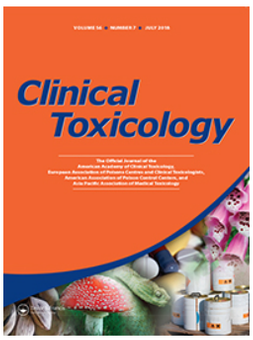

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REVIEW

Challenges in the diagnosis of acute cyanide poisoning

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ABSTRACT

Objective: The aim of this systematic review was to identify isolated acute cyanide poison cases and to identify reported signs, symptoms, and laboratory findings.

Methods: We searched MEDLINE, Cochrane Reviews, and Web of Science case reports and series using a number of MeSH descriptors pertaining to cyanide, toxicity, and poisonings. We excluded studies on plants, laboratory analyses, smoke inhalation poisonings, animals as well as non-English language articles and those in which data were not available. Data extracted included demographics, exposure characteristics, acute signs/symptoms, and medical management and outcome.

Results: From the initial 2976 articles retrieved, 65 articles (52 case reports, 13 case series) met inclusion criteria and described 102 patients. Most patients were unresponsive (78%), hypotensive (54%), or had respiratory failure (73%); other signs and symptoms included cardiac arrest (20%), seizures (20%), cyanosis (15%), cherry red skin (11%), and had an odor present (15%). Medical management included cyanide antidote kit (20%), sodium thiosulfate (40%), and hydroxocobalamin (29%). The majority of cases (66%) required intubation with mechanical ventilation and a substantial number (39%) developed refractory hypotension requiring vasopressor support.

Conclusions: Contrary to general reviews published on cyanide toxicity, reports of cherry red skin and bitter almond odor were rare among published cyanide cases. Consistent with other studies, metabolic acidosis with significant lactic acidosis were the laboratory values consistently associated with cyanide toxicity. Healthcare providers may overlook cyanide toxicity in the differential diagnosis, if certain expected characteristics, such as the odor of almonds or a cherry red color of the skin are absent on physical examination.

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Cyanide; poisoning; lactic acidosis; bitter almond

Introduction

Acute cyanide poisoning may cause rapid hemodynamic and neurological dysfunction. Early recognition in the emergency department and appropriate antidotal treatment of toxicity is crucial to survival [1]. Healthcare providers may overlook cyanide toxicity in the differential diagnosis if certain characteristics are absent on physical examination. Common teaching in medical Schools mention the odor of bitter almond and cherry red skin as expected findings of cyanide poisoning, despite their poor utility in clinical use.

Potential sources of cyanide exposure include smoke, amygdalin, nitriles, mining, manufacturing, agriculture, and hydrogen cyanide gas [2]. Cyanide salts have a long history of use for murder and suicide, and they continue to appear in modern cases. Two highly publicized cases of homicidal poisoning both eluded antemortem diagnosis in the ED and ICU [3,4].

Cyanide poisoning accounted for 1951 exposures reported to the American Association of Poison Control Centers from 2007 to 2014 [5–12]. Bebarta et al. reviewed poison center data and found that 8.3% of intentional exposure cases died and another 9% developed cardiac arrest but survived. Seventy-four percent of cases did not receive an antidote [13].

The clinical findings in a patient with cyanide toxicity depend on the route, duration, dosage, and source of exposure. Absorption of cyanide can occur through oral, dermal, inhalational, and parental routes. Cyanide is a potent decoupler of oxidative phosphorylation causing disruption of ATP synthesis via blockade of cytochrome oxidase aa3. Consequently, aerobic respiration ceases and anaerobic respiration ensues leading to excessive lactate formation [14,15]. Ultimately, a significant metabolic acidosis occurs despite adequate oxygen in the mitochondria. Ingestion of approximately 140–250 mg of cyanide salt is potentially lethal if left untreated [16]. Because cyanide poisoning is rare, healthcare professionals may overlook the diagnosis without an obvious history of exposure and may miss the fleeting opportunity to treat with an appropriate antidote [1].

The current medical literature contains inconsistencies concerning the expected clinical and laboratory findings after cyanide poisoning. Conventional reviews report that hydrogen cyanide has a bitter almond odor. Prior reports claim that only 20–40% and possibly 60–80% of individuals can discern the odor [17,18]. Cherry-red skin is another physical exam finding that is reported as characteristic of cyanide toxicity, due to increased venous hemoglobin oxygen saturation. However, there is not a predictable incidence in which cherry-red skin is present upon initial presentation. Patients

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may present after cardiovascular collapse with subsequent cyanosis rather than cherry-red skin [1]. In one case series of intentional cyanide ingestions pink lividity and a "bitter" almond smell were not prevailing signs [19]. Additional signs and symptoms associated with cyanide toxicity are dizziness, headache, nausea, vomiting, tachypnea, tachycardia, restlessness, seizures, and loss of consciousness. However, these signs and symptoms can occur from a multitude of medical conditions and are not specific to cyanide toxicity. Metabolic acidosis with associated hyperlactatemia has been a predominant laboratory finding in various reports.

The aim of the systematic review was to identify case reports and case series of live patients presenting to a healthcare facility after acute cyanide poisoning from a cyanide salt and identify the most prevalent initial documented clinical examination and laboratory findings.

Methods

We conducted a systematic literature review adhering to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines.

Literature search

In April 2015, the authors sought publications detailing human cases of cyanide poisoning by searching MEDLINE (via PubMed), the Cochrane Library, and the following Web of Science databases: the Core Collection, Biological Abstracts, KCI-Korean Journal Database, and the SciELO Citation Index. No limits were placed on language or publication year. The initial MEDLINE search strategy used was: ((((cyanides/toxicity[Mesh Terms]) OR cyanide toxi*)) OR (((Cyanides[mesh] OR "Cyanide" OR "Cyanides")) AND (toxicity[Subheading] OR toxi* OR toxic* OR ("poisoning"[Subheading] OR "poisoning"[MeSH Terms]) OR poison* OR))) OR cyanide poison*.

