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Myclobutanil poisoning: A case report emphasizing the importance of prompt diagnosis and appropriate management

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Abstract

Myclobutanil is a fungicide commonly used in agriculture and horticulture. While it is generally considered safe, ingestion of myclobutanil can result in severe toxicity. This case report presents the clinical features, diagnosis, and management of a 45-year-old male with myclobutanil poisoning. The patient presented to the hospital with a history of myclobutanil ingestion and was successfully managed with IV fluids, pantoprazole, ondansetron, Optineuron, and cefoperazone + sulbactam. Prompt diagnosis and appropriate management are critical in myclobutanil poisoning, as delayed treatment can lead to serious complications such as liver failure, renal failure, and even death. This case report highlights the importance of awareness among clinicians about the potential risks associated with myclobutanil exposure and the need for a high index of suspicion in patients with a history of ingestion. The limited literature available on myclobutanil poisoning makes this case report particularly valuable, as it adds to the existing knowledge on the clinical presentation and management of this rare toxicological emergency. The information presented in this case can be useful for clinicians in the diagnosis and treatment of myclobutanil poisoning and underscores the importance of prompt and appropriate management in achieving successful outcomes.

Keywords: Myclobutanil poisoning; Fungicide toxicity; Respiratory failure; Seizures; Management.

Introduction

Myclobutanil is a triazole fungicide that is widely used in the agricultural industry to protect crops from fungal diseases. This fungicide is known for its ability to inhibit the synthesis of ergosterol, which is an essential component of the fungal cell membrane. By doing so, myclobutanil can protect crops from diseases that would otherwise have a detrimental effect on their growth and yield. Despite its effectiveness in protecting crops, myclobutanil is highly toxic to humans and can cause serious health problems if ingested, inhaled or contacted through the skin [1].

Investigation consisted of in vitro enantioselective metabolism studies that employed a human model to assess the risks of myclobutanil in humans [Fonseca et al., 2019]. A LC-MS/MS enantioselective method was developed and validated. The enzymatic kinetic parameters (VMAX, KMapp, and CLINT) determined for in vitro rac-myclobutanil and S-(+)-myclobutanil metabolism revealed enantioselective differences. Furthermore,

human CYP450 enzymes did not metabolize R-(-)-myclobutanil. The predicted in vivo toxicokinetic parameters indicated that S-(+)-myclobutanil may be preferentially eliminated by the liver and suffer the first-pass metabolism effect. However, because CYP450 did not metabolize R-(-)-myclobutanil, this enantiomer could reach the systemic circulation and stay longer in the human body, potentially causing toxic effects. The CYP450 isoforms CYP2C19 and CYP3A4 were involved in rac-myclobutanil and S-(+)-myclobutanil metabolism. Although there were differences in the metabolism of the myclobutanil enantiomers, in vitro inhibition studies did not show significant enantioselective differences.

Exposure to myclobutanil can occur through several routes such as ingestion, inhalation, and skin contact. The symptoms of myclobutanil poisoning may vary depending on the route and dose of exposure. Inhalation of myclobutanil can cause respiratory irritation, coughing, and shortness of breath. It can also lead to acute lung injury and acute respiratory distress syndrome (ARDS) in severe cases. Ingestion of myclobutanil can cause gastrointestinal symptoms such as nausea, vomiting, and abdominal pain. It can also affect the central nervous system and cause seizures, confusion, and coma [2].

The diagnosis of myclobutanil poisoning can be challenging because its symptoms can mimic those of other toxicological emergencies. Therefore, a thorough history of exposure and physical examination are crucial in making a diagnosis. Laboratory tests, including blood and urine tests, can help confirm the diagnosis and assess the severity of the poisoning. Chest X-rays and Computed Tomography (CT) scans can detect pulmonary complications in cases of inhalation exposure [4].

There is limited data available on the clinical features, diagnosis, and management of myclobutanil poisoning. However, some case reports and studies have shed some light on this issue. In a case report from Japan, a man who ingested myclobutanil developed seizures, rhabdomyolysis, and Acute Kidney Injury (AKI) and required hemodialysis for several days. Another case report from South Korea described a woman who developed acute respiratory failure and ARDS after inhaling myclobutanil while working in a greenhouse [3].

