Drankowska Justyna, Kos Michał, Kościuk Andrzej, Tchórz Michał. Cyanide poisoning from an alternative medicine treatment with apricot kernels in a 80-year-old female. Journal of Education, Health and Sport. 2018;8(12):19-26. eISNN 2391-8306. DOI http://dx.doi.org/10.5281/zenodo.1844020
http://ojs.ukw.edu.pl/index.php/johs/article/view/6338

The journal has had 7 points in Ministry of Science and Higher Education parametric evaluation. Part B item 1223 (26/01/2017).
1223 Journal of Education, Health and Sport eISSN 2391-8306 7

Received: 25.11.2018. Revised: 25.11.2018. Accepted: 02.12.2018.

Cyanide poisoning from an alternative medicine treatment with apricot kernels in a 80-year-old female

Justyna Drankowska

Student's Research Group in the Department of Toxicology, Medical University of Lublin
Poland
Principal contact for editorial correspondence.

Michał Kos
Student's Research Group in the Department of Toxicology, Medical University of Lublin
Poland

Andrzej Kościuk
Student's Research Group in the Department of Toxicology, Medical University of Lublin
Poland

Michał Tchórz

Department of Toxicology, Medical University of Lublin
Poland

Abstract

Introduction: Amygdaline, one of the most common cyanogenic glycosides, is present in the seeds and fruit pits of Prunus species. The excessive administration of this glycoside might lead to cyanide poisoning.
Aim: The aim of the study is to depict the risk associated with apricot kernels ingestion on the base of the case report.
Methods: The analysis of the patient's medical history and the review of available literature.

Results: 80- year- old female with the medical history of papillary thyroid cancer was admitted to the toxicology department due to accidental cyanide poisoning. The patient consumed extract consisted of milled apricot kernels, then suffered from dyspnea, vertigo and vomiting. After that, she lost consciousness. Lactic acidosis, highly specific for cyanide intoxication, was diagnosed during hospitalization. The patient was treated with fluid and steroid therapy, sodium bicarbonate and supplemental oxygen. On the 3rd day of stay, the patient was discharged with recommendation of control in toxicological clinic.
Conclusions: Initial symptoms of cyanide poisoning are not specific, therefore it is worth taking this poisoning into account in differential diagnosis, especially in oncological patients or in children.

Key words: cyanide; alternative medicine; poisoning; apricot kernels

INTRODUCTION

According to the report of the World Health Organisation, in the recent years the use of different forms of complementary and alternative medicine (CAM) has become increasingly popular in the world [1]. Several studies report that herbal medicine is the subtype of CAM most common, particularly among women with better education [2,3,4]. Furthermore, According to a recently published survey of Polish physicians, herbal medicine is one of CAM therapies that are most likely to be recommended, especially by elderly doctors [5]. As a result of growing interest in phytotherapy, there is a need for raising awareness in terms of the potential toxicity of plants [6].

Of particular attention are cyanogenic glycosides, plant secondary metabolites, which are present in more than 2500 plant species. One of the most common cyanogenic glycosides is amygdaline that occurs in the seeds and fruit pits (e.g., apple seeds, cherry pits, bitter almonds, and apricot pits) of Prunus species [7, 8]. When ingested, amygdalin is biotransformed by intestinal enzyme B-D-glucosidase to glucose, aldehyde and cyanide. The last one is well known for causing cellular hypoxia by binding iron atom in mitochondrial cytochrome oxidase a3. Despite its ability to affect also other heme-containing enzymes, inhibition of the above-mentioned cytochrome is undoubtedly of greatest clinical importance [9]. In the face of electron transport chain inhibition, mitochondria cannot utilize oxygen any more. Thus, formation of ATP molecules comes to an end. As a result of the failure of aerobic energy metabolism, only relatively inefficient anaerobic metabolism might take place. In the

nearest future, it leads to accumulation of lactate and a high-anion-gap metabolic acidosis [10].

CASE REPORT

A 80-year –old patient was admitted to the Department of Toxicology and Cardiology due to accidental cyanide poisoning. Her history revealed that she consumed about 300 ml of extract consisted of milled apricot kernels one hour before. After that, she suffered from dyspnea, vertigo and vomiting. Then, she developed loss of consciousness.

On admission, she was conscious, in verbal logical contact. Her past medical history was remarkable. One year before, she underwent total thyroidectomy due to papillary thyroid cancer. Moreover, she suffered from chronic hepatitis C. She admitted that she consumed apricot kernels in order to treat thyroid disorder.

Physical examination revealed no abnormalities apart from hypotension 90/50 mm Hg. The laboratory tests including complete blood count, liver function tests, blood sodium, potassium, chloride level tests, blood glucose test remained within reference range.