Study selection

The search in the selected databases resulted in 2976 publications, and initial removal of duplicates [JPV] yielded 2905 retrieved articles. We included case reports or case series implicating cyanide poisoning. We excluded non-English language articles, animal studies, medication assessments, plant studies and analyses, smoke inhalation, technical reports, and articles without laboratory data. Figure 1 depicts the flow chart of the systematic review search and selection of final articles.

Data extraction and analysis

For each case, we extracted and recorded data in a standard format and excluded any duplicate cases. Data included publication characteristics (case report versus series, year of publication), demographics (age, sex, race/ethnicity), and exposure characteristics (cyanide salt type, route, amount ingested, exposure reason, coingestants). We assessed acute signs and symptoms including level of consciousness (lethargic, unresponsive, normal), seizures, posturing, change in pupils, respiratory failure, vomiting, cardiac arrest, arrhythmias up to three time points, hypothermia, hypertension, hypotension, cherry red skin, presence of an odor, cyanosis, and death. We classified arrhythmias as asystole, atrial fibrillation, bradycardia, tachycardia, ventricular arrhythmia, or other. We also extracted data on medical management (supplemental oxygen, IVF, cyanide antidote kit, hydroxocobalamin, sodium thiosulfate, sodium bicarbonate, vasopressors, and intubation) and laboratory results (levels of lactic acidosis, anion gap, cyanide, and thiocyanate). For demographics, exposure and clinical characteristics, and medical management we used descriptive statistics including the frequencies and percentages for nominal data.

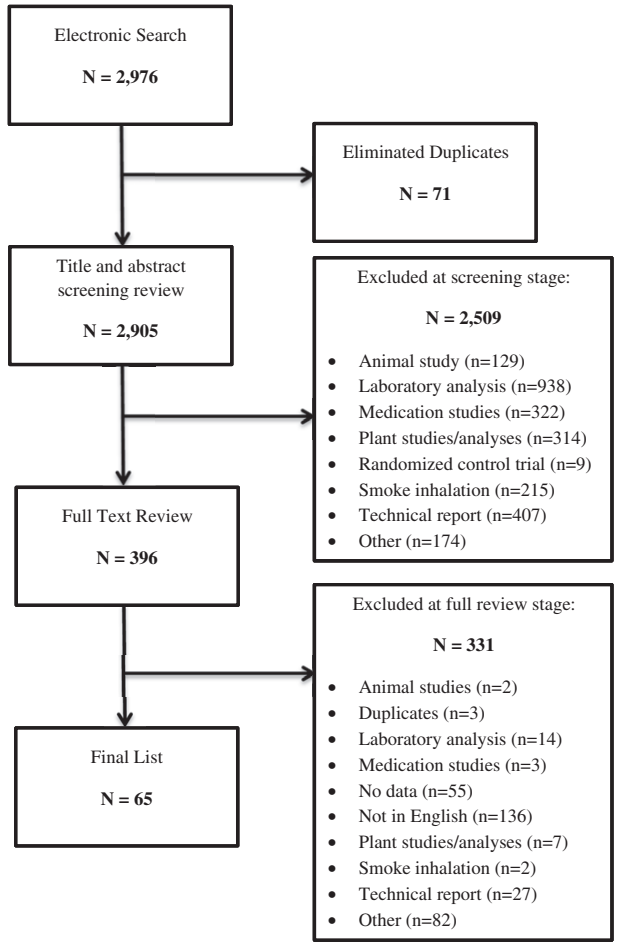

Figure 1. Systematic review search and selection flow chart.

Quality assessment

Two authors [J. P. C., J. R.] independently conducted title and abstract screening, full article review, and data extraction. We randomly selected a sub-sample of 30 cases for review by two reviewers prior to full stage review. This analysis demonstrated a strong inter-rater agreeability (Cohen's Kappa value: 0.98). A third reviewer [JPV] identified discrepancies, which a fourth reviewer [CPH] resolved.

Results

General characteristics

Publications and cases

There were 65 studies [3,20–83] (52 case reports, 13 case series) that met the study criteria (Table 1). The publication years covered approximately 48 years (from 1967 through 2015). The number of surviving cases, fatalities, and publications are presented in Figure 1. We identified 102 unique cases from these reports. Cases were predominantly males (72%) and often had unknown race/ethnicity (84%). The distribution of cases by age was: ≤5 (44%); 6–12 (0%); 13–19 (10%); 20–39 years (51%); 40–59 (28%); ≥60 (7%).

Exposure characteristics

Exposure characteristics and circumstances appear in Table 2. The majority of cases (91%) involved single agent exposures, of which approximately half involved potassium cyanide. Among polysubstance exposures, the other substances included ethanol, methanol, medications (e.g. acetaminophen, benzodiazepines, ephedrine, pseudoephedrine, fluoxetine), and others (e.g. gold, nitrobenzene, sodium arsenic). Among oral ingestions, less than one-quarter of cases reported estimates of amount ingested. Approximately two-thirds of cases were suspected suicide cases.

Clinical characteristics

Clinical characteristics of the patients appear in Table 3. Findings mentioned included unresponsiveness (78% of cases), respiratory failure (73%), hypotension (54%), arrhythmia (72%), cardiac arrest (20%), seizures (20%), cyanosis (15%), unusual or bitter almond odor (15%), and cherry red skin (11%).

There were 26 (26%) deaths identified among the studies. Most frequent presenting clinical characteristics of fatalities included: respiratory failure (96%), unresponsiveness (92%), hypotension (85%), cardiac arrest (58%), and bradycardia (43%). Not all reported deaths had clinical information available.

