Case Report DOI: http://doi.org/10.4038/sjdem.v12i1.7438

Glibenclamide or captopril, inaccurate medication identity with clinical implications: A case report

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Abstract

Background:

Medication errors are known to occur during prescribing, transcribing, dispensing, administration and monitoring. Look-alike medications can be an important cause of dispensing errors. We report a case of a look-alike medication error occurring in a patient presenting with hypoglycaemia.

Case presentation:

A 68-year-old female with a past history of rheumatic heart disease on warfarin, carvedilol and captopril, presented to hospital with three episodes of reduced level of consciousness. Hypoglycaemia was identified as the cause of the patient's episodic reduction in the level of consciousness and investigations were commenced. During the hospital stay her all usual medications were continued from the hospital ward, while carvedilol was substituted with verapamil to minimize hypoglycaemic unawareness. After hospital admission the patient did not develop any further episodes. All her investigations including fasting blood glucose, HbA1c, and prolonged fasting test were within normal limits. Detailed evaluation of the patient's medication history, laboratory evaluation of the medications and root-causes analysis confirmed that the identical appearance of both captopril and glibenclamide (colour, shape and size) and similarities in the two containers of the medications was responsible for a dispensing error at the local hospital pharmacy. In light of cases similar to our patient, preventive strategies to reduce look-alike dispensing errors need to be customised and tailor-made depending upon the requirements of the local hospital setting.

Conclusions:

As highlighted in the present case, clinicians need to be vigilant and consider medication errors in the differential diagnosis, especially when other possible causes have been reasonably eliminated.

Keywords: Case report; medication error; hypoglycaemia; diabetes

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Background

A medication error is defined as a failure in the treatment process that leads to or has the potential to lead to patient harm [1]. Medication errors are known to occur during prescribing, transcribing, dispensing, administration and monitoring. A dispensing error is a discrepancy between a prescription and the medicine that the pharmacy delivers to the patient, including the dispensing of a medicine with inferior pharmaceutical or informational quality [2]. Dispensing errors as a proportion of total medication errors show a wide variation, with some studies reporting nearly 45% [3]. The rates of dispensing errors are generally low, however further improvements in pharmacy distribution systems are still important because pharmacies dispense such high volumes of medications that even a low error rate can translate into a large number of errors [3]. Some of the common causes of medication errors identified in studies are: being busy (21%), being short-staffed (12%), being subject to time constraints (11%), fatigue of healthcare providers (11%), interruptions during dispensing (9.4%), and look-alike/ sound-alike medicines (LASA) (8.5%) [4].

The World Health Organization (WHO) has identified confusing medication names as a common cause for errors [5]. Currently referred to as LASA medications, they are an important cause of dispensing errors. They are either visually similar in physical appearance/packaging or have similarities in the spelling/phonetics of the medication name. The availability LASA medication at the pharmacy puts the onus of patient safety on vigilance and perfection on part of the health-care providers, leaving margins for human errors [6]. We report a case of a look-alike medication error occurring in a 68-year-old female patient, presenting with hypoglycaemia. Since such errors are generally not considered during the differential diagnosis of hypoglycaemia, clinicians need to be aware about this rare and potential life-threatening medication error and hospitals need to institute adequate preventive measures.

Case Presentation

A 68-year-old female with a past history of rheumatic heart disease, leading to severe mitral valve stenosis complicated with atrial fibrillation (on warfarin and carvedilol) and hypertension (on captopril), presented to the National Hospital of Sri Lanka with three episodes of reduced level of consciousness occurring during a period of one week in November 2019. These episodes were not accompanied by symptoms of sympathetic activation, such as palpitations and sweating. Furthermore, there were no accompanying features to suggest seizures. Review of the other systems were normal. On all three occasions the patient has recovered spontaneously after consumption of sugar containing liquids given at home, where hypoglycaemia has been noted on glucometer measured capillary blood glucose (28 mg/dl). There were no known allergies to food or drugs. Furthermore, no other person at home were taking oral hypoglycaemic medications. On examination at the hospital, she was afebrile, fully conscious with a GCS of 15, with normal vital signs. Her body mass index was 22.1 kg/m2 (normal range 18.5-24.9 kg/m2). The rest of the systemic examination was normal. Hypoglycaemia was identified as the cause of the patient's episodic reduction in the level of consciousness and investigations were commenced. During the hospital stay her usual medications, warfarin and captopril were continued from the hospital ward, while carvedilol was substituted with verapamil, to minimize hypoglycaemic unawareness. After hospital admission the patient did not develop any further episodes of reduced level of consciousness.

