# SUCCESSFUL MANAGEMENT IN OTHERWISE LETHAL SUICIDAL POISONING WITH 2,4-DICHLORPHENOXYACETIC ACID

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**CASE REPORT**

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**Abstract**

Herbicides are widely used to control the growth of broadleaf plants and among these 2,4-dichlorphenoxyacetic acid (2,4-D) has become dominant in both agriculture and households. However, despite being rare, acute intoxication with 2,4-D has lethal potential if early diagnosis and management are misguided. 2,4-D poisoning can mimic OP intoxication, so neuromuscular toxicity and coma can orient towards a correct symptom identification. We report the case of a 46-year-old male patient brought into the emergency department after voluntary herbicide ingestion that family confirmed as 2,4-D. Initial assessment revealed an agitated, confused, drowsy patient with a CGS of 9. Laboratory tests revealed mild metabolic acidosis and rhabdomyolysis. Patient management included early sodium bicarbonate administration, low dose mannitol, injectable furosemide and supplemental potassium to induce urine alkalinization. He was discharged five days later in good clinical condition. Acute 2,4-D intoxication has an increased risk of mortality, especially since no antidote is available. Diagnosis should be made promptly and urine alkalinization to accelerate poison clearance is the mainstay treatment.

**Keywords:** herbicides, 2,4-dichlorphenoxyacetic acid, acute poisoning, urine alkalinization, critical care

## Introduction

2,4-dichlorphenoxyacetic acid (2,4-D) is an auxin-analogue, being one of the most frequently used herbicide to eliminate unwanted weeds in the agriculture field [1]. Its worldwide use has proven beneficial to preserve grasses and crops like rice, wheat or corn. 2,4-D can be used individually or can be mixed with other compounds in various herbicides, leading to large market availability of the substance [2]. The substance can take the form of colorless crystals or white powder and its production depends on two main processes, namely forming the phenoxyacetic acid which is later chlorinated. In a secondary phase phenol is chlorinated leading to 2,4-dichlorophenol formation condensed with chloroacetic acid. Esterification of the latter induces a butyl ester derivative of 2,4-D [3].

Human exposure to 2,4-D is a consequence of ingestion, inhalation or skin absorption and it usually occurs as an occupational peril during herbicide

manufacturing or use or if significant contact is made with contaminated foods, water, soil, air [4].

Contamination with herbicide products can be assessed through adequately designed measurements using chromatography – spectrometry methods in biological samples or the environment [5].

Analyzing urine samples for the presence of 2,4-D is the most broadly utilized technique to evaluate human contamination, since the acid has a urinary excretion.

Long-term exposure to 2,4-D has been linked to a hypothyroid state or thyroid tumors in experimental studies. Moreover, the thyroid gland seems to enlarge while hormone production is suppressed. Genitalia seems to decrease in size, connecting 2,4-D to infertility in occupational or non-occupational chronic exposure [6]. There is strong evidence that this herbicide component induces oxidative stress in humans and a possibly chronic inflammatory state but the link to cell apoptosis or carcinogenicity is yet to be confirmed [7].

Despite a moderately-low proven toxicity, an intake of more than 300 mg kg-1 can be responsible for acute poisoning. Acute intoxication with this compound is not common and the main cited cause is voluntary ingestion in suicidal attempts [8].

Clinical signs of acute toxicity include vomiting, abdominal pain, rhabdomyolysis, hypotension or damage of the central nervous system and coma [9].

There is no antidote to acute poisoning with 2,4-D acid but given its structure and metabolism, alkalinization of urine seems an elective therapy together with support of vital functions and fluid administration [10]. Forced alkaline diuresis with intravenous administration of bicarbonate to maintain an urinary output >200ml/h and an urinary pH >7,5 [11-12] is an available therapeutic strategy. Osmotic diuresis is a frequently used method for elimination of renally excreted toxic substances, but reports of this practice in 2,4-D poisoning were not found in published literature [13]. Reported mortality is high, reaching almost 100%, depending on the amount ingested [14], [15].

**Case report**

A 46-year-old patient was brought into the emergency room (ER) six hours after voluntary ingestion of an unknown herbicide in a suicidal attempt. Upon admission the patient was diaphoretic and complained of myalgia, diffuse abdominal pain, nausea and vomiting. The cholinergic symptoms initially led to suspicion of OP acute exposure but plasma cholinesterase levels were within normal range.

Patient's family confirmed ingestion of around 100ml of 2,4-D acid and patient was transferred to the Toxicology Unit.

The initial assessment revealed an agitated, confused, drowsy patient with a CGS of 9 points, miosis. He had a respiratory rate of 24 breaths per minute, oxygen saturation on ambient air 77%, severe bronchorrhea and sialorrhea, thus orotracheal intubation was imposed. Patient's blood pressure was 123/73mmHg, pulse rate of 125 beats/min and body temperature of 38.9 ˚C.

Laboratory tests revealed mild metabolic acidosis, leukocytosis and rhabdomyolysis with high levels of transaminases, creatin kinase and muscle brain-creatin kinase. The latter reached its peak on second day of admission, with return to normal values in the following days.

Gastrointestinal decontamination was promptly performed, consisting of gastric lavage and administration of activated charcoal. Therapy also included the administration of balanced crystalloids, atropine (bolus and continuous infusion), loop diuretics. Hours later, the patient developed hypotension unresponsive to volume replacement therapy, so that vasopressor infusion was initiated.

