AMANITA PHALLOIDES POISONING, EARLY ACTIVATED CHARCOAL PLUS N-ACETYL CYSTEINE TREATMENT: CASE REPORT ANDA BRIEF LITERATURE REVIEW

LOUI M. AL-HUSINAT[1‡], GIUSEPPE FERRARA[2], ALAMEEN ALSABBAH[3],ANTONELLA COTOIA[2], RENATA BECK[2‡]

[1]Department of Clinical Medical Sciences, Faculty of Medicine, Yarmouk University, Yarmouk, Jordan; [2]Department of Anesthesia and Intensive Care Unit, University of Foggia, Foggia, Italy; [3]Faculty of Medicine, Yarmouk University, Yarmouk, Jordan

[‡]equal contribution

Consumption of wild poison mushrooms is one of the serious poisonings which may end in death. The present case report and recent literature review describe *Amanita phalloides* mushroom poisoning and possible treatment for this emergency state. A 59-year-old male presented in the Emergency Unit of the Foggia University Hospital, Italy, with clinical signs of extreme dizziness, nausea, vomiting, and diarrhea, 12 h after consuming one ovule of a wild mushroom that was mistaken for an edible ovule of the *Boletus edulis* mushroom. The suspected poison mushrooms were collected in the forest near the city of Foggia, Italy. Urgent examination of urine showed the presence of α-amanitin. After 6 days of intensive and supportive treatment with activated charcoal and N-acetyl cysteine, the patient was transferred to the internal medicine department and discharged without organ complications 10 days after mushroom ingestion. Early recognition of mushroom poisoning and immediate intensive treatment with supportive care give the patients a better chance for survival after this fatal poisoning.

Key words: **activated charcoal, *Amanita phalloides,* amatoxins, mushrooms, poisoning, N-acetyl cysteine**

Address for correspondence: **Renata Beck, MD**
Department of Clinical Medical Sciences
Faculty of Medicine, Yarmouk University
Yarmouk, Jordan
E-mail: beckrenata64@gmail.com

INTRODUCTION

Out of thousands of mushroom species found in the world, just up to 100 are toxic to humans; most of them are *Amanita* species. Two toxins produced by amanita species, phallotoxins and amatoxins, are responsible for phalloidin syndrome. Amatoxin-containing mushrooms (*Amanita, Lepiota,* and *Galerina*) are responsible for 90% of mushroom ingestion-related deaths (1). Although it is more dangerous in children, the amount that can be found in species like Amanita is sufficient to poison an adult person causing liver and renal damage (2, 3). The human lethal dose, LD50, is 0.1 mg/kg body weight (4). Amanita mushroom poisoning is one of the most serious food poisonings in the world characterized by a long incubation phase, gastrointestinal and liver phase, eventual coma, and death. *Amanita* species such as *A. phalloides*, *A. verna*, *A. virosa, A. amerivirosa,* and *A. vidua* sp. *nov.,* are responsible for almost all mushroom poisoning in Europe (5), but this health problem is present worldwide (6-9).

Amatoxins are heat- and frozen-stable toxic cyclic peptides (10-12). Two potent amatoxins are α- and β-amanitins (AMA). They irreversibly inhibit ribonucleic acid polymerase (RNA) II in the liver and kidneys, blocking the synthesis of proteins including intracellular enzymes (13-15). Studies on animal models suggest that α-AMA causes hepatocyte necrosis and apoptotic cell death (16,17).

The fatal course of mushroom poisoning can be avoided with early diagnosis, but despite intensive treatment, antidotes, and antioxidative therapies, mortality rate in this type of poisoning remains high (18-22). Our case report describes mushroom *Amanita phalloides* poisoning in one of our patients (Figure 1).

Figure 1. *The Amanita phalloides mushroom (original photo). This photo shows the second mushroom ovule that was not ingested by our patient.*

METHODS

Using the PubMed, Medline, Ovid, Google, Google Scholar, and Cochrane databases, the keywords (activated charcoal, *Amanita phalloides*, amatoxins, mushrooms, poisoning, N-acetyl cysteine [NAC]) as the medical subject headings were searched with results limited to the past 20 years (2002-2022), including only peer-reviewed scientific articles on amatoxin-containing mushroom poisonings and new treatment guidelines over the study period to meet the main objectives of this report. Attention was mainly on the therapies used in case reports, case series, short communications, and letters to the editor in the study period.

CASE REPORT

Our patient was a 59-year-old male with suspected *Amanita phalloides* poisoning. The patient was received to the Emergency Unit with a red code, about twelve hours after the suspected ingestion of a poison mushroom. The circumstances under which the poisoning occurred were unintentional and accidental. He was conscious, oriented, and eupneic. He reported symptoms of dizziness, nausea, uncontrollable vomiting, diarrhea, and severe abdominal pain. The Apulian Regional Poison Center was contacted and emergency blood chemistry and gas tests, blood pressure, electrocardiogram, and echocardiogram were performed. The patient was transferred to the Intensive Care Unit (ICU) for continuous intensive care and monitoring.

In ICU, after cardio-circulatory monitoring, a nasogastric tube was placed and activated charcoal administered every 6 hours in doses of 20 g. The patient was hydrated with Ringer lactate intravenously (IV) at 63 mL/h; it was administered in a bolus of NAC 150 mg/kg body weight in 60 minutes, then 300 mg/kg body weight (2 mL/h[1] in glucose 5% 500 mL) in continuous infusion. Biological samples were sent for detection of AMA toxins (with confirmation of the presence of the α-AMA toxins in the urine sample). We contacted immediately the University Hospital Polyclinic of Bari for a possible liver transplant. We began monitoring hepatic, renal, and coagulation function and hemachrome every six hours (Table 1, Figure 2). On day 6 of ICU stay and after normalization of all examinations, the patient was transferred to the internal medicine department.

