Chemical Emergency Medical Guideline

Information and recommendations for medical personnel

Aminonitrile

CAS No.: 13893-53-3

GHS symbols:

GHS06
Acute toxicity

Signal word: Danger

Hazard statements:

H301+H311+H331 Toxic if swallowed, in contact with skin or if inhaled.

Overview

- Before the paramedic/emergency doctor on site approaches a patient, who has been or is exposed to acrylonitrile, it must be ensured that there is no danger to themselves from acrylonitrile. Acrylonitrile contains free cyanide (hydrogen cyanide or prussic acid) and can cause acute poisoning.
- There is no relevant danger from contact with patients who have only been exposed to aminonitrile vapors. However, a patient who is wet with liquids containing aminonitrile, or whose clothing is wet with such liquids, may endanger other people through direct contact or through evaporating aminonitrile. Immediate cleaning of the skin and hair with water is crucial.
- Aminonitrile poisoning can be fatal within minutes. If the presence of aminonitrile-containing material is suspected and there are signs of severe oxygen deficiency, aminonitrile poisoning should be assumed, even if no blue-red discoloration of the skin and mucous membranes is visible.
- If aminonitrile poisoning is suspected, immediate administration of pure oxygen is crucial. If the patient shows signs of poisoning, the recommended antidotes (4-DMAP) should be administered.

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1. Information on the substance

2-Amino-2,3-dimethylbutyronitrile, (CAS 13893-53-3)
Synonym: Aminonitrile
The composition is as follows: 2-amino-2,3-dimethylbutyronitrile (~ 80%) CAS 13893-53-3 and toluene (~ 20%). The liquid is colorless to yellowish brown, oily and has a musty smell of toluene. Under normal conditions, a small proportion decomposes into free cyanide (HCN), both in the pure liquid and in the non-reactive toluene-containing solution. Hydrogen cyanide is in equilibrium with 2-amino-2,3-dimethylbutyronitrile and can be easily expelled by heating 2-amino-2,3-dimethylbutyronitrile. Significant amounts of hydrogen cyanide are produced during the thermal decomposition of 2-amino-2,3-dimethylbutyronitrile. In the body, metabolic breakdown of 2-amino-2,3-dimethylbutyronitrile can form cyanides, which lead to cyanide poisoning. The smell of cyanide does not provide sufficient warning of dangerous exposure. The solvent toluene is flammable.

2. Exposition

2.1. Inhalation

Gaseous amine nitrile is rapidly absorbed through the lungs. Intensive exposure to respirable toluene can cause severe irritation of the lungs.

2.2. Skin/eye contact

Aminonitrile is rapidly absorbed through the skin and mucous membranes, causing general poisoning. Although the onset of poisoning symptoms may be slightly delayed in the case of skin exposure, a potentially lethal dose is possible even if only a very small area of skin is contaminated with aminonitrile. Exposure to aminonitrile may cause mild skin and eye irritation.

2.3. Ingestion

Accidental ingestion of aminonitrile is unlikely. Aminonitrile is immediately absorbed in the gastrointestinal tract. Ingestion can lead to serious poisoning.

3. Acute health effects

Initial symptoms may include skin redness, rapid pulse, shortness of breath, headache and dizziness. This may eventually lead to agitation, immobility, unconsciousness, respiratory arrest, seizures, slow pulse, drop in blood pressure and death. Aminonitrile can lead to cyanide poisoning. The cyanide ion binds to the trivalent iron of mitochondrial cytochrome oxidase C, thereby inhibiting oxidative phosphorylation and ATP production. The cellular oxygen deficiency and inhibition of cellular oxidation processes result in increased anaerobic glycolysis, which then leads to lactic acidosis.

3.1. Central nervous system

Central nervous system disorders and symptoms generally develop very quickly. Initially, there are often non-specific symptoms, e.g. agitation, dizziness, nausea, vomiting and headaches. Eventually, this can lead to impaired consciousness, respiratory paralysis, seizures and coma.