Medical management

The severity of clinical symptoms typically guided the intensity of medical intervention. Of the therapies reported, the majority of patients received supportive care with supplemental oxygen (79%) and intravenous fluids (66%). A substantial number of patients developed respiratory failure requiring intubation (66%) and refractory hypotension requiring vasopressor support (39%). Eighty-nine percentage of cases that died required intubation while 73% required hemodynamic support with vasopressors. The choice of antidote therapy was variable and most likely influenced by availability and approval for use. Overall, 20% received Cyanide Antidote Kit (amyl nitrite, sodium nitrate, and sodium thiosulfate), 29% received hydroxocobalamin, and 40% received sodium thiosulfate alone. Some patients received multiple antidotes. A summary of patient management and therapies provided appears in Table 4.

Limitations

This systematic review assessed the characteristics of all published case reports and case series of cyanide salt ingestions. As a result, the potential for publication bias exists as we are relying on select cases that may have been unique to be published. However, the purpose of this study was to identify reported signs and symptoms of cases, which may not be possible to extract from larger or more robust studies such as cohort studies or clinical trials. Limitations to our review include recall and reporting biases of the clinician's recollection of signs and symptoms. In addition, while this is the largest sample size of patients studied, the overall sample size of 102 remains low. Many of the effects assessed lacked consistent reporting among this heterogeneous collection of case reports and case series. Cutaneous assessment and odor are subjective findings influenced by the clinician's perception and prior experiences. Although the majority of cases were isolated cyanide salt ingestions, there were a few cases of co-ingestants, which may have affected findings and outcomes. Also, exclusion of non-English language cases or cases that were unobtainable may have prevented us from identifying pertinent findings in other languages within this topic.

Discussion

Of reported cases in the literature, very few described cutaneous signs. Only 11% of cases reported "cherry red skin." There were various descriptions of skin color, but only 15% reported cyanosis. Cyanide toxicity inhibits aerobic respiration by inhibition of cytochrome oxidase. Oxygen is not utilized in the tissues and venous oxygen content increases. Cyanide victims may lack classic cutaneous manifestations of "cherry red skin", and may appear to have an absence of expected cyanosis in the setting of hemodynamic collapse. In one case report, a family member commented on "how unusually good" the patient appeared even though he was unstable and unconscious [60]. Initial cutaneous findings depend upon the latency of ingestion of a cyanide salt: cases presenting later after ingestion were unresponsive for longer periods of time appearing more cyanotic, and earlier presentations report more normal cutaneous findings. Therefore, the absence or presence of cherry red skin is not a reliable indicator for cyanide toxicity.

Fifteen cases reported an odor with various descriptions. Seven cases directly describe the odor of bitter almonds on the breath [21,27,30,35,37,38,82]. Others described an "burned" [83], "unpleasant" [68], "ammonia-like" [31], "musty" [40], and "putrid" [55] odor. Very few cases state the absence of an odor. The majority of cases do not comment on the presence or absence of an odor. Based on these discrepancies, a clinician should not rely on the presence of a bitter almond odor to verify cyanide toxicity.

Table 1. Characteristics of included studies.

Citation	Title	Country	Gender	Age	Race/ethnicity	Exposure type	Death
Bain, 1967 [81]	Successful treatment of cyanide poisoning	UK	Male	61		Accidental	No
De Busk, 1969 [21]	Attempted Suicide by Cyanide	USA	Male	22	Caucasian	Suicide	No
			Female	24	Caucasian	Suicide	No
Mascarenhas, 1969 [22]	Cyanide poisoning, medical emergency	USA	Male	18	Caucasian	Suicide	No
Thomas, 1970 [23]	Accidental cyanide poisoning	UK	Male	19		Accidental	No
Juskowa, 1972 [24]	Electrocardiogram in Poisoning with Mercuric Oxycyanide	Poland	Female	26		Suicide	No
			Female	25		Suicide	No
Hillman. 1974 [79]	The use of dicobalt edetate (Kelocyanor) in cyanide poisoning	UK	Male	68		Accidental	Yes
Nagaratnam, 1974 [25]	Acute Renal Failure Following Potassium Ferrocyanide Poisoning Treated with Peritoneal Dialysis	Netherlands	Male	16		Suicide	No
Naughton, 1974 [83]	Acute cyanide poisoning	Australia	Male	35		Suicide	No
			Male	u		Suicide	No
Stewart, 1974 [26]	Cyanide Poisoning	USA	Male	22	Caucasian	Suicide	No
Buchanan, 1976 [27]	Abnormal Fundal Appearances in a Case of Poisoning by a Cyanide Capsule	UK	Male	23	Asian	Suicide	Yes
Graham, 1977 [28]	Acute Cyanide Poisoning Complicated by Lactic Acidosis and Pulmonary Edema	USA	Male	21		Suicide	No
Bryson, 1978 [29]	Cyanide Poisoning	UK	Male	48		Suicide	No
Nagler, 1978 [30]	Hydrogen Cyanide Poisoning: Treatment with Cobalt EDTA	Belgium	Male	42		Accidental	No
			Male	42		Accidental	No
			Male	46		Accidental	No
Peters, 1982 [31]	Acute Cyanoid Poisoning: The treatment of a suicide attempt	UK	Male	31		Suicide	No
Brivet, 1983 [32]	Acute Cyanide Poisoning: Recovery with Non-Specific Supportive Therapy	France	Male	43		Suicide	No
Litovitz, 1983 [33]	Cyanide Poisoning Treated with Hyperbaric Oxygen	USA	Female	23		Suicide	No
			Female	25		Suicide	Yes
Dodds, 1985 [82]	Cyanide toxicity after immersion and the hazards of dicobalt edetate	UK	Male	43		Other	No
Wesson, 1985 [34]	Treatment of Acute Cyanide Intoxication with Hemodialysis	USA	Male	59		Suicide	No
Wright IH, 1986 [35]	Acute Poisoning with Gold Cyanide	UK	Female	42		Suicide	Yes
Hall, 1987 [36]	Nitrite/Thiosulfate Treated Acute Cyanide Poisoning: Estimated Kinetics After Antidote	USA	Male	34		Suicide	No
Krieg, 1987 [37]	Cyanide Poisoning from Metal Cleaning Solutions	USA	Male	23	Asian	Accidental	No
			Female	3	Asian	Accidental	No
van Heijst, 1987 [38]	Therapeutic Problems in Cyanide Poisoning	Netherlands	Male	32		Suicide	No
			Male	23		Suicide	No
			Male	21		Suicide	Yes
Johnson, 1988 [39]	Arteriolization of Venous Blood Gases: A Clue to the Diagnosis of Cyanide Poisoning	USA	Male	30		Suicide	No
DiNapoli, 1989 [40]	Cyanide and Arsenic Poisoning by Intravenous Injection	USA	Male	29		Suicide	No
Johnson, 1989 [41]	Cyanide Poisoning Successfully Treated without 'Therapeutic Methemoglobin Levels'	USA	Female	24		Suicide	No
Rosenberg, 1989 [42]	Cyanide-Induced Parkinsonism: clinical, MRI, and 6-fluorodopa PET studies	USA	Male	46		Suicide	No
Schreiner, 1989 [43]	A near-fatal poisoning	USA	Male	42		Suicide	No
Singh, 1989 [80]	The metabolic effects of fatal cyanide poisoning	UK	Male	24		Accidental	Yes
El-Harasis, 1990 [44]	Collapse and Coma	USA	Female	40		Suicide	No
Binder, 1991 [45]	Poisonings in Laboratory Personnel and Health Care Professionals	USA	Female	34	Latin American	Suicide	No
CDC, 1991 [46]	Cyanide Poisonings Associated with Over-the-Counter Medication - Washington State, 1991	USA	Female	28		Homicide	No
			Female	40		Homicide	Yes
			Male	44		Homicide	Yes
Hantson, 1991 [47]	Successful Pancreas and Renal Transplantations from a Donor who died of Cyanide Poisoning	Belgium	Male	29		Other	Yes

