Assessment and Management of Poisonous Mushrooms in Türkiye: An Overview

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Received: May 18, 2023 **Accepted**: July 4, 2023 **Published:** 29 August, 2023
To cite this article: Şahin A, Arıcı MA, Korkut S, Tunçok Y. (2023) Assessment and Management of Poisonous Mushrooms in Türkiye: An Overview. Recent Trends in Pharmacology, vol 1, issue 2: 92-109.

Abstract

Patients exposed to poisonous mushrooms may present to emergency rooms with severe clinical conditions ranging from simple gastrointestinal complaints to liver failure. The clinical findings of mushroom poisoning differ according to the toxin of the mushroom species consumed. Poisonings are typically classified as acute-onset (<6 hour), late-onset (6-24 hours) and delayed-onset (>24hours) toxicity. Acute onset mushroom poisonings occur within 6 hours after consuming the mushroom and cause cholinergic toxicity, gastrointestinal findings, disulfiram-like reaction, seizures and hallucinations. Late-onset mushroom poisonings occure within 6-24 hours with the hepatotoxicity, nephrotoxicity and erythromelalgia. Delayed onset mushroom poisonings occure one day after consuming mushrooms with nephrotoxicity, neurotoxicity and rhabdomyolysis. While the prognosis is good in the case of early onset of symptoms in mushroom poisoning, the prognosis is poor in the case of late onset of symptoms. Most of the mushroom poisoning cases that present gastrointestinal symptoms improve with adequate supportive treatment. Hepatotoxic mushrooms containing cyclopeptide are mainly responsible for deaths due to mushroom poisonings. In all cases, basic laboratory evaluation and symptomatic supportive treatment approachs are required. There are no antidotes with proven efficacy in the treatment of mushroom poisoning. Specific treatment approaches should be applied according to mushroom species.

Keywords: Mushroom poisoning, Acute onset, Late onset, Delayed onset, Treatment

Introduction

Mushroom poisoning is often caused by the consumption of wild mushrooms, as they cannot be easily distinguished from edible mushrooms (Yardan et al., 2010). It is a common habit to pick and eat mushrooms from nature due to their delicious taste, especially in rainy spring months. Invalid methods, such as mushrooms turning black when cooked with a silver spoon and precluding an insect living on it, are still used to discriminate between toxic and edible mushrooms. However, it is difficult to distinguish between edible and toxic species (Kirchmair et al., 2012).

Approximately 100 of the 10,000 mushroom species found worldwide cause toxicity. Data on the frequency of mushroom poisonings are limited due to the difficulty of diagnosis. However, approximately 7500 mushroom poisoning cases are reported annually to Poison Control Centers in the United States (Gold et al., 2021). According to the data of the Turkish National Poison Information Center, the frequency of mushroom poisoning in Türkiye was between 1.2-1.8% among all poisonings in 2018 and the following 2 years (Koç İ., 2021), and approximately 1000 toxic mushroom poisonings are reported annually (Colak et al., 2015). Due to its climate and vegetation, Türkiye has very rich mushroom diversity, and the majority of mushroom poisonings are observed in rural areas (Akata, 2017; Durukan et al., 2007). It has been reported that poisoning with all types of mushrooms, especially Coprinus species, *Amanita phalloides*, *Amanita pantherina* and mushrooms that cause simple gastrointestinal symptoms, has been observed in Türkiye (Diaz, 2005). *Amanita phalloides*-type mushrooms, containing cyclopeptides, are the most common toxic mushrooms that cause severe symptoms in emergency room admissions in Türkiye in childhood and adults and are responsible for nearly 95 % of fatal mushroom poisonings (Karahan et al., 2016).

According to clinical findings, mushroom poisonings are classified into three groups: early-onset (<6 hours), delayed-onset (6-24 hours), or late-onset (>24 hours) (Diaz, 2005). Early-onset mushroom poisonings cause neurotoxic effects, cholinergic symptoms, disulfiram-like reactions or gastrointestinal manifestations, and late-onset mushroom poisonings cause toxic effects on the liver or kidney or cause erythromelalgia. Delayed-onset mushroom poisonings also cause toxic effects on the kidney with rhabdomyolysis or have neurotoxic effects(Diaz, 2005). Although the prognosis varies according to the type of mushroom

ingested, the most common cause of death in mushroom poisoning is the ingestion of cyclopeptide-containing mushrooms (Diaz, 2018).