3.2. Cardiovascular system

Severe poisoning can cause cardiac arrhythmia. Elevated blood pressure and heart rate may occur temporarily immediately after exposure, followed by bradycardia and low, barely measurable blood pressure and cardiovascular arrest.

3.3. Acid-base status

In severe poisoning, elevated lactic acid levels in the blood can lead to an anion gap and thus to metabolic acidosis.

3.4. Respiratory

Shortness of breath and tightness in the chest may occur even at the onset of systemic poisoning. The respiratory rate has increased, and breathing has deepened. As the poisoning progresses, breathing may become slow and difficult. Cyanosis may occur, but is not necessarily present, as cyanide blocks oxygen utilization in the respiratory chain and not oxygen transport by the erythrocytes.

3.5. Skin contact

Skin contact may cause irritation. As acrylonitrile is readily absorbed through the skin, systemic toxic effects are possible.

3.6. Eye contact

If liquids containing acrylonitrile come into contact with the eyes, irritation and swelling may occur. Acrylonitrile is also rapidly absorbed into the body in this way.

3.7. Oral ingestion

A burning sensation in the mouth and throat has been reported. Smell or taste of bitter almonds, but only about 50% of people can perceive this due to genetic factors. Aminonitrile is absorbed very quickly into the body when ingested.

3.8. Possible consequences

Survivors of life-threatening exposure should be monitored for possible cerebral or cardiac damage. These patients have an increased risk of central nervous system disorders, including memory loss or Parkinson's syndrome; clinical follow-up examinations should continue for several weeks to months after exposure.

4. Measures

4.1. Self-protection of first aiders

If there is suspicion that the area the helper must enter contains acrylonitrile, a self-contained breathing apparatus and a chemical protection suit must be worn. Contaminated equipment must not be used. A patient who is wet with liquids containing acrylonitrile, or whose clothing is wet with such liquids, may endanger other people through direct contact or through cyanide gas emissions. Acrylonitrile is present in a toluene solution, so the precautions for handling flammable liquids must be strictly observed.

4.2. Rescue

Patients should be removed from the danger zone immediately. If they are unable to walk unaided, they should be removed from the danger zone quickly using appropriate means, taking care to protect themselves. The "A, B, C procedure" then has absolute priority.

A) Clear the airways (check for blockages caused by the tongue or foreign objects)
B) Ventilation (check the patient's breathing, if necessary, begin ventilation with adequate self-protection, e.g. breathing mask)
C) Circulation (begin resuscitation for any person who does not respond to verbal commands and is not breathing normally)

"CRASH" decontamination

- Rescue patients contaminated with acrylonitrile who are unconscious or unable to move (critically ill/injured patients according to the ABCDE scheme) from the immediate danger zone, taking care to protect yourself with suitable personal protective equipment.
- If necessary, perform emergency measures ("basic life support"; e.g. bleeding control using tourniquets, chest compressions, etc.)
- At a suitable location outside the danger zone, completely undress the contaminated patient using an emergency rescue knife, taking care to protect yourself (duration: approx. 1 minute).
- Shower/rinse with plenty of water (duration: approx. 1 minute).
- Transfer to a clean stretcher. Ensure body heat is maintained. Transport/handover to the emergency services/emergency doctor (duration: approx. 1 minute).

4.3. Cleaning

Patients suspected of having contact with cyanide-containing solutions such as aminonitrile must undergo mandatory decontamination. When cleaning persons or objects, the recommended protective measures should be observed, e.g. butyl rubber or Viton® gloves, safety goggles, etc. Equipment used should be cleaned thoroughly (e.g. with 5.25% hypochlorite).
If possible, patients should assist in their own cleaning. Contaminated clothing should be removed as quickly as possible, securely wrapped and disposed of, while affected skin and hair areas should be rinsed with water for 15 minutes. This should be followed by further cleaning with soap and water. The patient's eyes should be protected during the cleaning of skin and hair areas.
Exposed or irritated eyes should be rinsed with water or neutral saline solution for 15 minutes. Eye rinsing should be continued during other emergency measures or transport. Contact lenses should be removed, if possible, without additional risk to the eye.

