **Austin Clinical School, Melbourne Medical School, University of Melbourne, Victoria, Australia.**
3. **Centre for Integrated Critical Care, Department of Medicine and Radiology, Melbourne Medical School, University of Melbourne, Victoria, Australia.**
4. **Department of Medicine, School of Clinical Sciences at Monash Health, Monash University, Victoria, Australia.**

Corresponding author:

Associate Professor Anselm Wong

Emergency Department

Austin Health

Studley Road

Heidelberg, Victoria, Australia.

Email: anselm.wong@austin.org.au

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/1742-6723.13343

A case of liraglutide toxicity presenting to the emergency department and literature review.

Dear Editor

We report a case of a 36-year-old male who presented to our Emergency Department following an accidental overdose of liraglutide. He was prescribed liraglutide for weight loss (BMI 30.7) and did not have a history of diabetes mellitus. He was not on any other prescribed medication and he denied any recreational substance use.

The patient commenced liraglutide on the day of presentation and misread the instructions provided with the medication. Instead of the prescribed dose of 0.5mg, he injected 3.0mg subcutaneously. Three hours later he developed profuse vomiting and epigastric pain. As it was not resolving, he initially presented to the Emergency Department at 12 hours post injection and left after being given 4mg ondansetron, which temporarily resolved his symptoms. He subsequently represented at 16 hours post overdose with severe vomiting episodes followed by dry retching. He did not report any other symptoms. On examination, he had normal vital signs and some mild epigastric tenderness. He had a normal full blood count, urea, creatinine and electrolytes and was treated with metoclopramide, oral and IV ondansetron. He was admitted overnight, symptoms had improved the following day and he was discharged 26 hours post injection. There were no episodes of hypoglycaemia on admission.

Discussion:

Liraglutide is from a newer class of antidiabetic medications. It is a glucagon-like peptide 1 (GLP-1) agonist, which mimics the effects of native GLP-1 (sharing 97% structural similarity)[1]. It stimulates glucose-dependent insulin secretion from pancreatic islets, suppresses glucagon secretion, slows gastric emptying and increase satiety[1]. Hence, it has potential benefit for the treatment of Type 2 Diabetes Mellitus but also as a treatment that may assist with weight loss, as observed in our patient.

Liraglutide is slowly absorbed via subcutaneous injection with a plasma half-life of approximately 13 hours prior to metabolism in the plasma by Dipeptyl-peptidase-4 and neutral endopeptidase (NEP) and excreted in the urine[2]. This likely contributed to the ongoing symptomatology in our case. There is limited information available regarding the toxicity of liraglutide. We performed a search of PubMed and Medline for overdoses using the search terms ‘liraglutide’, ‘toxicity’ and ‘overdose’ with an unrestricted timeline. Out of 2059 articles, 4 were relevant.

From the available literature (table 1), liraglutide overdose in isolation appears relatively benign in diabetic patients with predominantly prolonged gastrointestinal features (vomiting and nausea). In addition, hypoglycaemia requiring dextrose infusion has been observed in a non-diabetic patient.

This is likely due to the stimulation of insulin release and reduction in glucagon secretion facilitated by liraglutide, which would have a more marked effect in a non-diabetic patient. In this instance, regular blood glucose measurement and utilisation of intravenous dextrose when required is recommended. Supportive care, observation for hypoglycaemia and antiemetics are the mainstays of management.

References:

1. Sisson EM. Liraglutide: clinical pharmacology and considerations for therapy. Pharmacotherapy. 2011; 31: 896_911.
2. Jacobsen LV, Flint A, Olsen AK, Ingwersen SH. Liraglutide in Type 2 Diabetes Mellitus: Clinical Pharmacokinetics and Pharmacodynamics. Clinical Pharmacokinetics. 2016;55:657-672. doi:10.1007/s40262-015-0343-6.
3. Elmehdawi RR, Elbarsha AM. An accidental liraglutide overdose: case report. *The Libyan Journal of Medicine*. 2014;9:10.3402/ljm.v9.23055. doi:10.3402/ljm.v9.23055.
4. Solverson KJ, Lee H, Doig CJ. Intentional overdose of liraglutide in a non-diabetic patient causing severe hypoglycaemia. CJEM. 2018; Feb 5:-3. Doi: 10.107/cem.2017.439 [Epub ahead of print]
5. Nakanishi R, Hirose T, Tamura Y, Fujitani Y, Watada H. Attempted suicide with liraglutide overdose did not induce hypoglycaemia. Diabetes Res Clin Pract. 2013 Jan; 99(1):e3-4. Doi: 10.1016/j.diabres.2012.10.017. Epub 2012 Nov 11
6. Bowler M, Nethercott DR. Two lessons from the empiric management of a combined overdose of liraglutide and amitriptyline. A A Case Rep. 2014 Feb 1; 2(3): 28-30. Doi: 10.1097/ACC.0b013e3182a526fa

Table 1: Case summary of literature search.

Report	Gender/ Age	T2DM*	Dose	Route	Symptoms	Treatment	Outcome
Elmehdawi RR & Elbarsha AM[3]	49F	Yes	18mg	S/C#, accidental	Nausea, vomiting within 1 hour (stopped 13 hours post overdose)	Intravenous fluids, intravenous metoclopramide	Recovered, discharged after 24 hours
Solverson KJ et al[4]	46M	No	36mg	S/C#, intentional	Nausea, vomiting within five hours, **2 episodes of hypoglycaemia**	Admission to intensive care unit, dextrose infusion, octreotide	Recovered
Nakanishi R et al.[5]	33F	Yes	72mg	S/C#, intentional	Nausea, vomiting	Intravenous saline	Recovered
Bowler MR & Nethercott DR[6]	52M	Exocrine Pancreatic insufficiency	36mg + TCA	S/C#, intentional	Seizure, PEA arrest	CPR, adrenaline 1mg, sodium bicarbonate, calcium chloride, lipid emulsion therapy	Recovered

*Type 2 Diabetes Mellitus, # subcutaneous, TCA – tricyclic antidepressant