1. Early-onset mushroom poisoning (<6 hours) (Table 1, Figure 1)

Table 1. Mushroom types, toxins, symptoms and time of onset of symptoms in acute onset mushroom toxicity (<6 hours)

Type of mushroom	Toxin	Symptoms	Time of onset of symptoms
Boletus, Chlorophyllum, Entoloma, Lactarius, Omphalotus and Tricholoma	Not identified	Acute gastroenteritis	0.5- 3 hours
Inocybe, Clitcybe	Muscarine	Cholinergic poisoning	0.5-2 hours
Amanita muscaria, Amanita pantherina	Ibotenic acid Muscimol	Central nervous system excitation and depression	0.5-2 hours
Gyromitra species	Gyromitrin	Epileptogenic	5-10 hours
Psilocybe species	Psilocybin	Hallucination	0.5-1 hours
Coprinus atramentarius	Coprin	Disulfuram like reaction	0.5-2 hours

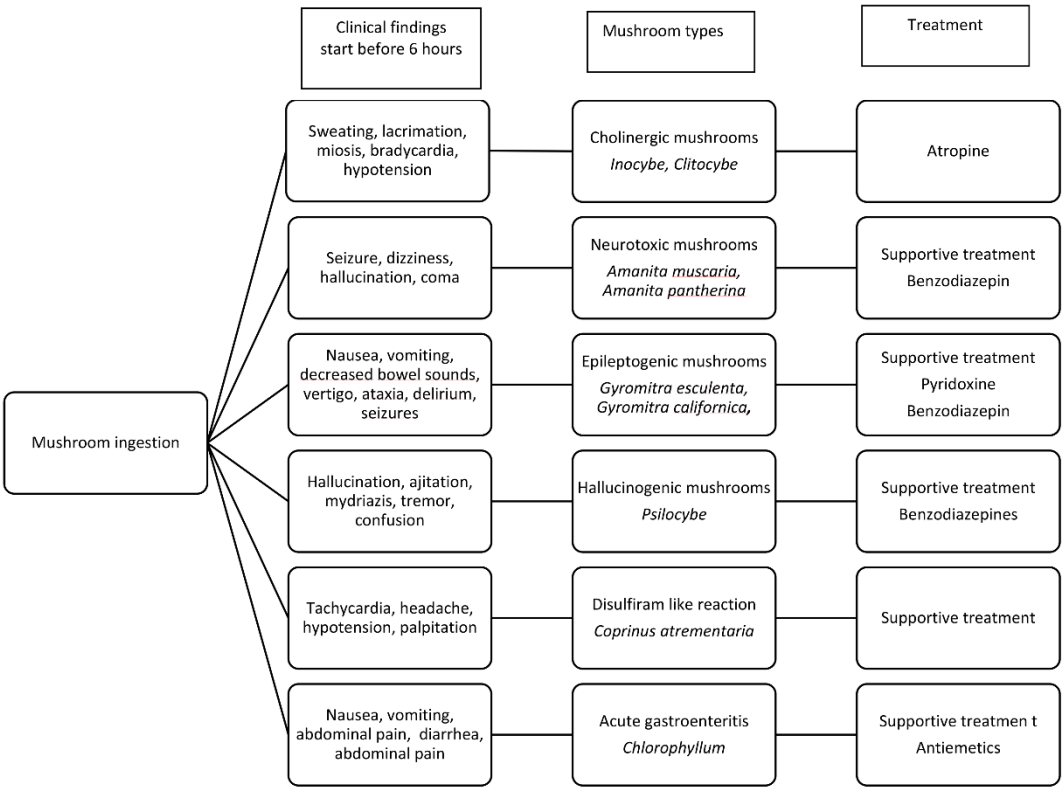

Figure 1. Diagnosis and treatment algorithm in early-onset mushroom poisoning

Gastrointestinal toxin-containing mushrooms: Although there are hundreds of mushrooms in this group, *Boletus, Chlorophyllum, Entoloma, Lactarius, Omphalotus* and *Tricholoma* ingestions are the main types that cause acute gastrointestinal symptoms. The toxins of these mushrooms have not been identified. It is claimed that the observed clinical findings are due to allergy or malabsorption due to these mushrooms. Clinical findings include acute gastroenteritis findings such as abdominal pain, cramps, nausea, and vomiting, which may be watery or bloody, severe diarrhea and profuse sweating. In some cases, autonomic nervous system changes and blurred vision, dizziness, lacrimation, salivation, hypotension and tachycardia may be observed. Rarely, it may be associated with hematological abnormalities, bleeding, and disseminated intravascular coagulation (Colomer-Carbonell et al., 2022). Symptoms generally start within 0.5-4 hours of ingestion and resolve within 6-24 hours with supportive treatment, including fluid resuscitation and antiemetics (Diaz, 2005). If symptoms persist, physicians should consider other types of toxic mushrooms.