(*continued*)

Table 1. Continued

Citation	Title	Country	Gender	Age	Race/ethnicity	Exposure type	Death
Barkoukis, 1992 [48]	Multiorgan Procurement from a Victim of Cyanide Poisoning	USA	Male	19		Suicide	Yes
Wananukul, 1992 [49]	Acute cyanide poisoning: Case report with Toxicokinetic Study	Thailand	Male	19		Accidental	No
Nakatani, 1993 [50]	Changes in the Parameters of Oxygen Metabolism in a Clinical Course Recovering from Potassium Cyanide	Japan	Male	31		Suicide	No
Swanson-Biearman, 1993 [51]	Successful donation and transplantation of multiple organs from a victim of cyanide poisoning	USA	Male	38		Suicide	Yes
Saincher, 1994 [52]	Cyanide Overdose: Survival with Fatal Blood Concentration without Antidotal Therapy	USA	Male	23		Suicide	No
Benaissa, 1995 [53]	Mercury Oxycyanide and Mercuric Cyanide Poisoning: Two Cases	France	Female	27		Suicide	Yes
			Male	14		Suicide	No
Baud, 1996 [20]	Relation between plasma lactate and blood cyanide concentrations in acute cyanide poisoning	France	Male	63		Suicide	Yes
Brueske, 1997 [54]	ED Management of Cyanide Poisoning	USA	Male	35		Accidental	No
Martin-Bermudez, 1997 [55]	Venous blood arteriolization and multiple organ failure after cyanide poisoning	Spain	Female	19		Other	No
Chin, 2000 [56]	Acute Cyanide Poisoning: A Case Report	USA	Female	19		Homicide	No
Kampe, 2000 [57]	Survival from a lethal blood concentration of cyanide associated with alcohol intoxication	Germany	Male	29		Suicide	No
Baud, 2002 [58]	Value of lactic acidosis in the assessment of the severity of acute cyanide poisoning	France	Male	38		Other	Yes
			Female	30		Other	Yes
			Male	52		Other	No
			Female	28		Other	No
			Male	26		Other	Yes
			Male	32		Other	No
			Female	53		Other	No
			Male	39		Other	No
			Male	44		Other	No
Mannaioni, 2002 [59]	Acute Cyanide Intoxication Treated with a Combination of Hydroxycobalamin, Sodium Nitrate, and Sodium Triosulfate	USA	Male	80		Accidental	No
Mutlu, 2002 [60]	An Unresponsive Biochemistry Professor in the Bathtub	USA	Male	83		Suicide	Yes
Dreykluft, 2004 [61]	Blue acid blues	Germany	Male	36		Suicide	No
Weng, 2004 [62]	Elevated Plasma Cyanide Level After Hydroxocobalamin Infusion for Cyanide Poisoning	USA	Male	51		Suicide	No
Prieto, 2005 [63]	Acute Cyanide Poisoning by Subcutaneous Injection	Spain	Female	30		Suicide	No
Peddy, 2006 [64]	Acute Cyanide Poisoning	USA	Male	17	Caucasian	Homicide	Yes
Borron, 2007 [65]	Hydroxocobalamin for Severe Acute Cyanide Poisoning by Ingestion or Inhalation	USA	Male	25		Suicide	No
			Male	51		Other	No
			Male	39		Suicide	Yes
			Male	22		Suicide	No
Hung, 2009 [66]	Cyanide Poisoning in Taiwan	Taiwan	Female	32		Other	No
Matsuoka, 2009 [67]	Lung Injury and Renal Failure Caused by Potassium Cyanide Poisoning	Japan	Male	54		Suicide	No
Coentrao, 2010 [68]	Hydroxocobalamin treatment of acute cyanide poisoning with a jewelry-cleaning solution	Portugal	Male	50		Suicide	No
Fortin, 2010 [69]	Hydroxocobalamin for Poisoning Caused by Ingestion of Potassium Cyanide: A Case Study	USA	Male	48		Suicide	No
Holstege, 2010 [3]	A Case of Cyanide Poisoning and the Use of Arterial Blood Gas Analysis to Direct Therapy	USA	Male	47		Suicide	Yes
Kon, 2010 [70]	Pink toes and red urine: What is the Poison	Hong Kong	Male	4		Accidental	No
Payen, 2010 [71]	Lethal Acute Poisoning with Potassium Ferrocyanide	USA	Male	56		Suicide	Yes
Sutter, 2010 [72]	Hemodialysis Complications of Hydroxocobalamin: A Case Report	USA	Female	34		Other	No

