Mushrooms

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Abstract

The incidence of fungal poisoning varies considerably globally and is related to local habits, economic factors and lifestyle. Mushroom poisoning is mostly an accidental result of a mix-up between edible and toxic fungi. However, intentional ingestion of psychotropic ('magic') mushrooms has become a problem. Among thousands of mushroom species worldwide, fewer than a hundred are severely toxic. Most fungal toxins cause mild or moderate poisoning, often only gastroenteritis; the ingestion of a few species of extremely poisonous fungi defines the medical dimension of the problem. The most dreaded poisonings are those caused by cytotoxic fungi, for example amatoxins in death cap (*Amanita phalloides*) and destroying angel (*Amanita virosa*); both cause severe gastroenteritis and liver damage. Orellanine, occurring in certain *Cortinarius* spp., can induce severe and persistent kidney damage. Dramatic, but rarely lethal, effects are caused by fungi containing neurotoxins such as muscarine (*Clitocybe* and *Inocybe* spp.), psilocybin (*Psilocybe* and *Panaeolus* spp. – 'magic' mushrooms), isoxazoles (fly agaric, panther cap) and gyromitrin (false morels). Treatment is focused on general symptomatic and supportive care, although antidotes exist for fungi containing muscarine (atropine), gyromitrin (pyridoxine) and amatoxins (silibinin [silibinin is approved e.g. in Sweden and Germany (Legalon SIL D)], penicillin); the benefit of the latter has not yet been fully established.

Keywords amatoxin; antidotes; gyromitrin; isoxazoles; muscarine; mushroom poisoning; orellanine; psilocybin

Introduction

The incidence of mushroom poisoning varies geographically depending on climate, occurrence of toxic fungi, lifestyle and local traditions. Toxic mushroom ingestion can be related to:

- confusion between edible and poisonous species
- ignorance of the risks (careless harvesting)
- intentional ingestion of psychotropic mushrooms
- accidental ingestion by children
- suicidal ingestion (rare).

Diagnosis involves a careful history, assessment of the clinical features and, sometimes, examination of mushroom specimens by a mycologist. If available, chemical analysis can be useful in the acute phase for detecting and measuring the concentrations of, for example, amatoxin.

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Cytotoxic mushrooms containing amatoxins, orellanine and gyromitrin

Amatoxins

These occur in *Amanita phalloides* (Figure 1), *Amanita virosa*, *Amanita verna*, *Galerina marginata* and in some *Lepiota* spp.

Mechanisms of toxicity and toxicokinetics: amatoxins are highly toxic, and large doses can result in death in spite of treatment. Amatoxins are cyclic octapeptides that inhibit transcription from DNA to mRNA because of the blockade of nuclear RNA polymerase II. This will result in impaired protein synthesis and cell death.[1] Other suggested mechanisms are induction of apoptosis, formation of oxygen free radicals and depletion of hepatic glutathione.

Amatoxins are rapidly absorbed and distributed, and uptake is particularly high in the parenchymal cells of the liver, the kidneys and the intestinal mucosa. Excretion is mainly renal, but significant amounts are also excreted in bile and faeces.[2]

Clinical features:[1–3] intense gastrointestinal symptoms, with severe watery diarrhoea, start 8–24 hours (mean 12 hours) after ingestion and persist for 24 hours or longer. Patients become dehydrated, exhausted, hypovolaemic, hypotensive and sometimes hypoglycaemic. Signs of liver damage appear during the second day and hepatic failure can ensue. Impaired kidney function is often seen initially because of dehydration and shock, but its later occurrence is due to amatoxin-induced renal damage, which is a poor prognostic sign. Taken together, these features may suggest a probable fatal outcome.

Management:[1–3] all patients who have eaten a mushroom meal containing amatoxin fungi should be given fluids to replace the heavy loss of body fluids and electrolytes. Acid–base correction should be performed. Hepatic and renal function are supported conventionally.

Repeated doses of charcoal can enhance the excretion of amatoxin. In adults, an initial dose of activated charcoal 50 grams should be given and should be followed by repeated doses of activated charcoal 25 grams every 4 hours for 3 days. In children, an initial dose of activated charcoal 25 grams is given and followed by charcoal 10 grams every 4 hours for 3 days. A modestly increased diuresis (around 200 ml/hour in adults) is advised for the first 24–48 hours to support toxin elimination, although the benefit has not been demonstrated.