Cholinergic toxin-containing mushrooms: *Inocybe*- and *Clitocybe*-type mushrooms are the most common mushrooms known to cause muscarinic poisoning. Muscarine, which is in the content of these mushroom species, binds to muscarinic receptors and causes the development of typical muscarinic cholinergic findings within approximately 30 minutes or 2 hours after ingestion. Additionally, psilocybin, which binds to 5-HT_{2A} receptors, was identified in *Inocybe*-type mushrooms (Kosentka et al., 2013). Nausea, vomiting, diarrhea, abdominal pain, tracheobronchial secretions, hypersalivation, sweating, rhinorrhea, lacrimation, miosis, blurred vision, bradycardia, and hypotension are observed. Since muscarine is in the quaternary amine structure, it does not cross the blood–brain barrier, and no findings related to the central nervous system are expected (Diaz, 2005; Kosentka et al., 2013; Lurie et al., 2009). Treatment of poisoning with mushrooms that cause cholinergic toxicity is symptomatic, and atropine (1-2 mg IV slowly) is an anticholinergic drug that may be used when necessary as an antidote.

Neurotoxin-containing mushrooms: *Amanita muscaria* and *Amanita pantherina* are mushrooms that cause the neurological symptoms known as Pantherina-Muscaria syndrome. The neurotoxic isoxazoles ibotenic acid and muscimol in the content of such mushrooms are responsible for the observed findings. Additionally, *Amanita pantherina*-type mushrooms often contain

toxins, such as stizolobic and stizolobinic acid. These are L-dopa oxidation products, and they could also produce anticholinergic effects. After the mushroom ingestion, its toxins are rapidly absorbed from the gastrointestinal tract and can be detected in the urine within one hour. Ibotenic acid is structurally similar to the stimulatory neurotransmitter glutamic acid, and muscimol is structurally similar to the neurotransmitter gamma-aminobutyric acid (GABA). Both of them cross the blood–brain barrier; ibotenic acid causes myoclonic movements and seizures, and muscimol causes somnolence, dizziness, hallucinations, dysphoria, delirium and coma. Glutamatergic manifestations and myoclonic movements are predominant in children. It has been reported that *Amanita muscaria*-type mushrooms containing more stimulant ibotenic acid often cause confusion and agitation, and *Amanita pantherina*-type mushrooms containing the inhibitor muscimol often cause coma (Vendramin & Brvar, 2014). Therefore, the syndrome, known as Pantherina-Muscaria syndrome, can be divided into two subtypes, *Amanita. Muscaria* and *Amanita Pantherina* poisoning. Most of the cases respond to benzodiazepines such as diazepam or lorazepam and supportive treatment for symptoms such as agitation and seizures. However, cases with respiratory depression starting with central nervous system symptoms and death have also been reported in the literature (Meisel et al., 2022).

Hallucinogenic toxin-containing mushrooms: *Psilocybe caerulipes, Psilocybe cubensis, Gymnopilus spectabilis*, *Panaeolus spp*. (e.g., *Panaeolus foenisecii*) and *Psathyrella foenisecii* are hallucinogenic mushrooms. The toxicity of such mushrooms is caused by the psilocybin (4-phosphoryloxy-N,N-dimethyltryptamine) in their content, which turns into psilocin. Although psychoactive mushrooms are considered to be natural and harmless due to their low toxicity, their use is restricted in many countries due to their potential for abuse. Psilocybin is rapidly absorbed, and the biological activity of its metabolite psilocin continues for 2-4 hours. Toxic findings may be evident for 24-48 hours. Psilocybin activates presynaptic $5HT_{2A}$ receptors and prevents the release of presynaptic serotonin, while at high doses, it inhibits muscarinic receptors in the central nervous system. The effects of psilocybin are dose-dependent and cause controllable changes in consciousness at moderate doses (Borowiak et al., 1998; Passie et al., 2002). In this type of mushroom poisoning, hallucinations or delusions, agitation, anxiety, nervousness, confusion, tachycardia, nausea, vomiting, mydriasis, and tremor are among the most

common toxic findings. In case reports, rhabdomyolysis, end-stage renal disease, myocardial infarction and neurotoxic effects related to psilocybin have been reported (Borowiak et al., 1998; Forrester, 2020). Treatment of poisoning with such mushrooms requires supportive treatment and administration of intravenous fluids. In rare cases, benzodiazepines may be used (Forrester, 2020).