4.4. Initial treatment (preclinical or clinical)

Speed is crucial. If the patient shows signs of poisoning, they should be treated with 100% oxygen until specific antidotes are available. Treatment should be carried out simultaneously with cleaning. If available, amyl nitrite beads can be used until intravenous treatment can be started (see below).

If swallowed, do not induce vomiting under any circumstances.

Patients who are conscious and able to swallow should receive 50 g of activated charcoal (or 1 g/kg body weight for children weighing up to 50 kg) within two hours of exposure. Repeated administration of activated charcoal is possible at any time to complete decontamination if there are signs or suspicion of ongoing absorption.
For multiple doses, start with the single-dose amount mentioned above, followed by the same dose every four hours or half the dose every two hours. Avoid inhaling the product.

If possible, administer activated charcoal immediately. Avoid inhalation of the product. Isolate gastric lavage fluid and vomit, as they may release cyanide.
In case of respiratory insufficiency, perform endotracheal intubation or alternative airway management. If this is not feasible, perform coniotomy if necessary.

4.5. Antidote treatment

Critical or unconscious patients with known or highly probable amine nitrile poisoning should be treated with antidotes by emergency medical services. If symptoms occur, immediate intravenous treatment should be started, e.g. after relevant skin contamination.
The availability of antidotes may vary from country to country due to legal regulations or ordinances. The attending emergency physician should be informed whether and, if so, which antidotes have already been administered.

Antidote treatment is usually divided into two steps:

Methemoglobin agents (4-dimethylaminophenol = 4-DMAP or amyl and/or sodium nitrite) for rapid elimination of cyanide from the affected enzymes of the respiratory chain, followed by an active ingredient

to form less harmful compounds with cyanide and their excretion (sodium thiosulphate).

Use of 4-dimethylaminophenol = 4-DMAP or amyl and/or sodium nitrite only in cases of high suspicion of cyanide poisoning. These antidotes must not be used in cases of smoke inhalation poisoning with simultaneous release of cyanides, as methemoglobin formation would further reduce oxygen transport capacity in addition to carboxyhemoglobinemia.

An alternative antidote is hydroxocobalamin (=vitamin B12). The intravenous dose for an adult is 5g in 100 ml of saline solution (hydroxycobalamine 70mg/kg body weight). A second and third dose, but not more than 15 g in total, may be considered if available, especially in cases of persistent cardiovascular failure. However, in cases of severe cyanide poisoning, the binding capacity of a standard dose of hydroxycobalamine is insufficient. In such cases, the use of 4-DMAP is preferable.

Step 1:
Note: In some countries, 0.2-0.4ml amyl nitrite inhalation ampoules (pearls) are available, the use of which is recommended until intravenous treatment can be started. The patient should be lying down during administration, as nitrite lowers blood pressure. The contents of the amyl nitrite bead should be placed in a cloth and held close to the patient's nose for 15-30 seconds. Oxygen should then be administered for 15-30 seconds. The administration of amyl nitrite and oxygen is repeated alternately. A new bead should be used every three minutes.

If 4-dimethylaminophenol (4-DMAP) is available, inject 4-DMAP intravenously immediately. Normally, a dose of 1 ampoule containing 250mg of 4-DMAP is sufficient in adults to achieve a therapeutic methemoglobin level (target methemoglobin level approx. 30-40%).