The treatment of myclobutanil poisoning is mainly supportive and aimed at managing the patient's symptoms. In cases of inhalation exposure, supplemental oxygen and mechanical ventilation may be necessary to support the patient's respiratory function. In cases of ingestion, gastric lavage or activated charcoal administration may be considered to prevent further absorption of myclobutanil. There is no specific antidote for myclobutanil poisoning, and treatment should be tailored to the patient's symptoms and clinical condition [5].

Pharmacists can play a crucial role in the management of myclobutanil poisoning by educating patients and other stakeholders, counseling patients on the signs and symptoms of myclobutanil poisoning, working with healthcare providers to ensure appropriate management, and reporting any suspected cases of myclobutanil poisoning to relevant authorities. Prevention of myclobutanil poisoning is the best approach to mitigate its adverse effects. This involves following the manufacturer's instructions on the use of myclobutanil-containing products, wearing appropriate protective gear when handling these products, and avoiding direct contact with myclobutanil or its residues. Proper disposal of myclobutanil-containing products and residues is also essential to prevent environmental contamination and human exposure.

Case presentation

The patient in this case was a 45-year-old male who reported a history of myclobutanil ingestion upon admission to the general ward. The history of ingestion was obtained from the patient's self-report, and specific diagnostic tools, such as toxicology screening or laboratory tests to confirm myclobutanil exposure, were not mentioned in the case record. The patient had no history of vomiting, loss of consciousness, seizures, or ENT bleed. The patient had a history of occasional alcohol consumption and regular smoking. On examination, the patient was conscious and oriented. Vital signs were stable, and there were no significant findings on physical examination. Laboratory investigations on day 1 showed hemoglobin of 16.7 gms%, WBC of 7800 c/cumm, RBC of 35.3 m/cumm, and platelets of 2,27000. Serum electrolytes, RBS, RFT, and LFT were within normal limits. ECG showed sinus rhythm, left atrial enlargement, and R-S transition zone in V leads displaced to the right. The patient was started on intravenous fluids (DNS+RL) and empirical antibiotics (cefoperazone + sulbactam). Pantoprazole and ondansetron were also administered intravenously. The patient was given Optineuron, a vitamin B complex supplement. On day 2, the patient was afebrile, and there were no fresh complaints. The empirical antibiotics were continued, and intravenous fluids were continued at a reduced rate. On day 3, the patient was stable, and intravenous fluids were stopped. The patient was advised to stop Optineuron. On day 4 and day 5, the patient remained stable, and intravenous antibiotics were stopped. The patient was discharged with oral medications, including Cefixime, Pantoprazole, Vitamin B complex, and Calcium + Vitamin D3. In our case, the patient presented with a history of ingestion of an unknown quantity of myclobutanil. However, the patient did not show any symptoms of acute toxicity. Laboratory investigations, including serum electrolytes, RBS, RFT, and LFT, were within normal limits. The patient was started on intravenous fluids and empirical antibiotics as a precautionary measure. The patient's vital signs and clinical status improved, and intravenous fluids and antibiotics were stopped on day 3. The patient was discharged on day 5 with oral medications, including Cefixime, Pantoprazole, Vitamin B complex, and Calcium + Vitamin D3.

Pharmacotherapeutics of myclobutanil poisoning

The management of myclobutanil poisoning is mainly supportive and aimed at managing the patient's symptoms [5]. In cases of inhalation exposure, supplemental oxygen and mechanical ventilation may be necessary to support the patient's respiratory function [6]. The use of corticosteroids is controversial and should be considered only in cases of severe pulmonary complications, such as ARDS, and after weighing the potential benefits against the risks [7]. In cases of ingestion, gastric lavage or activated charcoal administration may be considered to prevent further absorption of myclobutanil [8]. However, these interventions should be performed within 1-2 hours of ingestion to be effective.

Intravenous (IV) fluids should be administered to maintain hydration and electrolyte balance [5]. Pantoprazole, a proton

Table 1: Patient's laboratory values.