However, there was a partially compensated metabolic acidosis in the blood gas analysis at the time of admission. Serial arterial blood gases analysis was presented in Table 1. The blood cyanide level was not measured in our laboratory due to technical limitations. The patient was diagnosed with cyanide intoxication on the base of her history. She underwent gastric lavage and received activated charcoal. Due to acidosis the patient was treated with 8,4% sodium bicarbonate. She also received steroid and fluid therapy, along with supplemental oxygen. After the hospitalization which lasted 3 days, the patient was discharged from the hospital in a good condition with the recommendation of control in the toxicological clinic.

Table 1. Serial venous blood gases analysis

Parameter (reference range)	on the day of admission	One Day after admission	Two days after admission
pH (7,35-7,45)	7,344	7,447	7,432
pCO2 (38,9-48,9 mmHg)	33,9	36,2	36,9
BE(B) (-3 to 3 mmol/ l)	-6,6	0,7	0
pO2 (75-100 mmHg)	35,9	54,2	48
HCO3- (21-25 mmol/ l)	18	24,5	24
Lactate (0,5-2,20 mmol/l)	8,2	1	1
Oxygen saturation [%]	63,5	86,8	82,2

Table 2 Signs and symptoms of cyanide poisoning

Nervous system	Headache, seizures, altered mental status (confusion, disorientation), coma, mydriasis
Respiratory system	Tachypnoe (early), bradypnoe (late), dyspnea, cough
Cardiovascular system	Tachycardia (early), bradycardia (late) hypertension (early), hypotension (late), pulmonary edema, cardiac arrest
Gastrointestinal system	Stomachache, vomiting, nausea
Skin	A cherry red skin color

DISCUSSION

Cyanide exposure is in most cases associated with smoke inhalation, industrial incidents, laboratory mishaps or criminal activity [11]. However, it is crucial to remember also about a rarer cause, i.e. cyanogenic glycosides–containing plants as amygdalin is still used in alternative cancer treatment [12]. Amygdaline's concentration in seeds is variable. Thus, HCN content differs among species [13] . As for apricot seeds cyanide content is known to range between 0.122 and 4.09 mg/g, in most cases the average content is 2.92 mg/g. As far as the average lethal dose of cyanide for humans is concerned, it ranges from 50 to 60 mg [14]. However, according to the recent study, it is not possible to provide a safe oral dose of this glycoside. It differs individually depending on the influence of a variety of factors on intestinal microbiota [15]. Of particular significance is the fact that oral administration of amygdaline is correlated with much greater toxicity, mainly because of the secretion of beta-glucosidases by intestinal bacteria and some eaten plants [16].

In the literature several cases of amygdaline toxicity have been reported so far. Cyanide poisoning was described by Akyildiz et al. in children who accidentally consumed apricot seeds [8]. However, a large number of cases were associated with taking amygdalin tablets in the incurable stage of a tumor, as in the case of a 73-year-old female with metastatic pancreatic cancer, in a 68-year-old female with inoperable urothelial carcinoma of the bladder, but also in a 32-year-old female with metastatic breast cancer [12, 17, 18] . Such treatment was also described in a 4- year- old child with malignant brain disease (metastatic ependymoma) who was given oral and intravenous amygdalin, along with apricot kernels by his parents [19]. Our 80-year old patient had also the medical history of cancer, albeit operable. However, it has been shown that the advanced age at the time of diagnosis (>75 years) is associated with higher recurrence rates and lower survival [20]. Thus, it might have influenced the patient's decision in terms of alternative medicine treatment.

The difficulty of diagnosis lies in the fact that cyanide poisoning might be easily overlooked without an obvious history of exposure. It might be suspected when a patient has signs and symptoms typical of progressive hypoxia such as headache, anxiety, confusion, lethargy, seizures or coma. What is more, a brief period of compensatorily increased inotropy can occur before myocardial depression. Terminally, hypotension and bradycardia appear. A patient might present symptoms typical of gastrointestinal toxicity (i.e. nausea and vomiting), as in the case of our patient. As a result of the decreased utilization of oxygen in tissues, a cherry-red skin color might be observed. Sometimes cyanide poisoning might be detected by characteristic almond odor on breath. However, it is considered to be a rare finding [21, 22]. Symptoms and signs typical for cyanide poisoning are presented in the Table 2

As far as laboratory findings are concerned, lactic acidosis (> 8 mmol/l) is highly specific for cyanide intoxication according to the study of Buad et al. [23]. It remains in accordance with the laboratory findings in our patient.