(*continued*)

Table 1. Continued

Citation	Title	Country	Gender	Age	Race/ethnicity	Exposure type	Death
Chen, 2011 [73]	Visual Loss Caused by Acute Cyanide Poisoning: A Case Report	USA	Male	30		Accidental	No
Coentrao, 2011 [74]	Acute cyanide poisoning among jewelry and textile industry workers	Portugal	Male	27		Suicide	No
			Female	3		Accidental	No
			Male	22		Suicide	No
			Male	33		Suicide	No
			Male	28		Suicide	No
			Female	50		Suicide	No
			Male	39		Suicide	No
			Male	52		Suicide	No
			Female	39		Suicide	No
Garlich, 2012 [75]	Poisoning and Suicide by Cyanide Jewelry Cleaner in the US Hmong Community: A case series	USA	Female	15	Asian	Suicide	Yes
			Female	72	Asian	Suicide	Yes
			Male	44	Asian	Accidental	Yes
			Female	41	Asian	Suicide	Yes
			Female	35	Asian	Suicide	Yes
			Female	43	Asian	Suicide	No
			Male	24	Asian	Suicide	No
Jethava, 2014 [76]	Acute Cyanide Intoxication: A Rare Case of Survival	India	Male	30		Accidental	No
Prochalska, 2014 [77]	Poisoning with gold potassium cyanide and other metallic cyanides in a jeweler	USA	Male	69		Accidental	No
Zakharov, 2015 [78]	Successful Use of Hydroxocobalamin and Sodium Triosulfate in Acute Cyanide Poisoning: A Case Report with Follow-up	Czech Republic	Male	58		Suicide	No

Table 2. Exposure characteristics.

Exposure characteristic	*n*	%
Cyanide salt type		
Sodium cyanide	10	9.8
Potassium cyanide	47	46.1
Other	45	44.1
Route		
Oral	86	84.3
Inhalational	8	7.8
Inhalational/dermal	1	1.0
IV	1	1.0
Oral and inhalational	1	1.0
Subcutaneous	1	1.0
Unknown	4	3.9
Most Frequent sources of exposure		
Electroplating factory	5	4.9
Jewelry cleaning, industry	17	16.7
Laboratory	18	17.6
Coin cleaner	3	2.9
Amount ingested (mg)[a]		
$\leq$399	1	1.1
400–800	6	6.9
800–1500	9	10.3
$>$1500	11	12.6
Unknown	60	69.0
Exposure reason		
Accidental	18	17.6
Homicide	5	4.9
Suicide	64	62.7
Other	15	14.7

[a]Oral exposures only.

Table 3. Clinical characteristics and outcomes.

	All		Deaths	
	n	%	*n*	%
Total	102	100.0	26	100.0
Consciousness				
Lethargic	5	4.9	1	3.8
Unresponsive	79	77.5	24	92.3
Normal	16	15.7	1	3.8
Unknown	2	2.0	0	0.0
Seizure				
Yes	20	19.6	1	3.8
No	36	35.3	22	84.6
Unknown	6	5.9	3	11.5
Posturing[a]				
Yes	9	8.8	4	15.4
No	36	35.3	7	26.9
Unknown	57	55.9	15	57.7
Respiratory failure				
Yes	74	72.5	25	96.2
No	28	27.5	1	3.8
Unknown	0	0.0	0	0.0
Vomiting				
Yes	24	23.5	2	7.7
No	28	27.5	6	23.1
Unknown	50	49.0	18	69.2
Cardiac arrest				
Yes	20	19.6	15	57.7
No	81	79.4	12	46.2
Unknown	1	1.0	1	3.8
Arrhythmias[b]				
Asystole	1	1.0	0	0.0
Atrial fibrillation	9	8.8	2	7.7
Bradycardia	17	16.7	11	42.3
Tachycardia	41	40.2	6	23.1
Ventricular arrhythmias	6	5.9	3	11.5
Other	19	18.6	13	50.0
Hypothermia				
Yes	6	5.9	5	19.2
No	18	17.6	1	3.8
Unknown	78	76.5	20	76.9

(*continued*)

Table 3. Continued

	All		Deaths	
	n	%	*n*	%
Hypertension				
Yes	8	7.8	0	0.0
No	72	70.6	20	76.9
Unknown	22	21.6	6	23.1
Hypotension				
Yes	55	53.9	22	84.6
No	39	38.2	2	7.7
Unknown	8	7.8	2	7.7
Cherry red skin				
Yes	11	10.8	5	19.2
No	35	34.3	4	15.4
Unknown	56	54.9	17	65.4
Cyanosis				
Yes	15	14.7	3	11.5
No	32	31.4	6	23.1
Unknown	55	53.9	17	65.4
Odor				
Yes	15	14.7	3	11.5
No	16	15.7	4	15.4
Unknown	71	69.6	19	73.1

[a]Decerebrate or decorticate posturing.
[b]Any documented, up to three documented when available for each patient.

Table 4. Management and therapies.