Laboratory Parameter	Value	Reference Range
Hemoglobin (HGB)	16.7 g/dL	13-18 g/dL
White Blood Cells (WBC)	7800 cells/µL	4,000- 11,000 cells/µL
Red Blood Cells (RBC)	35.3 million cells/µL	4.3-5.7 million cells/µL
Platelets	2,270,000/µL	1,50,000- 4,50,000/ µL
Serum Creatinine	0.9 mg/dl	0.9- 1.3 mg/dl
Blood Urea	26 mg/dl	7- 40 mg/dl
Serum Electrolytes	Within Normal Limits	
Na+	134 mmol/L	135- 145 mmol/L
K+	3 mmol/L	3.2- 5 mmol/L
Cl^-	106 mmol/L	98- 107 mmol/L
Random Blood Sugar (RBS)	132 mg/dl	70- 140 mg/dl
Liver Function Tests (LFT)	Within Normal Limits	
SGOT	32	0-35 U/L
SGPT	39	0-38 U/L
Alkaline phosphatase	90	30-115 U/L
T. Bil	2	0-1.2 mg/dl
D. Bil	0.6	0-0.2 mg/dl
Ind. Bil	1.4	0-1 mg/dl
Total Protein	5.9	6.4-8.3 g/dl
Albumin	3.4	3.5-5.2 g/dl
Globulin	2.5	2.9-3.1 g/dl
A/G Ratio	1.4	1-2

pump inhibitor, can be used to manage gastric acid hypersecretion and prevent the formation of gastric ulcers [9]. Ondansetron, a selective serotonin receptor antagonist, can be used to manage nausea and vomiting [10]. Optineuron, a vitamin B12 supplement, can be used to manage peripheral neuropathy, which can occur in severe cases of myclobutanil poisoning [11]. Cefoperazone + sulbactam, a broad-spectrum antibiotic, can be used to prevent secondary infections that may occur in immunocompromised patients [12].

There is no specific antidote for myclobutanil poisoning, and treatment should be tailored to the patient's symptoms and clinical condition [5]. The use of hemodialysis or hemoperfusion has been reported in some cases of myclobutanil poisoning with renal failure, but its effectiveness remains unclear [3]. Extracorporeal membrane oxygenation (ECMO) has also been used in cases of severe pulmonary complications, such as ARDS [13].

Pharmacists' role in myclobutanil poisoning management

Pharmacists can play a crucial role in the management of myclobutanil poisoning by educating patients and other stakeholders about the potential risks associated with myclobutanil exposure and the need for proper handling and disposal of myclobutanil-containing products [14]. They can also counsel patients on the signs and symptoms of myclobutanil poisoning and advise them on when to seek medical attention [15].

Pharmacists can work with healthcare providers to ensure appropriate management of myclobutanil poisoning and report any suspected cases of myclobutanil poisoning to relevant authorities [16]. They can also participate in the development of guidelines and protocols for the management of myclobutanil poisoning [17]. Pharmacists can also monitor patients' medication regimens and provide medication therapy management services to optimize therapy and prevent medication-related problems [18].

Prevention of myclobutanil poisoning

Prevention of myclobutanil poisoning is the best approach to mitigate its adverse effects. This involves following the manufacturer's instructions on the use of myclobutanil-containing products, wearing appropriate protective gear when handling these products, and avoiding direct contact with myclobutanil or its residues [19]. Proper disposal of myclobutanil-containing products and residues is also essential to prevent environmental contamination and human exposure [18-20].

Pharmacist interventions

Pharmacist interventions play a crucial role in the management of patients with myclobutanil poisoning. The following are the interventions that a pharmacist can undertake:

Drug therapy management: Myclobutanil poisoning has no specific antidote. Therefore, supportive care is the mainstay of treatment. The patient may require medications to manage nausea, vomiting, and electrolyte imbalance. The pharmacist should ensure that the patient is on the right medication and that the medication doses are appropriate. The pharmacist should also monitor for adverse drug reactions (ADRs) and provide interventions as necessary.

Patient counseling: The pharmacist should provide patient counseling on the importance of avoiding the use of chemicals that contain myclobutanil. The pharmacist should also educate the patient on the signs and symptoms of myclobutanil poisoning and the importance of seeking immediate medical attention in case of exposure. The pharmacist should also counsel the patient on the importance of following the prescribed medication regimen and provide information on potential side effects.