If 4-DMAP is not available, sodium nitrite should be administered intravenously immediately. The patient should be lying down during administration, as nitrite lowers blood pressure. The usual adult dose is 300mg (10ml of a 3% solution) and should be administered over at least 5 minutes (2–4ml/minute). The solution can be mixed with 50-100ml of saline solution. A dose of sodium nitrite (300mg) should not increase the methemoglobin level above 30-40%. Blood pressure must be monitored closely and the infusion rate reduced if a drop in blood pressure becomes apparent. A drop in blood pressure should be treated with a volume of 10-20ml/kg body weight of saline solution, and the patient should be placed in shock position. In the event of clinical shock, the administration of adrenergic substances should be considered.

Step 2: After administering 4-DMAP or sodium nitrite, sodium thiosulphate should be infused over a period of 10 minutes. The adult dose of sodium thiosulphate is 100mg/kg body weight.

Methemoglobinemia should only be treated if 4-DMAP or nitrite has been overdosed, or the diagnosis of cyanide poisoning has been revised. If signs/symptoms of poisoning persist or recur, the administration of sodium thiosulphate should be repeated one hour later at 50% of the initial dose. In the event of seizures, 5 mg of diazepam or alternative benzodiazepines may be administered intravenously.
All patients should/must be transported to a hospital with intensive care facilities.

Sodium thiosulphate can also be administered to symptomatic, non-critical and non-unconscious patients with suspected cyanide poisoning. However, it should be noted that patients without impaired consciousness should not receive either 4-DMAP or sodium nitrite.

4.6. Further procedure and treatment

In addition to medical history, physical examination and vital signs, arterial blood gases, hemoglobin and methemoglobin levels, venous oxygen content and cyanide blood levels should be determined. A chest X-ray should also be performed.
After treatment with 4-DMAP or sodium nitrite, serum methemoglobin levels should be monitored. A methemoglobin level of 30-40% should not be exceeded if there is no anemia.
Signs of cyanosis occur at methemoglobin concentrations of approximately 15% or higher. In case of overdose or incorrect use of the methemoglobin-forming agent, methemoglobinemia must be treated. Methylene blue or toluidine blue are available as specific antidotes. All patients who have been treated with systemic antidotes for amine nitrile poisoning/exposure must remain in intensive care for at least 24 hours.

4.7. Laboratory tests

The diagnosis of aminonitrile poisoning is based primarily on the clinical picture, with rapidly onset central nervous and cardiopulmonary symptoms, as well as known or suspected very probable aminonitrile exposure. Laboratory tests are useful for monitoring the course of poisoning and early detection of complications. Routine laboratory tests should include complete blood count, glucose and electrolytes. After treatment with 4-DMAP or sodium nitrite, methemoglobin levels must be monitored closely.

Arterial blood gas concentrations should be determined to assess acid-base status, oxygen saturation and oxygen uptake. Pulse oximetry is not sufficient. Additional tests include ECG monitoring and serum lactate determination.

Metabolic acidosis should be treated with bicarbonate if the blood pH falls below 7.15. Care should be taken to ensure the timely detection and treatment of electrolyte imbalances (e.g. hyperkaliemia, hypercalcemia).

4.8. Discharge of the patient / instructions for further rules of conduct

Patients who show unremarkable clinical examination findings and no signs of toxic effects after an appropriate follow-up after or had only a minor exposure to aminonitrile and have not received any antidotes may be discharged under the following circumstances:

- Information and recommendations for patients with instructions for further action were provided verbally and in writing. The patient was instructed to seek immediate medical attention if any health problems arise.
- The patient is aware of and understands the toxic effects of amine nitriles and the instructions given for further rules of conduct.
- The attending physician has been informed that regular contact between the patient and the physician is possible in the following 24 hours.
- Heavy physical work should not be carried out in the following 24 hours.
- Do not smoke and avoid cigarette smoke for at least 72 hours; smoke can impair lung function.

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Contact	ESG/CH: Dr. M. Conzelmann, T. Schröck ESG/AS: Dr. D. Frambach

BASF SE
Corporate Health Management
Carl-Bosch-Straße 38
67056 Ludwigshafen
Germany