	Overall		Deaths	
	n	%	*n*	%
Total	102	100.0	26	100.0
Supplemental oxygen				
Yes	81	79.4	24	92.3
No	3	2.9	0	0.0
Unknown	18	17.6	2	7.7
IVF				
Yes	67	65.7	18	69.2
No	0	0.0	0	0.0
Unknown	35	34.3	8	30.8
Cyanide antidote kit				
Yes	20	19.6	3	11.5
No	79	77.5	21	80.8
Unknown	3	2.9	2	7.7
Hydroxocobalamin				
Yes	30	29.4	9	34.6
No	69	67.6	15	57.7
Unknown	3	2.9	2	7.7
Sodium thiosulfate				
Yes	41	40.2	13	50.0
No	58	56.9	11	42.3
Unknown	3	2.9	2	7.7
Sodium bicarbonate				
Yes	38	37.3	7	26.9
No	39	38.2	8	30.8
Unknown	25	24.5	11	42.3
Vasopressors				
Yes	40	39.2	19	73.1
No	49	48.0	2	7.7
Unknown	13	12.7	5	19.2
Intubation				
Yes	67	65.7	23	88.5
No	29	28.4	1	3.8
Unknown	6	5.9	2	7.7

No predominant arrhythmia was noted among cases of cyanide toxicity. The variable report of arrhythmias could be attributable from the latency between exposure and presentation to a healthcare facility. Victims most likely would have had a catecholamine surge that caused more tachydysrythmias earlier in toxicity, prior to myocardial depression. Whereas, cases with later presentations and sustained a prolonged hemodynamic collapse, were more likely present with bradycardia and hypotension. Fatalities undoubtedly presented with more dire findings such as hypotension, bradycardia, unresponsiveness, and respiratory failure. Reported arrhythmias with acute cyanide toxicity included: asystole, atrial fibrillation, bradycardia, tachycardia, and ventricular arrhythmias.

A few cases reported suspected amounts of cyanide ingested and cyanide or thiocyanate levels, but this is not a reliable marker to predict severity of toxicity or outcomes. Cyanide is volatile and dissipates rapidly in blood samples [20]. Only minute amounts of unmetabolized cyanide appear in urine [84]. Consequently, obtaining an accurate and clinically meaningful concentration at the time of treatment will not alter management.

Conclusion

The majority of cyanide salt cases did not report cherry red skin or odor bitter almonds. Neither the absence nor presence of these clinical signs should be relied upon for accurate diagnosis of cyanide toxicity. Overall, few cases reported specific cutaneous signs. Clinicians should keep a high level of suspicion for cyanide toxicity for an unresponsive, hemodynamically unstable patient with significant persistent lactic and metabolic acidosis, with potential access to cyanide salts. Vigilance in obtaining a history from pre-hospital personnel of the victim's environment can lead to an accurate diagnosis. Earlier diagnosis and delivery of an effective antidote can improve outcomes and increase chances of survival.

Disclosure statement

The authors report no declarations of interest

References

[1] Holstege C, Chapter 126: cyanide and hydrogen sulfide. In: Goldfran L, editor. Goldfrank's toxicologic emergencies. New York: McGraw HIll; 2015. p. 5039–5053.
[2] Peck MD. Structure fires, smoke production, and smoke alarms. J Burn Care Res. 2011;32:511–518.
[3] Holstege CP, Forrester JD, Borek HA, et al. A case of cyanide poisoning and the use of arterial blood gas analysis to direct therapy. Hosp Pract (1995). 2010;38:69–74.
[4] News C. Pa. medical researcher gets life for wife's cyanide death; [Cited 2016 Jun 24]. Available from: http://www.cbsnews.com/news/pennsylvania-medical-researcher-gets-life-for-wifes-cyanide-death/.
[5] Bronstein AC, Spyker DA, Cantilena LR Jr. 2007 annual report of the American association of poison control centers' national poison data system (NPDS): 25th annual report. Clin Toxicol. 2008;46:927–1057.
[6] Bronstein AC, Spyker DA, Cantilena LR Jr, et al. 2008 annual report of the American association of poison control centers' national poison data system (NPDS): 26th annual report. Clin Toxicol. 2009;47:911–1084.
[7] Bronstein AC, Spyker DA, Cantilena LR Jr, et al. 2009 annual report of the American association of poison control centers' national poison data system (NPDS): 27th annual report. Clin Toxicol. 2010;48:979–1178.