Her fasting blood glucose value on day 1 was 98 mg/dl and the HbA1c was 5.4%. Furthermore, initial laboratory tests on admission showed a normal haemoglobin of 12.9 g/dl, a white blood cell count of 8,900/μL and a platelet count of 291,000/μL. Her serum sodium, potassium, calcium and magnesium levels were normal, with a PT/INR of 3.2, while serum creatinine was 76 μmol/l. Inflammatory markers were not elevated (C-Reactive Protein <6mg/dl), with normal liver enzymes and thyroid function tests. The initial investigations also included an ultrasound scan of the abdomen, which did not reveal any abnormalities. The summary of the investigations is presented in Table 1. On day 3 of the admission, it was decided to conduct a supervised fast for the evaluation of hypoglycaemia, which was stopped at 72 hours as the patient did not develop hypoglycaemic symptoms. Lowest blood glucose value noted during the entire 72-hour period was 64 mg/dl. At the end of the 72 hours samples taken for random blood glucose, C-peptide and serum insulin were all within normal limits (Table 1).

Since the patient did not develop any hypoglycaemic episodes during the hospital stay of 1 week, it was decided to undertake a detailed evaluation of the patient's medication history. She has attended the routine cardiology clinic at the local hospital in the last week of October 2019, where she was continued

Table 1 : Results of the laboratory investigations

	Patient's value	Normal range
Fasting blood glucose (mg/dL)	98 mg/dl	60-100 mg/dl
Glycosylated haemoglobin (HbA1c) (%)	5.4	<6.5
Haemoglobin (g/dl)	12.9	
White blood cell count (per μL)	8,900	7,000-11,000
Platelet count (per μL)	291,000	150,000-450,000
Serum sodium (mmol/l)	140	135-145
Serum potassium (mmol/l)	3.9	3.5-5.2
Serum calcium (mg/dl)	9.3	8.7-10.2
Serum magnesium (mmol/l)	0.95	0.65-1.05
Serum creatinine (μmol/l)	76	62-106
Alanine transaminase (AST) (U/l)	25	5-40
Aspartate transaminase (ALT) (U/l)	23	5-40
Thyroid stimulating hormone (TSH) (mIU/l)	1.35	0.4-4.0
Free thyroxine (ng/dl)	1.47	0.7-1.8
Serum 9am cortisol (nmol/l)	388.7	118.6-618.0
Random blood glucose (mg/dl) – 72 hours fast	63	<200
Serum insulin (mIU/l) – 72 hours fast	14	<25
Serum C-peptide (nmol/l) – 72 hours fast	0.41	0.26-0.62

on warfarin, carvedilol and captopril. These medications were dispensed at the pharmacy of the hospital, and patient has started using this new supply of clinic medicines, one week prior to the index admission (since there were leftover medications from the previous month). The medications were taken from containers at the pharmacy and dispensed in 3 separate envelopes to the patients, one each for warfarin, carvedilol and captopril. The onset of symptoms was closely related in time to the commencement of this new supply of medications, which were discontinued only after the index admission, since the patient was given the medications from the ward. Close examination of the medications given from the clinic revealed that the captopril dispensed from the pharmacy was identical in appearance (colour, shape and size) to the currently available tablets of glibenclamide in the ward (Figure 1). Further evaluation revealed that the containers of captopril and glibenclamide at the local hospital pharmacy were similar in appearance, although from different manufacturers.

Subsequently, the tablets that was claimed to be captopril dispensed from the local hospital pharmacy were sent for analysis to the National Drug Quality Assurance Laboratory (NDQAL) of the National Medicine Regulatory Authority (NMRA), Ministry of Health Care and Indigenous Medicine of Sri Lanka. The analysis revealed that the tablets given in the local hospital pharmacy, contained glibenclamide, which has led to hypoglycaemia in this patient. Using the Naranjo adverse drug reaction probability scale (our patient scored 8, which makes the drug reaction 'probable') the patient's diagnosis was confirmed as hypoglycaemia caused by glibenclamide [7]. Root-cause analysis revealed that similar physical appearance of glibenclamide and captopril (colour, shape and size) and similarities of the containers of both medications (colour, shape and size) available at the local hospital pharmacy, and close proximity of storage in containers with similar exterior appearance was the reasons for the mix-up in the two medications at the local hospital pharmacy.

