Chemical Emergency Medical Guideline

Information and recommendations for healthcare professionals

N-Methylpyrrolidone

CAS No.: 872-50-4

GHS symbols:

GHS07
Acute toxicity

GHS08
Health hazard

Signal word: Danger

Hazard statements:

H315	Causes skin irritation.
H319	Causes serious eye irritation.
H335	May cause respiratory irritation.
H360D	May damage the unborn child.

Overview

- There is no danger from contact with patients who have only been exposed to N-Methylpyrrolidone vapors. A patient who is wet with liquid N-Methylpyrrolidone (boiling point 202°C) or whose clothing is wet with it may endanger other people through direct contact or through N-Methylpyrrolidone vapours.
- N-Methylpyrrolidone irritates the skin, eyes and respiratory tract and can lead to general health problems.
- There is no known specific antidote. Treatment depends on the extent of exposure and the symptoms.

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1. Information on the substance

N-Methylpyrrolidone (C_5H_9NO), CAS 872-50-4
Synonyms: N-Methylpyrrolidione, 1-methyl-2-pyrrolidone, NMP.
N-Methylpyrrolidone is a clear, colorless liquid at room temperature (boiling point 202°C). The liquid is highly flammable. N-Methylpyrrolidone has an amine-like odor. It is miscible with water and organic solvents. Combustion produces carbon monoxide and nitrogen oxides.
N-Methylpyrrolidone is a low-volatility organic solvent for resins in the microelectronics and pharmaceutical industries. It can replace other solvents in paint strippers and lubricant extraction and be used as a solvent for pesticides, paints, adhesives and plastics.

2. Exposition

2.1. Inhalation

Exposure to N-Methylpyrrolidone occurs mainly through inhalation. N-Methylpyrrolidone is rapidly absorbed through the lungs.

2.2. Skin/eye contact

N-Methylpyrrolidone can be rapidly absorbed through the skin.

2.3. Ingestion

N-Methylpyrrolidone is absorbed through the gastrointestinal tract. However, ingestion is rare in the workplace. If swallowed, it can enter the respiratory tract.

3. Acute health effects

3.1. Dose-response relationship

N-Methylpyrrolidone concentration		Effect
10 ppm	-	OEL (European Union)
20 ppm	-	TLV-STEL
20 ppm	-	Occupational exposure limit (AGS, Germany)
40 ppm	-	Short-term value (Germany)

OEL: Occupational Exposure Limit
TLV-STEL: Threshold Limit Value-Short-Term Exposure Limit → Average concentration over 15 minutes to which workers may be exposed up to four times per day with at least 60 minutes between successive exposures without adverse health effects.
Occupational exposure limit AGW: According to the Hazardous Substances Ordinance, the occupational exposure limit (AGW) is the limit value for the time-weighted average concentration of a substance in the air at the workplace in relation to a given reference period. It specifies the concentration of a substance at which acute or chronic adverse health effects are generally not to be expected.
AGS: Committee for Hazardous Substances

3.2. Systemic effects

High concentrations can lead to general symptoms of poisoning such as headaches, nausea and dizziness. Disorders of the central nervous system and functional disorders of the liver and kidneys may occur, as well as changes in blood count.

3.3. Respiratory tract

N-Methylpyrrolidone irritates the upper respiratory tract.

3.4. Skin

Local exposure to liquid N-Methylpyrrolidone can cause skin irritation. Prolonged or chronic exposure can cause burning, redness, inflammation and blistering of the skin.

3.5. Eyes

Local exposure to liquid N-Methylpyrrolidone or high vapor concentrations may cause eye irritation with redness, burning, tearing or spasmodic eyelid closure.

3.6. Possible consequences

If the patient survives 48 hours after exposure, further improvement in symptoms can be expected. After acute exposure, lung function usually returns to normal within 7 to 14 days. Complete recovery is usually achieved. Increased sensitivity to irritants may persist and cause bronchospasm or chronic bronchitis. Such "reactive airways dysfunction syndrome" (RADS) may persist for several years. Destruction of lung tissue or scarring can lead to chronic dilation of the bronchi and increased susceptibility to infection.

4. Measures

4.1. Self-protection of first aiders

If there is a suspicion that the area the helper must enter contains N-Methylpyrrolidone, a self-contained breathing apparatus and a chemical protection suit must be worn.
There is no danger from contact with patients who have only been exposed to N-Methylpyrrolidone vapors. A patient who is wet with liquid N-Methylpyrrolidone or whose clothing is wet with it may endanger other people through direct contact or through evaporating N-Methylpyrrolidone.

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" has absolute priority in this case.