[8] Bronstein AC, Spyker DA, Cantilena LR Jr, et al. 2010 annual report of the American association of poison control centers' national poison data system (NPDS): 28th annual report. Clin Toxicol. 2011;49:910–941.
[9] Bronstein AC, Spyker DA, Cantilena LR Jr, et al. 2011 annual report of the American association of poison control centers' national poison data system (NPDS): 29th annual report. Clin Toxicol. 2012;50:911–1164.
[10] Mowry JB, Spyker DA, Cantilena LR Jr, et al. 2012 annual report of the American association of poison control centers' national poison data system (NPDS): 30th annual report. Clin Toxicol. 2013;51:949–1229.
[11] Mowry JB, Spyker DA, Cantilena LR Jr, et al. 2013 annual report of the American association of poison control centers' national poison data system (NPDS): 31st annual report. Clin Toxicol. 2014;52:1032–1283.
[12] Mowry JB, Spyker DA, Brooks DE, et al. 2014 annual report of the American association of poison control centers' national poison data system (NPDS): 32nd annual report. Clin Toxicol. 2015;53:962–1147.
[13] Bebarta VS, Pitotti RL, Borys DJ, et al. Seven years of cyanide ingestions in the USA: critically ill patients are common, but antidote use is not. Emerg Med J. 2011;28:155–158.
[14] Baud FJ. Cyanide: critical issues in diagnosis and treatment. Hum Exp Toxicol. 2007;26:191–201.
[15] Baud FJ, Barriot P, Toffis V. Elevated blood cyanide concentrations in victims of smoke inhalation. N Engl J Med. 1991;325: 1761–1766.
[16] Hall AH, Rumack BH. Clinical toxicology of cyanide. Ann Emerg Med. 1986;15:1067–1074.
[17] Gresham C, Industrial toxins. In: Tintinalli JE, Stapczynski JS, Ma OJ, et al. editors. Tintinalli's emergency medicine: a comprehensive guide. 8th ed. New York: The McGraw-Hill Companies; 2016.
[18] Gwilt JR. The odour of (potassium) cyanide. Med Leg J. 1961;29:98–99.
[19] Gill JR, Marker E, Stajic M. Suicide by cyanide: 17 deaths. J Forensic Sci. 2004;49:826–828.
[20] Baud FJ, Borron SW, Bavoux E, et al. Relation between plasma lactate and blood cyanide concentrations in acute cyanide poisoning. BMJ. 1996;312:26–27.
[21] De Busk RF, Seidl LG. Attempted suicide by cyanide. A report of two cases. Calif Med. 1969;110:394–396.
[22] Mascarenhas BR, Geller AC, Goodman AI. Cyanide poisoning, medical emergency. N Y State J Med. 1969;69:1782–1784.
[23] Thomas TA, Brooks JW. Accidental cyanide poisoning. Anaesthesia 1970;25:110–114.
[24] Juskowa J. Electrocardiogram in poisoning with mercuric oxycyanide. Pol Med J. 1972;11:297–303.
[25] Nagaratnam N, Alagaratnam K, Thambapillai AJ, et al. Acute renal failure following potassium ferrocyanide poisoning treated with peritoneal dialysis. Forensic Sci. 1974;4:87–89.
[26] Stewart R. Cyanide poisoning. Clin Toxicol. 1974;7:561–564.
[27] Buchanan IS, Dhamee MS, Griffiths FE, et al. Abnormal fundal appearances in a case of poisoning by a cyanide capsule. Med Sci Law. 1976;16:29–32.
[28] Graham DL, Laman D, Theodore J, et al. Acute cyanide poisoning complicated by lactic acidosis and pulmonary edema. Arch Intern Med. 1977;137:1051–1055.
[29] Edwards AC, Thomas ID. Cyanide poisoning. Lancet 1978;1:92–93.
[30] Nagler J, Provoost RA, Parizel G. Hydrogen cyanide poisoning: treatment with cobalt EDTA. J Occup Med. 1978;20:414–416.
[31] Peters CG, Mundy JV, Rayner PR. Acute cyanide poisoning: the treatment of a suicide attempt. Anaesthesia. 1982;37:582–586.
[32] Brivet F, Delfraissy JF, Duche M, et al. Acute cyanide poisoning: recovery with non-specific supportive therapy. Intensive Care Med. 1983;9:33–35.
[33] Litovitz TL, Larkin RF, Myers RA. Cyanide poisoning treated with hyperbaric oxygen. Am J Emerg Med. 1983;1:94–101.
[34] Wesson DE, Foley R, Sabatini S, et al. Treatment of acute cyanide intoxication with hemodialysis. Am J Nephrol. 1985;5:121–126.
[35] Wright IH, Vesey CJ. Acute poisoning with gold cyanide. Anaesthesia. 1986;41:936–939.
[36] Hall AH, Doutre WH, Ludden T, et al. Nitrite/thiosulfate treated acute cyanide poisoning: Estimated kinetics after antidote. J Toxicol Clin Toxicol. 1987;25:121–133.
[37] Krieg A, Saxena K. Cyanide poisoning from metal cleaning solutions. Ann Emerg Med. 1987;16:582–584.
[38] van Heijst ANP, Douz JMC, Van Kesteren RG, et al. Therapeutic problems in cyanide poisoning. J Toxicol Clin Toxicol. 1987;25: 383–398.
[39] Johnson RP, Mellors JW. Arteriolization of venous blood gases: a clue to the diagnosis of cyanide poisoning. J Emerg Med. 1988;6: 401–404.
[40] DiNapoli J, Hall AH, Drake R, et al. Cyanide and arsenic poisoning by intravenous injection. Ann Emerg Med. 1989;18:308–311.
[41] Johnson WS, Hall AH, Rumack BH. Cyanide poisoning successfully treated without 'therapeutic methemoglobin levels'. Am J Emerg Med. 1989;7:437–440.
[42] Rosenberg NL, Myers JA, Martin WR. Cyanide-induced parkinsonism: clinical, MRI, and 6-fluorodopa PET studies. Neurology. 1989;39:142–144.
[43] Schreiner RD, Morgan HJ. A near-fatal poisoning. J Tenn Med Assoc. 1989;82:138.
[44] el-Harasis A, Panlasigui L, Lee M. Collapse and coma. Hosp Pract (off Ed). 1990;25:16–17.
[45] Binder L, Fredrickson L. Poisonings in laboratory personnel and health care professionals. Am J Emerg Med. 1991;9:11–15.
[46] Centers for Disease Control (CDC). Cyanide poisonings associated with over-the-counter medication–Washington state, 1991. MMWR Morb Mortal Wkly Rep. 1991;40:161, 167–168.
[47] Hantson P, Squifflet JP, Vekemans MC, et al. Successful pancreas and renal transplantations from a donor who died of cyanide poisoning. Clin Transplant. 1991;5:419–421.
[48] Barkoukis TJ, Sarbak CA, Lewis D, et al. Multiorgan procurement from a victim of cyanide poisoning. A case report and review of the literature. Transplantation. 1993;55:1434–1436.
[49] Wananukul W, Kaojarern S. Acute cyanide poisoning: a case report with toxicokinetic study. J Med Assoc Thai. 1992;75: 304–309.
[50] Nakatani T, Kosugi Y, Mori A, et al. Changes in the parameters of oxygen metabolism in a clinical course recovering from potassium cyanide. Am J Emerg Med. 1993;11:213–217.
[51] Swanson-Biearman B, Krenzelok EP, Snyder JW, et al. Successful donation and transplantation of multiple organs from a victim of cyanide poisoning. J Toxicol Clin Toxicol. 1993;31:95–99.
[52] Saincher A, Swirsky N, Tenenbein M. Cyanide overdose: Survival with fatal blood concentration without antidotal therapy. J Emerg Med. 1994;12:555–557.
[53] Benaissa ML, Hantson P, Bismuth C, et al. Mercury oxycyanide and mercuric cyanide poisoning: two cases. Intensive Care Med. 1995;21:1051–1053.
[54] Brueske PJ. ED management of cyanide poisoning. J Emerg Nurs. 1997;23:569–573.
[55] Martin-Bermudez R, Maestre-Romero A, Goni-Belzunegui MV, et al. Venous blood arteriolization and multiple organ failure after cyanide poisoning. Intensive Care Med. 1997;23:1286.
[56] Chin RG, Calderon Y. Acute cyanide poisoning: a case report. J Emerg Med. 2000;18:441–445.
[57] Kampe S, Iffland R, Korenkov M, et al. Survival from a lethal blood concentration of cyanide with associated alcohol intoxication. Anaesthesia. 2000;55:1189–1191.
[58] Baud FJ, Borron SW, Megarbane B, et al. Value of lactic acidosis in the assessment of the severity of acute cyanide poisoning. Crit Care Med. 2002;30:2044–2050.
[59] Mannaioni G, Vannacci A, Marzocca C, et al. Acute cyanide intoxication treated with a combination of hydroxycobalamin, sodium nitrite, and sodium thiosulfate. J Toxicol Clin Toxicol. 2002; 40:181–183.