Mushrooms that cause disulfiram-like reactions: *Coprinopsis atramentaria* is an edible mushroom that contains coprin and causes a disulfiram-like reaction that has been known for many years. The metabolite of coprin, 1-aminocyclopropanol, inhibits aldehyde dehydrogenase and causes acetaldehyde accumulation. Accumulation of acetaldehyde causes undesirable effects such as vomiting, nausea, tachycardia, flushing, headache, dizziness, hypotension, palpitations and shortness of breath (Nowakowski et al., 2020). In these poisonings, disulfiram-like reactions develop when alcohol is consumed simultaneously or within 48-72 hours after the mushroom ingestion. Coprinus species cause a disulfiram-like reaction when ingested with alcohol, which is well recognized, but additionally, disulfiram-like reactions have been reported in five different cases who consumed alcohol ingested with *Lepiota aspera*, but the toxin of this type of mushroom could not be described (Haberl et al., 2011). Treatment is symptomatic with fluid repletion and used antiemetics such as metoclopramide as needed. In the presence of severe hypotension, direct-acting vasopressors such as norepinephrine are used.

Epileptogenic toxin-containing mushrooms: Mushrooms such as *Gyromitra esculenta, Gyromitra californica, Gyromitra brunnea* and *Gyromitra infula* contain gyromitrin. Gyromitrin (N-methyl-N-formyl hydrazone) is broken down into acetaldehyde and N-methyl-N-formyl hydrazine. Hydrazine is structurally similar to pyridoxine, inhibits enzymatic reactions related to pyridoxal phosphate and causes seizures by decreasing GABA levels. Monomethylhydrazine can induce lipid peroxidation in the liver to form hydrazones that cause cytotoxic effects and acute liver injury. Additionally, cytochrome p450 enzymes, amino oxidases and glutathione pathways are affected. The severity of the toxicity depends on the amount of toxin ingested. Symptoms of Gyromitra-type mushroom poisoning usually occur after 5 to 12 hours of ingestion with abdominal pain and nausea sometimes with headache. Dryness of the skin and mucous membranes, decreased bowel sounds, and

confusion may be observed in poisoned patients. Some patients may have vomiting and watery diarrhea. Nervousness, vertigo, ataxia, delirium, seizures and at the end of three days jaundice can be observed in high amounts of toxin ingestion (Arłukowicz-Grabowska et al., 2019; Michelot & Toth, 1991). First, fluid support is required in the treatment. In these cases, liver function tests, blood urea nitrogen and serum creatinine levels should be monitored. In the treatment of seizures, 25 mg/kg (intravenous) pyridoxine and, if there is no response, additional benzodiazepines are recommended. Most patients give response to treatment within 6 days with good supportive care and pyridoxine(Horowitz KM, Kong EL, 2023).

2. Late-onset mushroom poisoning (6-24 hours) (Table 2)

Table 2. Mushroom types, toxins, symptoms and time of onset of symptoms in late-onset mushroom toxicity (6-24 hours)

Type of mushroom	Toxin	Symptoms	Time of onset of symptoms
Amanita species *Gallerina* species *Lepiota* species	Amatoxins, Phallotoxins Virotoxins	Hepatotoxicity	6-24 hours
Amanita proxima *Amanita smithiana*	Norleucine Chlorocrotylglycine	Nephrotoxicity	12 hours
Clitocybe acromelalga *Clitocybe amoenolens*	Acromelic acid (ACRO) Clitidine	Erythromelalgia	1 day

Cylopeptid toxin-containing mushrooms: *Amanita phalloides*-type mushrooms are grown in many countries, including mainly European countries and Türkiye, America, Asia, Australia and even the African continent in the temperate and humid climate zone (Erden et al., 2013). These types of mushrooms can be confused with edible mushrooms such as young *Agaricus spp., Lepiota naucina and Leucoagaricus leucothites* (Yilmaz et al., 2015). This type of mushroom contains three main toxins, namely, amatoxins, phallotoxins and virotoxins (Garcia et al., 2015). Among these toxins, amatoxins are primary toxins that cause toxicity; phallotoxins are not absorbed by the gastrointestinal system and are toxic when they are injected, while virotoxins have less toxicity (Vetter, 1998). Since Amatoxin is resistant to heating and freezing, consuming canned food prepared with this type of mushroom can cause out-of-season poisoning (Erden et al., 2013).