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)

4.3. Cleaning

Patients who have only been exposed to N-Methylpyrrolidone vapors and show no signs of skin or eye irritation do not require any special cleaning measures, unlike all others. If possible, patients should assist in cleaning themselves. If liquid N-Methylpyrrolidone has been exposed and clothing is contaminated, it must be removed and securely wrapped.
In the event of exposure to N-Methylpyrrolidone, rinse the eyes with water or neutral saline solution for at least 15 minutes. Remove any contact lenses, if possible, without causing additional danger to the eye. Other important first aid measures must be continued during this time.
Rinse affected skin and hair with water for at least 15 minutes. Other important first aid measures must be continued during this time. Protect eyes while rinsing.

Rinse mouth and then administer 200ml-300ml of water for dilution if the patient is conscious and responsive. Do not induce vomiting; this may cause irritation of the esophagus and aspiration. Patients who are conscious and able to swallow should be given 30g of activated charcoal with 240ml of water as soon as possible.

4.4. Estimation of inhaled dose

Patients with an exposure concentration of 100ppm or more (depending on the duration of exposure) and patients for whom no exposure can be estimated but for whom relevant exposure is likely should be transported immediately to a hospital with intensive care facilities.

4.5. Initial treatment (preclinical or clinical)

Empirical therapy; no specific antidote available.
The following measures are recommended if the N-Methylpyrrolidone concentration is 100ppm or more (depending on the duration of exposure), symptoms are present (e.g. irritation of the eyes or upper respiratory tract) or if no concentration can be estimated but exposure is very likely:

- Oxygen administration
- Administration of 8 sprays of beclomethasone (800µg beclomethasone dipropionate) from a metered dose inhaler.

If there are signs of airway constriction (e.g. bronchospasm or stridor)

- Nebulization of adrenalin (epinephrine): mix 2mg adrenalin (2ml) with 3ml NaCl 0.9% and administer via a nebulizer mask
- Administration of a $ß_2$ -selective adrenoceptor agonist, e.g. four puffs of terbutaline or salbutamol or fenoterol (one puff usually contains 0.25mg terbutaline sulphate; or 0.1mg salbutamol; or 0.2mg fenoterol); this can be repeated once after 10 minutes.

Alternatively, 2.5mg salbutamol and 0.5mg ipratropium bromide can be administered via a nebulizer mask.
If inhalation is not possible, administer terbutaline sulphate (0.25mg to 0.5mg) subcutaneously or salbutamol (0.2mg to 0.4mg over 15 minutes) intravenously.
Intravenous administration of 250mg methylprednisolone (or an equivalent steroid dose).

If there are signs of toxic pulmonary oedema (e.g. frothy sputum, moist rales)

- CPAP therapy
- Intravenous administration of 1000mg methylprednisolone (or an equivalent steroid dose)
  In case of (increasing) respiratory insufficiency, advanced airway management, e.g. endotracheal intubation or, if necessary, coniotomy.

Note: The efficacy of corticosteroid administration has not yet been proven in controlled clinical trials.

Skin contact with liquid N-Methylpyrrolidone may cause skin irritation; this should be treated as a burn.
Exposure to the eyes may also cause irritation; this should also be treated as a burn. Consult an ophthalmologist.

Note: Any contact with liquid N-Methylpyrrolidone in the facial area can have serious consequences.

The diagnosis of N-Methylpyrrolidone intoxication is based primarily on the clinical signs of upper respiratory tract and skin irritation, together with probable exposure to or contact with N-Methylpyrrolidone. Biomonitoring with determination of the 5-hydroxy-N-Methylpyrrolidone concentration in urine can be performed to estimate the systemic dose absorbed after exposure.

4.6. Further procedure and treatment

In addition to taking medical history, performing a physical examination and checking vital signs, spirometry should be performed. Laboratory tests may be performed to monitor and assess complications. Blood count, glucose and electrolytes should be determined routinely.

4.7. Biomonitoring

To assess the systemic dose absorbed after exposure, biomonitoring can be performed by determining the concentration of 5-hydroxy-N-Methyl-2-pyrrolidone (5-HNMP) in urine.

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

Clinically asymptomatic patients who have been exposed to an N-Methylpyrrolidone concentration of less than 40ppm (depending on the duration of exposure) and who show no abnormal clinical findings and no signs of toxic effects after an appropriate follow-up period 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 advised to seek immediate medical attention if any health problems arise.
- The patient is aware of and understands the toxic effects of N-Methylpyrrolidone.
- The attending physician has been informed that regular contact between the patient and the physician is possible in the following 24 hours.
- Drinking alcohol should be prohibited for at least 72 hours.
- Heavy physical work should not be done in the following 24 hours.
- Do not smoke or be exposed to cigarette smoke for at least 72 hours; smoke can impair lung function.
- Spirometry should be repeated at regular intervals after discharge until the values have returned to the patient's baseline values prior to exposure.

5. References

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