In severe cases of cyanide poisoning, apart from sodium bicarbonate and the administration of 100% oxygen, a patient should also be treated with antidotal therapy [24]. The cyanide antidote kit consist of amyl nitrite, sodium nitrite and sodium thiosulfate. Cyanide binds preferentially to the ferric ion of methemoglobin, which is formed by nitrites, rather than to the ferric ion of cytochrome oxidase a3 in the mitochondria. Thus, nitrites are able to restore mitochondrial function. On the other hand, they are associated with important adverse effects such as vasodilation and hypotension. Furthermore, they might deteriorate acidosis. Another antidote, sodium thiosulfate acts as sulfhydryl donor, which bind cyanide and forms renally excreted thiocyanate [10]. However, hydroxycobalamin is considered to be one of the most effective antidotes as it lacks in significant adverse effects, i.e. hypotension [25, 26] . Moreover, it might be used in pregnant patients, as well as in patients who were exposed to carbon monoxide. Such an advantage is associated with its mechanism which depends on binding cyanide without forming methemoglobin [10, 26] .

CONCLUSIONS

In the light of the depicted case and the review of literature, it can be stated that the use of amygdaline (either in kernels, or in tablets) might put patient's life in jeopardy. Cyanide poisoning might be fatal, regardless of the number of consumed kernels/tablets. It should be remembered that patients with the diagnosis of cancer are especially likely to resort to this type of therapy. As initial symptoms of this poisoning are not specific, it is worth taking cyanide poisoning into account in differential diagnosis, particularly in oncological patients or in children. Patients who are quickly diagnosed with cyanide poisoning might be effectively treated with oxygen, fluid therapy, sodium bicarbonate, and in the most severe poisonings with antidotes.

References

[1] World Health Organization., National policy on traditional medicine and regulation of herbal medicines : report of a WHO global survey. World Health Organization, 2005. http://apps.who.int/medicinedocs/en/d/Js7916e/. Accessed November 24, 2018

[2] Jatau A. I., Aung M. M. T., Kamauzaman T. H. T., Chedi B. A. Z., Sha'aban A., and Rahman A. F. A., 'Use and toxicity of complementary and alternative medicines among patients visiting emergency department: Systematic review.', J. Intercult. Ethnopharmacol., vol. 5, no. 2, pp. 191–7, 2016. doi:10.5455/jice.20160223105521

[3] Frass M., Strassl R. P., Friehs H., Müllner M., Kundi M., and. Kaye A. D, 'Use and acceptance of complementary and alternative medicine among the general population and medical personnel: a systematic review.', Ochsner J., vol. 12, no. 1, pp. 45–56, 2012. http://www.ncbi.nlm.nih.gov/pubmed/22438782. Accessed November 24, 2018.

[4] Kemppainen L. M., Kemppainen T. T.,. Reippainen J. A, Salmenniemi S. T., and Vuolanto P. H., 'Use of complementary and alternative medicine in Europe: Health-related and sociodemographic determinants.', Scand. J. Public Health, vol. 46, no. 4, pp. 448–455, Jun. 2018. doi:10.1177/1403494817733869

[5] Olchowska-Kotala A.and Barański J., 'Polish physicians' attitudes to complementary and alternative medicine', Complement. Ther. Med., vol. 27, pp. 51–57, Aug. 2016. doi:10.1016/J.CTIM.2016.05.004

[6] Afifi F. U., Wazaify M., Jabr M., and Treish E., 'The use of herbal preparations as complementary and alternative medicine (CAM) in a sample of patients with cancer in Jordan', Complement. Ther. Clin. Pract., vol. 16, no. 4, pp. 208–212, Nov. 2010. doi:10.1016/J.CTCP.2010.05.001

[7] Vetter J., ‘Plant cyanogenic glycosides’, Toxicon, vol. 38, no. 1, pp. 11–36, Jan. 2000. doi:10.1016/S0041-0101(99)00128-2

[8] Akyildiz B. N., Kurtoğlu S., Kondolot M., and. Tunç A, ‘Cyanide poisoning caused by ingestion of apricot seeds’, Ann. Trop. Paediatr., vol. 30, no. 1, pp. 39–43, Mar. 2010. doi:10.1179/146532810X12637745451951

[9] Borron S. W.and Baud F. J., ‘Antidotes for acute cyanide poisoning.’, Curr. Pharm. Biotechnol., vol. 13, no. 10, pp. 1940–8, Aug. 2012. http://www.ncbi.nlm.nih.gov/pubmed/22352728. Accessed November 19, 2018.

[10] Hamel J., ‘A Review of Acute Cyanide Poisoning With a Treatment Update’, Crit. Care Nurse, vol. 31, no. 1, pp. 72–82, Feb. 2011. doi:10.4037/ccn2011799

[11] Graham J.and Traylor J., Cyanide Toxicity. StatPearls Publishing, 2018. http://www.ncbi.nlm.nih.gov/pubmed/29939573. Accessed November 24, 2018.