[60] Mutlu GM, Leikin JB, Oh K, et al. An unresponsive biochemistry professor in the bathtub. Chest. 2002;122:1073–1076.
[61] Dreykluft T, Gobel U, Taveira O, et al. Blue acid blues. Nephrol Dial Transplant. 2004;19:2668–2671.
[62] Weng TI, Fang CC, Lin SM, et al. Elevated plasma cyanide level after hydroxocobalamin infusion for cyanide poisoning. Am J Emerg Med. 2004;22:492–493.
[63] Prieto I, Pujol I, Santiuste C, et al. Acute cyanide poisoning by subcutaneous injection. Emerg Med J. 2005;22:389–390.
[64] Peddy SB, Rigby MR, Shaffner DH. Acute cyanide poisoning. Pediatr Crit Care Med. 2006;7:79–82.
[65] Borron SW, Baud FJ, Megarbane B, et al. Hydroxocobalamin for severe acute cyanide poisoning by ingestion or inhalation. Am J Emerg Med. 2007;25:551–558.
[66] Hung DZ, Tsan YT, Yu YJ, et al. Cyanide poisoning in Taiwan. Lancet. 2009;374:1212.
[67] Matsuoka Y, Yasuda M, Hashizume M. Lung injury and renal failure caused by potassium cyanide poisoning. BMJ Case Rep. 2009;2009:bcr04.2009.1768.
[68] Coentrao L, Neves A, Moura D. Hydroxocobalamin treatment of acute cyanide poisoning with a jewellery-cleaning solution. BMJ Case Rep. 2010;2010:bcr01.2010.2603.
[69] Fortin JL, Waroux S, Giocanti JP, et al. Hydroxocobalamin for poisoning caused by ingestion of potassium cyanide: a case study. J Emerg Med. 2010;39:320–324.
[70] Hon KL, Cheung KL. Pink toes and red urine: what is this poison?. Hong Kong Med J. 2010;16:411–412.
[71] Payen C, Combe C, Le Meur C, et al. Lethal acute poisoning with potassium ferrocyanide. Am J Emerg Med. 2010;28:642.e3–642.e5.
[72] Sutter M, Tereshchenko N, Rafii R, et al. Hemodialysis complications of hydroxocobalamin: a case report. J Med Toxicol. 2010;6:165–167.
[73] Chen F, Jiang L, Yang B. Visual loss caused by acute cyanide poisoning: a case report. Clin Toxicol. 2011;49:121–123.
[74] Coentrao L, Moura D. Acute cyanide poisoning among jewelry and textile industry workers. Am J Emerg Med. 2011; 29:78–81.
[75] Garlich FM, Alsop JA, Anderson DL, et al. Poisoning and suicide by cyanide jewelry cleaner in the US Hmong community: a case series. Clin Toxicol. 2012;50:136–140.
[76] Jethava D, Gupta P, Kothari S, et al. Acute cyanide intoxication: a rare case of survival. Indian J Anaesth. 2014;58: 312–314.
[77] Prochalska C, Megarbane B, El Balkhi S, et al. Poisoning with gold potassium cyanide and other metallic cyanides in a jeweler. Clin Toxicol. 2014;52:907–908.
[78] Zakharov S, Vaneckova M, Seidl Z, et al. Successful use of hydroxocobalamin and sodium thiosulfate in acute cyanide poisoning: a case report with follow-up. Basic Clin Pharmacol Toxicol. 2015;117:209–212.
[79] Hillman B, Bardhan KD, Bain JTB. The use of dicobalt edetate (Kelocyanor) in cyanide poisoning. Postgrad Med J. 1974; 50:171–174.
[80] Singh BM, Coles N, Lewis P, et al. The metabolic effects of fatal cyanide poisoning. Postgrad Med J. 1989;65:923–925.
[81] Bain JTB, Knowles EL. Successful treatment of cyanide poisoning. Br Med J. 1967;2:763.
[82] Dodds C, McKnight C. Cyanide toxicity after immersion and the hazards of dicobalt edetate. Br Med J (Clin Res Ed). BMJ 1985;291:785–786.
[83] Naughton M. Acute cyanide poisoning. Anaesth Intensive Care. 1974;2:351–356.
[84] Nelson L. Acute cyanide toxicity: mechanisms and manifestations. J Emerg Nurs. 2006;32:S8–S11.