Amatoxin is absorbed from the gastrointestinal tract within 90-120

minutes, passes into the systemic circulation and reaches the target tissue liver by organic anionic transporter peptide 1B3 (OATP1B3) and sodium taurocolat cotransporting polypeptid (NCTP)(Gundala et al., 2004). The toxin is not metabolized, participates in the enterohepatic circulation and is excreted mainly through the kidneys. Amatoxin is a potent inhibitor of RNA polymerase II that blocks the production of mRNA and protein synthesis responsible for liver and kidney toxicity (Garcia et al., 2015; Walton JD, Hallen-Adams HE, 2010). As a result of increased free oxygen radicals and the inability of them to be eliminated by the body's antioxidant systems, the process of necrosis and/or apoptosis begins. Liver cell membrane is damaged and inflammatory mediators secreted contributes to the toxicity(Magdalan et al., 2011).

Amanita phalloides-type mushroom called "death cap" or "death angel" poisoning has three clinical stages. Poisoned patients are asymptomatic for the first 6-12 hours of ingestion. In the first stage, patients present with watery or bloody and mucous diarrhea, colic-like abdominal pain and vomiting. These findings begin at 6-24 hours of ingestion. If mushroom poisoning is not suspected, it may be confused with viral gastroenteritis. In the laboratory, liver enzymes are normal, and electrolyte abnormalities secondary to severe diarrhea and acute renal failure due to dehydration may occur. Dry mucosal membranes, tachycardia, and hypotension may be detected on the physical examination. In the second stage, the gastroenteritis improves, but the biochemical and clinical signs of liver toxicity become evident. In the third stage, approximately 2-4 days after the mushroom ingestion, liver and kidney failure develops. Hypoglycemia, coagulopathy, encephalopathy, seizure, respiratory failure, multiorgan failure and death within 3-15 days of ingestion may occur due to hepatic failure (Garcia et al., 2015; Horowitz BZ, 2022). It is noteworthy that in various case reports, cardiac toxic effects such as left ventricular failure and myocardial damage and dysfunction characterized by elevated cardiac enzymes have been reported in poisoning with *Amanita phalloides*-type mushrooms (Altintepe et al., 2014; Unverir et al., 2007).

In the diagnosis of poisoning with *Amanita phalloides*-type mushrooms, having a history of eating wild mushrooms and the time of onset of the findings suggest poisoning. It is not generally possible to evaluate the mushroom by a mycologist or routinely confirmatory testing of amatoxin exposure from blood or urine. For these reasons, the differential diagnosis of

mushroom poisoning is often based on clinical findings.

In treatment, decontamination methods cannot be applied because the diagnosis is made late in poisoning with such mushroom ingestions. However, repeated doses of activated charcoal (1 g/kg initially, followed by 0.5 g/kg orally) during the three days of poisoning may be beneficial as the toxin enters the enterohepatic circulation. In addition to supportive therapy, treatment alternatives that reduce toxin uptake into the main target liver cells or that can reverse toxicity-related oxidative stress or inflammation are used. Among these treatments are silibinin (20-50 mg/kg/day i.v. 48-96 hours), which prevents the uptake of the toxin into the liver cell by binding to its binding site in the liver; penicillin G (300.000- 1.000.000 U/kg i.v. infusion/day), which is an OATP substrate; and N-acetylcysteine (150 mg/kg infusion in the first 60 minutes, 50 mg/kg infusion over 4 hours, 6.25 mg/kg/hr infusion until the patient is clinically recovered), which acts as a glutathione donor. The common feature of all three treatments is antioxidant effects, but this effect is weak in penicillin (Arıcı A, 2021). There is no conclusive evidence regarding the efficacy of current antidote treatments. In experimental studies, resveratrol has been shown to be effective in preventing liver and kidney toxicity in poisoning with mushrooms containing amatoxin (Arici et al., 2020; Sahin et al., 2018). In addition, methylprednisolone was found to be effective by inhibiting NCPT and preventing the uptake of the toxin into liver cells (Garcia et al., 2015; Gundala et al., 2004). Extracorporeal treatment and liver support therapies should be considered by medical toxicologists, and clinical observation should be performed in intensive care units that have the capability of liver transplantation (Pilzvergiftungen, 2007) (Figure 2).