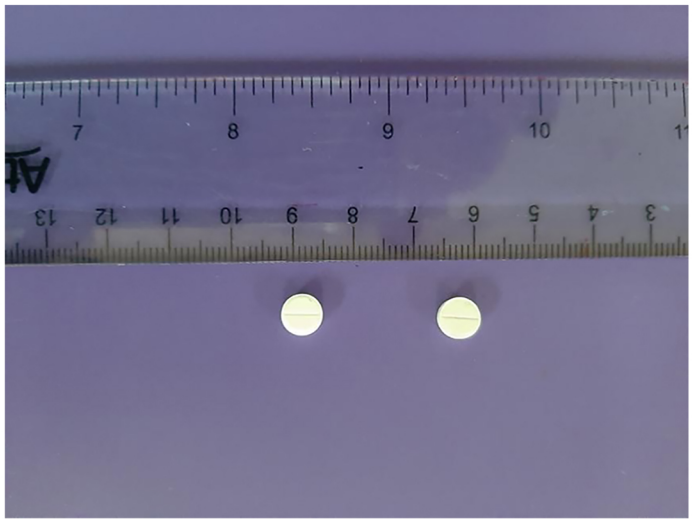

Figure 1

Discussion and Conclusions

Medication errors due to look-alike medicines has not been previously reported as a cause of hypoglycaemia in non-diabetic patients, who does not have access readily to oral hypoglycaemic medications. The causes of hypoglycaemia are quite broad in those who are not taking treatment for diabetes, and includes conditions like hepatic and renal failure, sepsis, trauma, burns, malnutrition, hormonal deficiencies (e.g cortisol), non-islet cell tumours (IGF-II secreting tumours), insulinoma, insulin and insulin receptor antibodies, post gastric bypass hypoglycaemia and genetic disorders [8]. However, most of these causes were not evident in our patient during the initial clinical evaluation, in spite clearly confirming that hypoglycaemia was the cause of the reduced level of consciousness as per the Whipple's trial (low plasma glucose concentration, clinical signs/symptoms consistent with hypoglycaemia, and resolution of signs or symptoms when the plasma glucose concentration increases) [8]. Hence, we had to broaden our differential diagnosis and consider medications as a possible cause for the presentation in this patient. The detailed evaluation of the medication history, laboratory evaluation and root-cause analysis confirmed that the look-alike nature of captopril and glibenclamide at the local hospital pharmacy was responsible for a dispensing error. Although the prescribing is done manually at the local hospital, the prescription was found to be legible, excluding a prescribing error. Glibenclamide causes hypoglycaemia due to the stimulation of insulin release and the minimal hypoglycaemic symptoms in our patient could have been due to the concurrent treatment with the beta-blocker carvedilol [9].

Accurate quantitative estimations regarding the incidence of look-alike medication errors are lacking, due to under reporting, fear of litigation, inability to determine causality and reluctance to admit error [10]. However, available estimates suggest that they are responsible for about one third of all dispensing errors [11]. Illegible handwriting, incomplete knowledge of drug names, new products and similarities in packaging and labelling act as contributing factors to this problem, which is further complicated by the presence of a multitude of brand names currently available in the Sri Lankan market [11].

Generally, LASA drugs are correlated to dispensing errors at the pharmacy level, however as evident in the current case multiple disciplines contribute towards the final appearance of look-alike medications at the pharmacy, including manufacturing, regulatory affairs and packaging. Furthermore, glibenclamide and captopril are not reported in the literature as LASA medications. Hence, when instituting preventive strategies for minimising dispensing errors due to LASA medications local factors also needs to be considered. Some of the strategies that have been proposed and tested to minimize the risks of LASA medication errors at hospitals settings include:

1) computer algorithms that detect potential LASA errors,
2) changes in the appearance of labelling and pack aging of LASA medicines,
3) inclusion of stickers with security symbols or pictograms on the packaging,
4) re-packaging
5) changing order and separate storage of products

with similar name,
6) tall man lettering of medication names in the Pharmacy area ,
7) the joint use of the brand name and the generic name (in brackets) in prescriptions and drug labelling and
8) constant review of new medications added in formularies and changes in packaging [12].