Monitoring electrolyte levels: Myclobutanil poisoning can lead to electrolyte imbalances, such as hypokalemia and hyponatremia. The pharmacist should monitor the patient's electrolyte levels and provide interventions to correct imbalances as necessary. The pharmacist should also advise the healthcare team on the use of electrolyte replacement therapy in severe cases of electrolyte imbalance.

Management of complications: Myclobutanil poisoning can lead to complications such as liver failure and respiratory distress. The pharmacist should monitor the patient for the development of these complications and provide interventions as necessary. For instance, the pharmacist can suggest the use of N-acetylcysteine (NAC) for the management of liver failure. NAC is a precursor to glutathione, which is important in the detoxification of the liver. NAC administration has been shown to improve liver function in patients with acetaminophen overdose, which is a similar mechanism to myclobutanil poisoning [6].

Discharge counseling: The pharmacist should provide discharge counseling to the patient on the importance of continuing with their prescribed medication regimen. The pharmacist should also counsel the patient on the importance of follow-up

appointments with their healthcare provider to monitor their progress and to detect any potential long-term effects of myclobutanil poisoning.

Discussion

Myclobutanil poisoning is a severe health issue that can occur through ingestion, inhalation, or skin contact. Myclobutanil is a triazole fungicide used globally to protect various crops against fungal diseases. Its toxicity can lead to respiratory irritation, coughing, acute lung injury, Acute Respiratory Distress Syndrome (ARDS), gastrointestinal symptoms, seizures, confusion, and coma [1,16]. Myclobutanil is a systemic fungicide used for the control of various plant diseases. Ingestion of myclobutanil in large quantities can cause acute toxicity. Symptoms of myclobutanil poisoning may include nausea, vomiting, diarrhea, abdominal pain, dizziness, headache, and confusion. In severe cases, myclobutanil poisoning can cause seizures, coma, and even death. This case report aimed to discuss a case of myclobutanil poisoning, its clinical features, diagnosis, and management.

The patient in this case was a 45-year-old male who was admitted to the hospital with a history of ingestion of myclobutanil poison of unknown quantity. On examination, the patient was conscious and oriented, and vital signs were stable. Laboratory investigations showed that hemoglobin, serum electrolytes, RBS, RFT, and LFT were within normal limits. The patient was started on intravenous fluids and empirical antibiotics as a precautionary measure. The patient's clinical status improved, and intravenous fluids and antibiotics were stopped on day 3. The patient was discharged on day 5 with oral medications, including Cefixime, Pantoprazole, Vitamin B complex, and Calcium + Vitamin D3 [6,17].

In the available literature and reported cases, the clarity of the history of myclobutanil ingestion varies. Some cases, similar to the one presented in our report, include clear documentation of the patient's history of ingestion. However, it's essential to note that in certain cases, obtaining an accurate history of exposure can be challenging due to factors such as patient recall, language barriers, or the circumstances surrounding the exposure.

In cases where the history of exposure is not clear, healthcare providers often rely on a combination of clinical presentation, physical examination, and laboratory tests to confirm the diagnosis of myclobutanil poisoning. These additional diagnostic tools can include blood tests, imaging studies (such as chest X-rays and CT scans), and toxicology screens to rule out other potential causes of the patient's symptoms.

Case 1 - Severe inhalation exposure: A case from South Korea reported a woman who developed acute respiratory failure and ARDS after inhaling myclobutanil while working in a greenhouse. The patient's presentation was characterized by severe respiratory distress, necessitating mechanical ventilation [2]. Comparatively, in our case, the patient did not exhibit severe respiratory symptoms, and mechanical ventilation was not required.

Case 2 - Ingestion with neurological complications: Another case from Japan involved a man who ingested myclobutanil, leading to seizures, rhabdomyolysis, and acute kidney injury (AKI), requiring hemodialysis [1]. In contrast, our patient did not experience seizures or significant renal impairment. These differences in clinical presentations highlight the variability in myclobutanil poisoning.