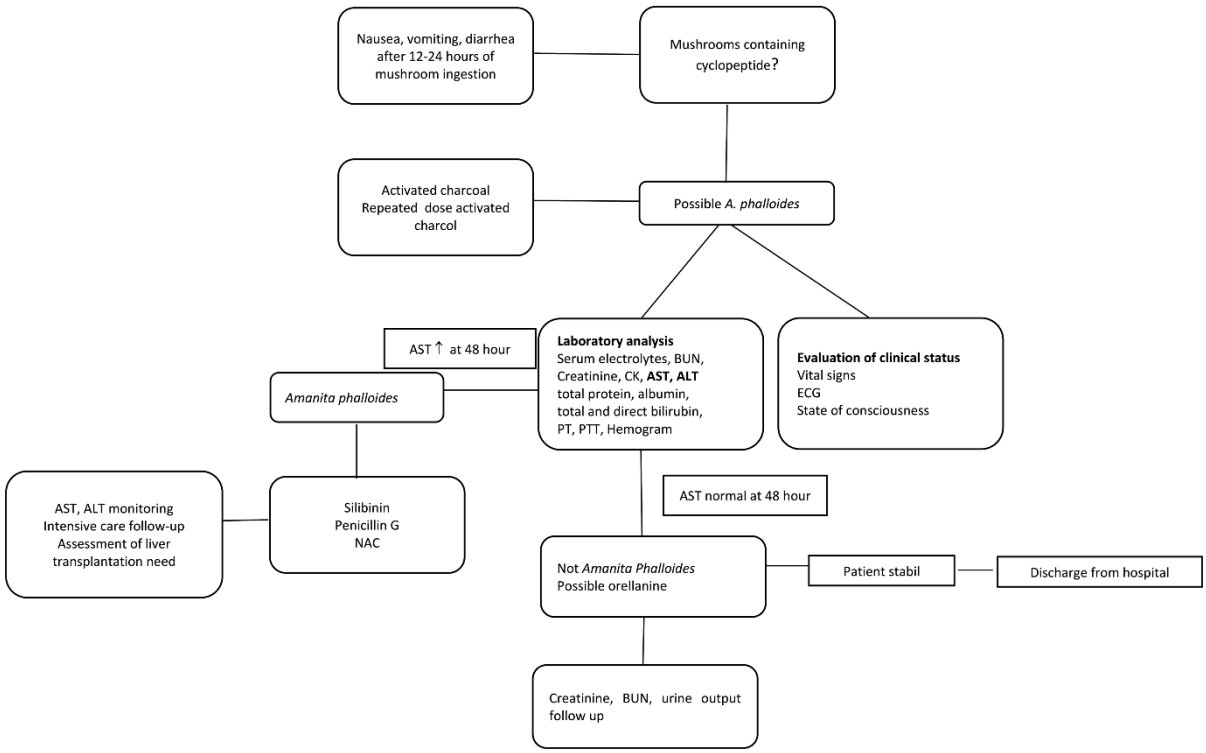

Figure 2. Diagnosis and treatment algorithm in late-onset mushroom poisoning. (BUN: Blood urea nitrogen, CK. Creatine kinase, AST: Aspartat aminotranspherase, ALT: Alanin aminotranspherase, ECG: Electrocardiogram, PT: Protrombin time, PTT: Partial tromboplastin time, NAC: N- acetylcysteine**)**

Nephrotoxic mushrooms: Amanita species are mushrooms that are similar in appearance and have different toxins. Among these species, *Amanita smithiana*, *Amanita proxima*, *Amanita boudieri*, *Amanita gracilior* and *Amanita echinocephala* are nephrotoxic mushrooms. Nephrotoxic toxins of *Amanita smithiana* are allenic norleucine and chlorocrotylglycine. The toxic mechanism of these toxins has not been identified. In these types of mushroom poisonings, gastrointestinal symptoms such as nausea and vomiting are observed within 2-12 hours, and renal failure develops within an average of 3.5 days of ingestion (2-6 days). In poisoning with this type of mushroom, symptoms are characterized by mild liver damage and severe but reversible acute renal failure due to acute interstitial nephritis. The well-known Orellanus syndrome, characterized by the absence of gastrointestinal symptoms and delayed onset of renal failure, should be considered in the differential diagnosis (Kirchmair et al., 2012). There is no specific treatment for *Amanita smithiana* poisoning available. Hemodialysis for acute renal failure and symptomatic supportive treatment are the main therapies for these types of poisonings (Yang et al., 2006).

