

Severe hypoglycaemia associated with ingesting counterfeit medication

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Cross-border importation of traditional and prescription medications is common, and many of these drugs are not approved by the Australian Therapeutic Goods Administration. Furthermore, counterfeit versions of prescription medications are also available (eg, weight-loss medications, anabolic steroids, and medications to enhance sexual performance). We describe a 54-year-old man with the first Australian case of severe hypoglycaemia induced by imported, laboratory-confirmed counterfeit Cialis. This serves to remind medical practitioners that counterfeit medication may be the cause of severe hypoglycaemia (or other unexplained illness). (MJA 2010; 192: 716-717)

Clinical record

A 54-year-old male truck driver was admitted to a regional hospital with profuse sweating, slurred speech, ataxia and confusion. He had a history of heavy smoking and moderate alcohol consumption, but denied taking any medications or using recreational drugs. On the evening before his illness, he had four standard alcoholic drinks.

On examination, his blood pressure was 150/97 mmHg, body mass index was 33.3 kg/m², and his score on the Glasgow Coma Scale was 12/15 (eye response, 3; motor response, 6; and verbal response, 3). The rest of the general and systemic examination was unremarkable.

In the emergency department, his blood glucose level indicated severe hypoglycaemia (1.1 mmol/L; reference range [RR], 3.0–6.0 mmol/L). After administering 50 mL of an intravenous infusion of 50% dextrose and giving an intramuscular injection of 1 mg glucagon, his Glasgow Coma Scale score improved to 15/15. Subsequently, apart from a high-carbohydrate diet, he required an intravenous infusion of 5% dextrose at a variable rate for 4 days to maintain euglycaemia. His glucose requirement decreased slowly over the following 4 days.

He was extensively investigated for hypoglycaemia while in hospital. All other haematological and biochemical parameters, except β -hydroxybutyrate, insulin and C-peptide, were normal. His serum insulin and C-peptide levels, measured on Day 1 and Day 2, were abnormally elevated relative to his low blood glucose level (ie, for the low blood glucose level in this case, the serum insulin level would be expected to be lower). The serum insulin and C-peptide levels had normalised by Day 9 (Box). The serum β -hydroxybutyrate level, measured on Day 2, was particularly low at 0.05 mmol/L (RR, <0.20 mmol/L), consistent with insulin excess. Magnetic resonance imaging of the pancreas gave negative results

for insulinoma. A plasma sulfonylurea screening test, first done on Day 9, gave a negative result.

No conclusive diagnosis about this self-limiting hypoglycaemic episode was made during admission. The patient was discharged after making a full recovery. He was advised to self-monitor his capillary blood glucose level and was referred to the endocrinology clinic at our hospital for further evaluation.

He attended the endocrinology clinic 2 weeks after discharge. In view of his self-limiting hypoglycaemic episode, specific enquiry was made about the use of oral medication that may have caused the hypoglycaemia. He admitted that, an hour before developing the symptoms, he took a sexual performance-enhancing medication. This was the first time he had taken any medication of this type. The medication had been bought in Vietnam by a friend. This raised the suspicion of contaminated or counterfeit medicine as the cause of the hypoglycaemia.

The medication from Vietnam was in a bottle labelled “Cialis 50”. When compared with Cialis manufactured by Eli Lilly, gross differences in packaging, labelling and dose strength were noticed. High-performance liquid chromatography performed by the Australian Therapeutic Goods Administration (TGA) confirmed that one tablet of counterfeit Cialis 50 contained 152.8 mg of glibenclamide and 0.5 mg of sildenafil. The TGA and Eli Lilly Australia were subsequently officially notified.

Discussion

This is the first report of a laboratory-confirmed counterfeit Cialis tablet in Australia. There have been recent warnings about this counterfeit drug and other similar sexual performance-enhancing medications on several health websites.¹⁻⁴

Cialis (tadalafil), a phosphodiesterase-5 (PDE-5) inhibitor, is a pharmaceutical drug manufactured and marketed by Eli Lilly. It can be obtained only with a prescription, and is dispensed in 5 mg, 10 mg and 20 mg, but not 50 mg, doses. Our case reveals the poor quality-control measures used during the manufacturing process of counterfeit Cialis, which not only contained a lethal dose of a sulfonylurea, but also a subtherapeutic amount of a different agent from the PDE-5 inhibitor class. Glibenclamide is not known to have any sexual performance-enhancing effect, and hypoglycaemia is not a known adverse reaction of tadalafil.

Consumption of counterfeit medicines may be harmful. As many countries have not yet enacted deterrent legislation, counterfeiters often do not need to fear prosecution.⁵ Medicines for

Glucose, insulin and C-peptide levels during admission

	Day 1	Day 2	Day 9
Glucose (RR, 3.0–6.0), mmol/L	2.4	2.8	4.7
Insulin (RR, 2–23), mU/L	17	11	0.3
C-peptide (RR, 0.3–1.4), nmol/L	2.6	Not done	0.7

RR = reference range. ◆

NOTABLE CASE

erectile dysfunction or sexual enhancement have a huge global market, and this is not the first report of this adverse reaction. An outbreak of hypoglycaemia, secondary to ingestion of sexual performance-enhancing drugs, including counterfeit Cialis and other unlicensed drugs, was reported recently from South-East Asia.⁶ These drugs also contained high doses of glibenclamide and low doses of sildenafil.