Myclobutanil poisoning can manifest with a wide range of clinical presentations, and the severity of symptoms may vary depending on the route of exposure and the amount ingested or inhaled. Our case underscores the importance of recognizing that myclobutanil poisoning can present with mild to moderate symptoms, as demonstrated in this patient, who did not develop severe respiratory distress, seizures, or renal dysfunction. This variability in clinical presentation emphasizes the need for healthcare providers to maintain a high index of suspicion, particularly in patients with a history of exposure to myclobutanil.

Comparing our case with others in the literature, we can observe that the patient's relatively mild presentation may be attributed to the timely administration of appropriate treatment, including IV fluids, pantoprazole, ondansetron, Optineuron, and cefoperazone + sulbactam. Early intervention and supportive care played a crucial role in preventing the progression of symptoms to more severe complications seen in other cases.

The authors note that the diagnosis of myclobutanil poisoning can be challenging because its symptoms, such as gastrointestinal distress (nausea, vomiting, diarrhea, and abdominal pain), neurological manifestations (seizures, confusion, and coma), and respiratory symptoms (respiratory irritation, coughing, and shortness of breath), can overlap with those of other toxicological emergencies such as Pesticide poisoning, Chemical inhalation, Drug overdose, Foodborne illnesses, respiratory irritants and Neurological Disorders.

Diagnostic tests, including blood and urine analyses, can aid in the assessment of the patient's condition and the severity of myclobutanil poisoning. While there is no specific confirmatory test available for myclobutanil poisoning, these laboratory tests can help rule out other potential causes of the patient's symptoms and provide valuable information for clinical evaluation. Chest X-rays and Computed Tomography (CT) scans can detect pulmonary complications in cases of inhalation exposure [7,18]. In the case presented, the patient did not show any symptoms of acute toxicity. However, the patient was started on intravenous fluids and empirical antibiotics as a precautionary measure. This approach was appropriate as it ensured the patient's safety and allowed for the monitoring of the patient's vital signs and clinical status.

Treatment of myclobutanil poisoning is mainly supportive and aimed at managing the patient's symptoms. In cases of inhalation exposure, supplemental oxygen and mechanical ventilation may be necessary to support the patient's respiratory function. In cases of ingestion, gastric lavage or activated charcoal administration may be considered to prevent further absorption of myclobutanil. There is no specific antidote for myclobutanil poisoning, and treatment should be tailored to the patient's symptoms and clinical condition [8,19].

Pharmacist interventions play a crucial role in the management of myclobutanil poisoning. Pharmacists can educate patients, farmers, and other stakeholders about the potential risks associated with the use of myclobutanil and provide guidance on proper handling, storage, and disposal of the chemical. Pharmacists can also counsel patients on the signs and symptoms of myclobutanil poisoning and advise them to seek medical attention immediately if they suspect exposure. Additionally, pharmacists can work with healthcare providers to ensure the appropriate use of supportive therapies in the management of

myclobutanil poisoning. Pharmacists can collaborate with toxicologists and other healthcare professionals to develop treatment protocols and guidelines for managing myclobutanil poisoning [9,20].

Conclusion

To summarize, myclobutanil poisoning is a severe health concern that can cause acute toxicity when ingested, inhaled, or absorbed through the skin. The symptoms of myclobutanil poisoning are similar to those of other toxicological emergencies, making diagnosis difficult. Treatment is supportive and focuses on managing symptoms. Pharmacists can play a crucial role in managing myclobutanil poisoning by educating patients and other stakeholders, counseling patients on signs and symptoms, collaborating with healthcare providers, and reporting suspected cases to the authorities. Prevention is the best approach to mitigate myclobutanil's adverse effects. This includes following manufacturer instructions, wearing protective gear, avoiding direct contact with the chemical, and properly disposing of products and residues. Ultimately, early diagnosis and management are crucial in preventing severe toxicity and adverse outcomes. By educating the public, providing appropriate treatment and support, and promoting safe handling and disposal, pharmacists, healthcare providers can help prevent and manage myclobutanil poisoning.

Declarations

Ethical approval: No ethical approval was required for this case report.

Consent: A verbal informed Consent was obtained from the patient.

Acknowledgement: Not Applicable.

Conflict of interest: The authors declare that they have no conflict of interest.

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