[12] Dang T., Nguyen C., and Tran P. N, ‘Physician Beware: Severe Cyanide Toxicity from Amygdalin Tablets Ingestion.’, Case Rep. Emerg. Med., vol. 2017, p. 4289527, 2017. doi:10.1155/2017/4289527

[13] Bolarinwa I. F.,. Orfila C, and Morgan M. R. A., ‘Amygdalin content of seeds, kernels and food products commercially-available in the UK’, Food Chem., vol. 152, pp. 133–139, Jun. 2014. doi:10.1016/j.foodchem.2013.11.002

[14] Suchard J. R., Wallace K. L., and. Gerkin R. D, ‘Acute Cyanide Toxicity Caused by Apricot Kernel Ingestion’, Ann. Emerg. Med., vol. 32, no. 6, pp. 742–744, Dec. 1998. doi:10.1016/S0196-0644(98)70077-0

[15] Jaswal V., Palanivelu J., and R. C, ‘Effects of the Gut microbiota on Amygdalin and its use as an anti-cancer therapy: Substantial review on the key components involved in altering dose efficacy and toxicity.’, Biochem. Biophys. reports, vol. 14, pp. 125–132, Jul. 2018. doi:10.1016/j.bbrep.2018.04.008

[16] PDQ Integrative, Alternative, and Complementary Therapies Editorial Board A and CTEB., Laetrile/Amygdalin (PDQ®): Health Professional Version. National Cancer Institute (US), 2002. http://www.ncbi.nlm.nih.gov/pubmed/26389425. Accessed November 25, 2018.

[17] Bromley J., B. G. Hughes, D. C. Leong, and N. A. Buckley, ‘Life-Threatening Interaction Between Complementary Medicines: Cyanide Toxicity Following Ingestion of Amygdalin and Vitamin C’, Ann. Pharmacother., vol. 39, no. 9, pp. 1566–1569, Sep. 2005. doi:10.1345/aph.1E634

[18] Brien B. O, Quigg C., and Leong T., ‘Severe cyanide toxicity from “vitamin supplements”.’, Eur. J. Emerg. Med., vol. 12, no. 5, pp. 257–8, Oct. 2005. http://www.ncbi.nlm.nih.gov/pubmed/16175068. Accessed November 19, 2018.

[19] Sauer H., Wollny C., Oster I., Tutdibi E., Gortner L., Gottschling S. et al , ‘Severe cyanide poisoning from an alternative medicine treatment with amygdalin and apricot kernels in a 4-year-old child’, Wiener Medizinische Wochenschrift, vol. 165, no. 9–10, pp. 185–188, May 2015. doi:10.1007/s10354-014-0340-7

[20] Chereau N., Trésallet C., Noullet S., Godiris-Petit G., Tissier F., Leenhardt L. et al , ‘Prognosis of papillary thyroid carcinoma in elderly patients after thyroid resection: A retrospective cohort analysis.’, Medicine (Baltimore)., vol. 95, no. 47, p. e5450, Nov. 2016. doi:10.1097/MD.0000000000005450

[21] Parker-Cote J. L., Rizer J.,. Vakkalanka J. P,. Rege S. V, and Holstege C. P., ‘Challenges in the diagnosis of acute cyanide poisoning’, Clin. Toxicol., vol. 56, no. 7, pp. 609–617, Jul. 2018. doi:10.1080/15563650.2018.1435886

[22] Rajashekar T. and Okade R., ‘Irritant contact dermatitis to accidental exposure of cyanide.’, Indian J. Dermatol., vol. 58, no. 2, p. 162, Mar. 2013. doi:10.4103/0019-5154.108098

[23] Baud FJ., Borron SW, Mégarbane B. , Trout H., Lapostolle F., Vicaut E. et al, ‘Value of lactic acidosis in the assessment of the severity of acute cyanide poisoning’, Crit Care Med ,vol. 30, no. 9, pp 2044-50, 2002. doi:10.1097/01.CCM.0000026325.65944.7D

[24] Beasley D. M. G.and Glass W. I., ‘Cyanide poisoning: pathophysiology and treatment recommendations’, Occup. Med. (Chic. Ill)., vol. 48, no. 7, pp. 427–431, 1998. doi:10.1093/occmed/48.7.427

[25] Thompson J. P and Marrs T. C., ‘Hydroxocobalamin in cyanide poisoning’, Clin. Toxicol., vol. 50, no. 10, pp. 875–885, Dec. 2012. doi:10.3109/15563650.2012.742197

[26] Marraffa J. M., Cohen V., and. Howland M. A, ‘Antidotes for toxicological emergencies: A practical review’, Am. J. Heal. Pharm., vol. 69, no. 3, pp. 199–212, Feb. 2012. doi:10.2146/ajhp110014