Mushrooms that cause erythromelalgia: *Clitocybe acromelalga*, belonging to the genus *Clitocybe*, is a species reported to cause erythromelalgia and is frequently found in Japan. *Paralepistopsis amoenolens,* which has caused similar findings, was previously known as *Clitocybe* species, and its presence in Türkiye has been shown recently (Kaygusuz et al., 2017). Acromelic acid (ACRO) in the content of *Clitocybe acromelalga* is considered a toxin that causes poisoning. Of the five types of ACRO isomers identified, ACRO-A and ACRO-B have been reported to be responsible for toxicity. Apart from acromelic acid, the clitidine contained in the mushroom is thought to be responsible for the toxicity, although its vasodilator effects are low. In addition, peripheral blood flow disorders and inflammatory mediators such as calcitonin gene-related peptides (CGRP) are thought to contribute to toxicity. Clinical findings present with redness, swelling and burning pain in the extremities that develops a few days after ingestion. High-dose intravenous administration of nicotinic acid may be efficacious in treating erythromelalgia associated with *Clitocybe acromelalga* poisoning (N. Nakajima et al., 2013; Nobuhito Nakajima et al., 2013).

3. Delayed onset mushroom poisonings (>1 day) (Table 3)

Table 3. Mushroom types, toxins, symptoms and time of onset of symptoms in delayed-onset mushroom toxicity (> 1 day)

Type of mushroom	Toxin	Symptoms	Time of onset of symptoms
Orellanine, Cortinarius species	Orellanin Cortinarin A, B, and C	Nephrotoxicity	Days-weeks
Tricholoma equestre *Russula* subnigrans	Russuphelins A, B, C, D, E, and F	Rhabdomyolysis	24-72 hours
Hapalopilus rutilans	Polyporic acid	Neurotoxicity	Not well known

Mushrooms that cause delayed nephrotoxicity: Cortinarius species are mushrooms that cause nephrotoxicity in the late period. *Cortinarius orellanus, Cortinarius rubellus,* formerly named *Cortinarius speciosissimus* or *Cortinarius orellanoides,* are among these nephrotoxic mushrooms. The toxin orellanin is a bipyridine N-dioxide in the content of such mushrooms, showing its toxic effects on the kidney with the development of oxidative stress and suppression of antioxidant enzyme systems. Additionally, *Cortinarius* species also contain cyclic decapeptides (cortinarin A, B, and C) that produce renal damage. The onset of symptoms in

orellanin poisoning occurs after a long latent period. The onset of symptoms is delayed for 2-4 to 14 days after ingestion. The higher the amount of mushrooms eaten, the shorter the latent period. Renal toxicity can develop in different ways as temporary, severe and irreversible. Clinical findings in the renal phase are vomiting, polydipsia, low back pain, nausea, vomiting, abdominal pain, headache, polyuria, asthenia, diarrhea, anorexia, myalgia, tremor, dizziness, sweating, tinnitus, burning in the mouth, visual defects, myalgia, oliguria, hematuria, proteinuria, anuria and glucosuria. In the laboratory analysis, leukocytosis and an increase in serum creatinine levels were observed. In the treatment of poisonings, hemodialysis/peritoneal dialysis, extracorporeal hemoperfusion, and plasmapheresis can be applied. Kidney transplantation can be performed in necessary cases (Dinis-Oliveira et al., 2016; Hedman et al., 2017).

Mushrooms that cause rhabdomyolysis: *Tricholoma equestre* is a mushroom known to cause late-onset rhabdomyolysis. The toxin of *Tricholoma equestre* has not been identified. It is a mushroom that causes rhabdomyolysis 24-72 hours after ingestion. In the case of poisoning with these mushrooms, fatigue, nausea, and excessive sweating without fever are observed. Acute kidney injury may be observed due to muscle wasting (Laubner & Mikulevičienė, 2016). Additionally, *Russula subnigricans* is the causative mushroom in cases of acute rhabdomyolysis. Russuphelins A, B, C, D, E, and F are isolated toxins from Russula subnigricans. Recently, isolated cycloprop-2-ene carboxylic acid was associated with fatal rhabdomyolysis (Lin et al., 2015). It is thought that this toxin may cause rhabdomyolysis by triggering some biochemical mechanisms. In rhabdomyolysis, ATP is mainly depleted in myocytes, resulting in an irregular increase in intracellular calcium, resulting in myocyte lysis. Therefore, hypocalcemia and hyperkalemia as electrolyte disturbances are evident in this type of mushroom poisoning (Cho & Han, 2016). Clinical findings of *Russula subnigricans* include rhabdomyolysis, serious electrolyte disturbances, respiratory failure, acute renal failure, pulmonary edema, ventricular tachycardia, and circulatory shock. In this type of mushroom poisoning, fluid support and correction of hyperkalemia are the main treatment approaches. Hypocalcemia does not need to be treated unless symptomatic. Although there is no evidence, patients may benefit from continuous venovenous hemofiltration or hemodiafiltration. In addition to seizure prophylaxis and ventilator support, hemodialysis and kidney or liver transplantation may be necessary

for patients with impaired kidney or liver function (Cho & Han, 2016).