However, in light of cases similar to our patient, it is important to understand that preventive strategies need to be customised and tailor-made depending upon the requirements of the local hospital setting. In the context of the present case-scenario, physical separation of the two medications at the pharmacy, clear and distinguishable labelling of the two containers and education of the pharmacist are important measures to minimize repetition of similar errors. Furthermore, manufacturers also need to be made aware regarding the identical appearance of the finished product and the similarity in the appearance of the containers.

In conclusion, medication errors due to look-alike medicines are under-reported. Glibenclamide and captopril are generally not considered LASA medications. However, as highlighted in the present case, clinicians need to be vigilant and consider medication errors in the differential diagnosis, especially when other possible causes have been reasonability eliminated.

List of Abbreviations

GCS – Glasgow Coma Scale
HbA1c – Glycosylated haemoglobin
IGF – Insulin like Growth Factor
LASA – look-alike/sound-alike medicines
NDQAL – National Drug Quality Assurance Laboratory
NMRA – National Medicine Regulatory Authority
PT/INR – Prothrombin Time/International Normalized Ratio
WHO – World Health Organization

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Written informed consent was obtained from the patient for publication of this case report.

Competing interests

The authors declare that they have no conflicts of interest

Availability of data and materials

Can be obtained by contacting the corresponding author

Authors' contributions

PR led the conception and design, acquisition of data, review of literature, and drafted the manuscript. DMDPC, AK and AHNF reviewed the manuscript. PR and DMDPC gave the concept of research paper, and critically reviewed the manuscript. All authors read and approved the manuscript.

Funding

Not applicable.

Acknowledgements

Not applicable.

References

1. Aronson JK: Medication errors: definitions and classification. *Br J Clin Pharmacol* 2009, **67**(6):599-604.

2. Cheung KC, Bouvy ML, De Smet PA: Medication errors: the importance of safe dispensing. *Br J Clin Pharmacol* 2009, **67**(6):676-680.

3. Cheung K-C, Bouvy ML, De Smet PAGM: Medication errors: the importance of safe dispensing. *Br J Clin Pharmacol* 2009, **67**(6):676-680.

4. Beso A, Franklin BD, Barber N: The frequency and potential causes of dispensing errors in a hospital pharmacy. *Pharm World Sci* 2005, **27**(3):182-190.

5. Naunton M, Gardiner HR, Kyle G: Look-alike, sound-alike medication errors: a novel case concerning a Slow-Na, Slow-K prescribing error. *Int Med Case Rep J* 2015, **8**:51-53.

6. Gangakhedkar GR, Waghalkar PV, Shetty AN, Dalvi AM: Look-Alike Drugs: Avoiding Potential Medical Errors. *Int J Prev Med* 2019,

10:9-9.

7. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, Janecek E, Domecq C, Greenblatt DJ: A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther* 1981, **30**(2):239-245.

8. Desimone ME, Weinstock RS: Non-Diabetic Hypoglycemia. In., edn. Edited by Feingold KR, Anawalt B, Boyce A, Chrousos G, Dungan K, Grossman A, Hershman JM, Kaltsas G, Koch C, Kopp P et al. *South Dartmouth: MDText.com*, Inc; 2000.

9. Luzi L, Pozza G: Glibenclamide: an old drug with a novel mechanism of action? A*cta Diabetol* 1997, **34**(4):239-244.

10. Ciociano N, Bagnasco L: Look alike/sound alike drugs: a literature review on causes and solutions. *Int J Clin Pharm* 2014, **36**(2):233-242.

11. Rahman Z, Parvin R: Medication Errors Associated with Look-alike/Sound-alike Drugs: *A Brief Review Journal of Enam Medical College* 2015, **5**(2):110-117.

12. Lizano-Díez I, Figueiredo-Escribá C, Piñero-López MÁ, Lastra CF, Mariño EL, Modamio P: Prevention strategies to identify LASA errors: building and sustaining a culture of patient safety. *BMC Health Services Research* 2020, **20**(1):63.