The value of silibinin or benzylpenicillin in reducing amatoxin-induced hepatic toxicity is not proven conclusively, but silibinin 5 mg/kg intravenously over 1 hour followed by 20 mg/kg/24 hours by continuous infusion should be considered in cases of substantial ingestion. Treatment is usually given for 3 days after ingestion. Benzylpenicillin 300 mg/kg/24 hours by continuous infusion can be used if silibinin is unavailable. Some recent experimental and clinical data suggest that acetylcysteine might also be of value. Liver transplantation occasionally has to be considered in severe, life-threatening poisoning, normally on day 4–8 after ingestion.

Orellanine

Orellanine is a potent nephrotoxin occurring in a number of fungi belonging to the *Cortinarius* genus, in particular *Cortinarius*

Figure 1 *Amanita phalloides* ('death cap') contains amatoxins that cause severe gastroenteritis and hepatic necrosis.

orellanus and *Cortinarius speciosissimus*. A large number of severe poisonings related to these toxic fungi have occurred in different parts of Europe. Confusion with other, non-toxic fungi is common.

Mechanism of toxicity: orellanine and its derivatives have a bipyridyl structure. Orellanine remains intact and stable in dry fungi for many years. Heating, freezing or drying does not reduce the toxicity of these fungi. The mode of action is not fully understood, but a metabolite of orellanine is believed to inhibit protein synthesis in the kidneys. A number of other hypotheses have been suggested, including free radical damage, peroxidative cell damage, immunological reactions and glutathione depletion. Histopathological changes of interstitial nephritis with oedema and leucocyte infiltration, tubular necrosis, basal membrane rupture and eventually fibrosis are observed.[1,4,5]

Clinical features:[1,4,5] typically, the onset of symptoms is delayed for 2–4 days (up to 14 days in cases where exposure is smaller). Some patients suffer mild gastrointestinal discomfort before developing signs of renal impairment. Headache, fatigue, intense thirst, chills, muscular discomfort and abdominal, lumbar and flank pain have been observed. Transient polyuria is followed by oliguria with proteinuria, haematuria and, characteristically, leucocyturia. Anuria can then follow. Renal function can recover completely or only partially. End-stage renal failure is reported in 10–40% of poisonings.

Management:[1,4,5] due to no or very mild initial symptoms, patients are generally admitted to hospital late and with renal impairment already present. Management involves careful monitoring of renal function and haemodialysis if renal failure supervenes. If renal function does not recover, renal transplantation can be required. If the patient is admitted within 24 hours of mushroom ingestion, haemodialysis to increase orellanine elimination should be considered but is of unproven benefit.

Gyromitrin

Gyromitrin is found in *Gyromitra* species, including in particular the false morel (*Gyromitra esculenta*) and *Cudonia circinans*.

Mechanism of toxicity:[1,6] gyromitrin is water-soluble and volatile. It can be removed partly by boiling or drying. It decomposes in the stomach to form hydrazines that are irritant. Hydrazines reduce the concentration of pyridoxine in the central nervous system, and hence diminish γ-aminobutyric acid (GABA) synthesis, cause glutathione depletion in red blood cells and can form free oxygen radicals that bind to hepatic macromolecules.

Clinical features:[1,6] vapours from the mushrooms are irritating to the eyes and respiratory tract and can also cause systemic poisoning. Systemic features, however, usually occur after ingestion of inadequately prepared morels. Gastrointestinal symptoms appear 5–8 hours or more after exposure. Vertigo, sweating, diplopia, headache, dysarthria, incoordination and ataxia can follow. Rarely, seizures, coma, haemolysis, methaemoglobinaemia, hypoglycaemia and hepatic damage have been observed.[1]

Management: symptomatic and supportive care is required, and it is wise to administer a glucose infusion to prevent hypoglycaemia. Pyridoxine, 25 mg/kg as an infusion over 30 minutes, should be given after substantial ingestion and if central nervous system toxicity is present.[1,6] Repeat doses can be required. If seizures persist, diazepam should be given.