Mushrooms cause delayed neurotoxic effects: *Hapalopilus rutilans* is a mushroom that causes delayed encephalopathy. Polyporic acid (PA) causes toxicity. What is known about this mushroom poisoning has often been described in experimental studies. It has been reported that PA inhibits the dihydroorotate dehydrogenase enzyme and has cytotoxic effects. It has been stated that it may have neurotoxic, hepatotoxic and nephrotoxic effects (Kraft et al., 1998; Villa et al., 2013).

The classification of mushroom poisonings into early-onset, delayed-onset, and late-onset groups based on clinical findings can be helpful, but it also has some challenges and limitations. Here are a few:

Overlapping symptoms: The clinical manifestations of mushroom poisonings can vary widely, and there can be overlapping symptoms between different categories. Some symptoms may not fit neatly into a specific group, making it challenging to assign a precise classification.

Variation in onset times: While the classification provides general time ranges for each group, the onset of symptoms can vary among individuals. Factors such as the type of mushroom ingested, the amount consumed, and individual variations in metabolism can affect the timing of symptom onset. This variation makes it challenging to rely solely on onset time for accurate classification.

Limited diagnostic tests: Diagnosing mushroom poisonings can be challenging due to the lack of specific diagnostic tests readily available in clinical settings. Identifying the exact mushroom species responsible for the poisoning often requires specialized expertise and laboratory analysis, which may not be easily accessible in all healthcare settings.

Limited data on toxicity: The classification is based on the available knowledge and understanding of mushroom toxicity. However, the toxic compounds in mushrooms can vary, and new toxins may be discovered over time. The current classification may not encompass all possible toxic effects and presentations of mushroom poisonings.

Individual variability: Different individuals may have varying sensitivities and reactions to mushroom toxins, leading to differences in symptom severity and clinical course. This individual variability makes it challenging to apply a uniform classification system to all cases.

Reporting bias: Mushroom poisonings are often underreported, especially in

milder cases or in regions with limited surveillance systems. This can lead to an incomplete understanding of the frequency and spectrum of mushroom poisoning cases, limiting the generalizability of the classification system.

Lack of specific treatments: While the classification provides a framework for understanding different types of mushroom poisonings, it does not necessarily guide specific treatment strategies. Treatment approaches primarily focus on supportive care, symptom management, and addressing complications. The classification may not offer clear guidance on targeted antidotes or definitive therapies for specific types of mushroom poisonings.

Conclusion

All mushroom poisonings' frequency varies regionally, and a very low rate causes fatal poisoning. It is important to distinguish mushroom poisoning from food poisoning. For this reason, the history of wild mushroom consumption, ingested amount, time of ingestion, and type and onset of symptoms are essential for medical evaluation and management.

In the diagnosis of poisoning with mushrooms, having a history ingestion of wild mushrooms and the time of onset of the findings suggest poisoning. It is often not possible to evaluate the mushroom by a mycologist or to measure toxins from blood or urine. For these reasons, the differential diagnosis of mushroom poisoning is often based on clinical findings. The treatment for early-onset mushroom poisoning is gastrointestinal decontamination with oral activated charcoal, fluid rehydration and symptomatic treatment. However, it should not be forgotten that even a single toxic mushroom that could mix with edible mushrooms can cause poisoning in all patients with a history of eating picking mushrooms, even if the findings are out before six hours. Late-onset mushroom poisoning may be life-threatening due to liver and renal failure. In poisoning with *Amanita phalloides*-type mushrooms, liver necrosis and death can be observed due to the late appearance of the findings after an asymptomatic period. Although there are antidotes such as silibinin, penicillin G, and N-acetylcysteine in the treatment of such mushrooms, their effectiveness has not been proven. The approach to mushroom poisoning is similar all over the world and treatment often includes symptomatic therapy. To prevent such mushroom poisoning, it is important to raise public awareness about not eating wild mushrooms.

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