Taking into account the ingested 2,4-D acid, patient management included early sodium bicarbonate administration, low dose mannitol, injectable furosemide and supplemental potassium to induce urine alkalinization. Additional measures were represented by antibiotics, thrombo-prophylaxis antiemetics, antitermics and external cooling.

Sedation was successfully stopped the next day and afterwards patient was weaned from vasopressors and ventilation. After a five-day stay in the intensive care unit he was discharged in good clinical condition and referred to a psychiatrist specialist to manage the suicidal attempt.

## Discussion

Herbicide poisoning is rare but associated with increased mortality rates. Apart from long-term exposure in professionals handling herbicide substances, acute poisoning is usually met in suicidal patients ingesting harmful products [16]. While paraquat and glyphosate are more commonly met in herbicidal intoxication reports, published data on poisoning with 2,4-D is scarce. 2,4-D is a herbicide in phenoxy group compounds and is widely used given it is readily available in every gardening shop, aiming to control unwanted weed growth [8]. Products containing 2,4-D acid can mimic OP poisoning but particular features are rhabdomyolysis, coma and hypo/hypertonia [17-18].

2,4-D has potentially toxic effects on every organ and system, namely the heart, central and peripheral nervous system, liver, kidneys, muscles, lungs and endocrine system [19].

2,4-D has an unknown mechanism of action, but it is believed that the neuromuscular toxicity is mediated through inhibition of a voltage-gated chloride channel [20]. Neuromuscular signs can manifest as myalgia, agitation/sedation, confusion, coma, miosis, hyperreflexia, rhabdomyolysis.

Due to damage of the blood-brain barrier, 2,4-D can be responsible for delayed nerved conduction or muscle contraction, suicidal ideas, depression, anxiety or aggressive manifestations [14].

The acid also has direct toxic effects on the gastrointestinal tract, the severity of manifestations depending on the quantity ingested, varying from nausea, vomiting, diarrhea to severe diffuse abdominal pain and ulcers [21]. Systemic signs can be present such as hypotension, hyperventilation, tachycardia, pyrexia, renal impairment.

Laboratory test results come as a consequence of organ dysfunction induced by 2,4-D and are often represented by metabolic acidosis, hypocalcemia, hyperkalemia, elevated creatin kinase, muscle brain creatin kinase, lactate dehydrogenase, transaminases [1,22].

Diagnosis can be established upon positive history of consumption and clinical signs and symptoms. Diagnosis assays do not have a validated role in the management of intoxication if the history is positive to acute ingestion [1, 22-23].

The scarcity of published data on 2,4-D acute poisoning makes it difficult to have management guidelines.

However, the mainstay treatment in 2,3-D intoxication is intravenous sodium bicarbonate, up to 40-80 mEq per liter in order to cause the alkalinization of urine (urine ph>7.5). This process will prevent the organic acid to reach the bloodstream from renal tubules where it is found in an ionized state. Urine alkalinization considerably stimulates the herbicide excretion [24].

Correction of alkaline diuresis-induced hypokalemia can be corrected by administering intravenous supplements. Aggressive poisoning cases can benefit from hemodialysis especially if associated with coma [14].

Plasma alkalinization has a potential to limit distribution from central circulation by ion trapping [11], [22]. The main purpose is to maintain an urinary output over 200ml/h or a urine flow of 4-6ml/min and an urinary pH >7,5 [11]. Literature reports cases of severe acute intoxication responding to hemodialysis and even plasmapheresis [24], [25].

Apart from primary above-mentioned measures, gastro-intestinal decontamination and charcoal administration can be tempted together with sorbitol and keeping an optimal electrolyte and acid-base balance. Patients need to be closely monitored for additional signs and symptoms [1], [10], [22] and receive supportive treatment to maintain vital signs if necessary. Alongside paraclinical tests should be performed such as renal function tests, electrolytes, blood gases, creatin kinase (for rhabdomyolysis), transaminases, urinalysis (pH, myoglobinuria) [1], [23].

In a study where human volunteers where dosed with 5mg/kg of 2,4-D, the elimination half-life from blood plasma was 11.6 hours.These human volunteers excreted more than 75% of 2,4-D in their urine within 96 hours of oral dosing [26–28].

Despite the 2,4-D spreading use, there is no specific antidote to treat acute intoxication and sodium bicarbonate aiming to alkalinize urine is the only strategy can has proven beneficial as to this point, being lifesaving [11,29].

Our management strategy, alongside routine clinical and paraclinical monitoring, fluids and alkaline diuresis, also included osmotic diuresis. Low-dose mannitol determines renal vasodilating effects and increased blood flow through the kidneys, thus enhancing elimination of renally excreted toxic substances.

A literature review published in 2017 by Hiran and Kumar on 2,4-D poisoning identified 16 reported cases in India with only 4 survivors. One of the cases exhibited severe muscle injury and cerebral oedema, while another patient was semiconscious and increased intracranial tension. All successful cases had induced alkaline diuresis [9].

## Conclusions

Despite being rare, acute 2,4-D intoxication has an increased risk of mortality, especially since no antidote is available.

Diagnosis should be made promptly and carefully, knowing that anticholinesterase poisoning can imitate clinical manifestations of 2,4-D intoxication. Thus, neuromuscular involvement, metabolic disturbances or coma should prompt correct diagnosis.

The rate of mortality is high if initial management is not properly applied and avoid systemic damage.

As published literature confirms, urine alkalinization has beneficial effects on these types of intoxications, but osmotic diuresis could be also helpful. Further research into the topic should be made before jumping to this conclusion, but preliminary results shown in the case report might be promising.

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