The World Health Organization estimates that up to 1% of medicines available in the industrialised countries, and 10% globally, may be counterfeit.⁷ In Australia, the TGA is an effective regulatory authority; however, despite the regulations, overseas travel and internet purchasing may allow counterfeit medicines to be imported. Under the "Personal import scheme", many complementary medicines can be legally imported without import permits.⁸ Additionally, drugs from the PDE-5 inhibitor class, such as tadalafil, which are prescription-only medicines, are not listed under "Prohibited imports and exports (drugs and precursor chemicals)" and so can be purchased on the internet with a prescription from Australia.⁹

A universal cyberlaw or some other form of international convention is needed to regulate promotion and sales of these types of products on the internet. The WHO acknowledges that increasing international trade in pharmaceuticals, as well as sales via the internet, has further facilitated the entry of counterfeit products into the supply chain. To combat this, in 2006 the WHO helped to create the International Medical Products Anti-Counterfeiting Taskforce (IMPACT).⁵

Consumers are encouraged to use web sources like the TGA, Health on the Net Foundation, and the WHO to get useful and reliable online health information on medicinal products.¹⁰⁻¹²

Based on this case, we suggest that health warnings about counterfeit sexual performance-enhancing medications should be published on the TGA website.

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Competing interests

None identified.

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References

- 1 New Zealand Medicines and Medical Devices Safety Authority. Director-General of Health warning about the personal importation of adulterated and counterfeit prescription medicines. Wellington: Medsafe, 2008. <http://www.medsafe.govt.nz/hot/alerts/CounterfeitMedicine/DGStatement.asp> (accessed Mar 2010).
- 2 Swiss Agency for Therapeutic Products. Swissmedic issues a warning regarding life-threatening, counterfeit erectile stimulants in the Asian

region. Bern: Swissmedic, 2009. <http://www.swissmedic.ch/aktuell/00003/00349/index.html?lang=en> (accessed Mar 2010).

- 3 Health Sciences Authority. HSA alerts on wider spread of harmful illegal health products [press release]. 11 Apr 2008. Singapore: HAS, 2008. http://www.hsa.gov.sg/publish/hsaportal/en/news_events/press_releases/2008.html (accessed Mar 2010).
- 4 Department of Health, Hong Kong. Public urged not to consume capsules for treating sexual dysfunction with undeclared drug [press release]. 5 Feb 2008. Hong Kong: Department of Health, 2008. <http://www.dh.gov.hk/textonly/english/press/2008/080205-2.html> (accessed Mar 2010).
- 5 World Health Organization. Medicines: counterfeit medicines. Media Centre. Fact sheet No. 275, Jan 2010. <http://www.who.int/mediacentre/factsheets/fs275/en/> (accessed Mar 2010).
- 6 Kao SL, Chan CL, Lim CC, et al. An unusual outbreak of hypoglycaemia [letter]. *N Engl J Med* 2009; 360: 734-736.
- 7 Therapeutic Goods Administration. Counterfeit medical products. TGA News Issue 58, April 2009. Canberra: TGA, 2009. <http://www.tga.gov.au/docs/html/tganews/news58/tganews58.htm> (accessed Mar 2010).
- 8 Therapeutic Goods Administration. Personal import scheme for unapproved medicines. Canberra: TGA, 2010. <http://www.tga.gov.au/import/persimp.htm> (accessed Mar 2010).
- 9 Australian Government Department of Health and Ageing. List of drug substances requiring import and or export authorisations. Canberra: Office of Chemical Safety and Environmental Health (OCSEH), 2010. <http://www.health.gov.au/internet/main/publishing.nsf/Content/list-of-drug-substances-requiring-import-and-or-export-authorisations> (accessed Mar 2010).
- 10 Therapeutic Goods Administration. Medical products and the Internet. A guide to finding reliable information. Canberra: TGA, 1999. <http://www.tga.gov.au/docs/html/whointer.htm> (accessed Mar 2010).
- 11 Health on the Net Foundation. Trustworthy health sites. <http://www.hon.ch/HONsearch/Patients/hunt.html> (accessed Mar 2010).
- 12 World Health Organization. Counterfeit medicines. <http://www.who.int/medicines/services/counterfeit/en/index.html> (accessed Mar 2010).

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The former colleagues, trainees and friends of the late Dr Edmund Hirst, of Sydney Hospital, will be pleased to know that Eddie's contribution to pathology in Australia has been recognised. A plaque in his honour has been placed on the Wall of Honour at the Royal Society of Medicine in London.

Eddie Hirst was one of the founding fathers of the Royal College of Pathologists of Australasia and was one of those early histopathologists who laid the foundations of the world-class pathology service enjoyed in Australia now.

Interested colleagues may inspect the Wall of Honour at the Wimpole Street, London, headquarters of the Society.

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