Table 1. *Laboratory parameters over time (T) in hours in our patient*

Recovery time (T) (hours)	PT (%)	PTT (sec)	INR (Ratio)	AST (U/L)	ALT (U/L)	LDH (U/L)	DB (mg/dL)	TB (mg/dL)	PLT (mm^3)	Hb (g/dL)	Cr (mg/dL)	BUN (mg/dL)
Normal range	70-120 %	30-40 sec	0.8-1.2	15-41 U/L	17-63 U/L	140-280 U/L	≤0.3 mg/dL	0.2-1.2 mg/dL	150-450 $x10^3$	M13.8-17.2; F12.1-15.1 g/dL	0.8-1.2 mg/dL	7-20 mg/dL
T0	93	39.7	1.04	32	32	507	0.1	0.7	171	14.9	0.82	43
T6	88	32.6	1.09	51	56	898	0.1	1,1	185	14.4	0.85	39
T12	81	33.6	1.14	147	169	923	0.2	1	168	14.3	0.84	39
T18	81	33	1.14	647	991	1156	0.2	1.5	175	14.3	0.75	37
T24	85	34.5	1.1	680	839	1762	0.3	1,9	160	13.6	0.81	37
T30	75	33.4	1.1	455	973	1091	0.3	1.9	164	13.8	0.85	34
T36	71	33.3	1.25	412	887	945	0.3	1.9	170	14.6	0.69	30
T42	71	31.4	1.25	315	836	1091	0.3	1.8	159	13.9	0.71	29
T48	65	32.4	1.34	295	789	698	0.3	1.8	169	14.3	0.8	29
T54	65	32.7	1.34	246	761	523	0.25	1.6	158	14	0.73	27
T60	63	32.6	1.35	152	566	498	0.2	1.3	157	13.3	0.74	23
T66	62	32.5	1.36	76	381	452	0.3	1.8	157	13.3	0.85	23
T72	60	32	1.37	60	326	380	0.2	0.8	156	12.4	0.79	20
T78	62	31	1.35	45	278	379	0.2	0.8	145	12.1	0.81	19
T84	60	29	1.41	34	227	424	0.2	0.8	139	12	0.75	20
T90	62	31.5	1.05	32	198	365	0.2	0.8	135	11.8	0.8	22
T96	50	32.3	1.57	22	151	344	0.2	0.8	130	11.6	0.83	19

PT = prothrombin time; PTT = partial thromboplastin time; INR = International Normalized Ratio; ALT = alanine aminotransferase; AST = aspartate aminotransferase; LDH = lactate dehydrogenase; DB = direct bilirubin; TB = total bilirubin; PLT = platelet; Hb = hemoglobin; Cr = creatinine; BUN = blood urea nitrogen; M=male; F=female

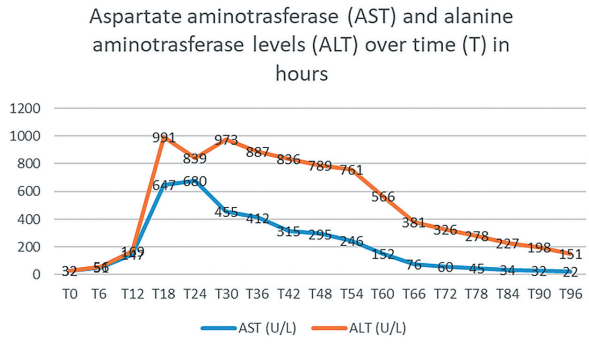

Figure 2. *Liver aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels in our poisoned patient over time (T) in hours during hospitalization. Serum ALT and AST have been used as sensitive indicators of liver injury caused by amatoxins.*

DISCUSSION AND CONCLUSION

Amanita phalloides is a toxic mushroom that can cause serious health problems in adults and in children, such as acute renal and liver injury, and even death(1-3). Angioi *et al.* report unusual end-stage kidney disease in a patient intoxicated with *A. phalloides* (2). Amanita poisoning mostly occurs worldwide as an un intentional poisoning due to false distinction between toxic and edible mushroom species.

The lethal dose (LD) for humans of AMA is 0.1 mg/kg body weight (4). This LD can be present in a single mushroom and can generate irreversible liver damage within 48 hours of ingestion (23).

The two toxins of Amanita species are phallotoxins and amatoxins. Phallotoxins are not absorbable in gastrointestinal tract and lead to irritation of gastric mucosa; as a result, their toxicity is limited to only gastrointestinal manifestations within the first 24 hours of ingestion. On the contrary, a massive amount of amatoxin α-AMA reaches the liver after gastrointestinal absorption. The two transporters of the liver cellular membrane that transport these toxins into cells are organic anion-transporting polypeptides (OATP1B3) and bile acid transporter Na(+)/taurocholate transport protein (NTCP) (14,28). OATPs mediate the uptake of a wide variety of organic compounds and also amatoxins into the liver cells. The presence of the OATP1B3 hepatic entry transporter, which mediates a rapid uptake of amatoxins, on hepatic cells, makes the liver a privileged target organ in case of amatoxins poisoning (14).

The toxic mechanism of AMAs is attributed to the non-covalent nuclear inhibition of RNA polymerase II in renal tubules, hepatocytes, and lymphocytes. The messenger RNA transcription process is suppressed, thus toxin-inhibited protein synthesis leads to cellular hepatic necrosis and apoptosis (1,4, 11-15).The hepatic centrilobular and periportal hemorrhagic hepatic necrosis brings to the rapid rise in hepatic damage biomarkers, principally serum transaminases, and coagulopathies result from deficiencies in the synthesis of hepatic clotting factors. As the liver function fails, tubulointerstitial nephropathy follows and precipitates the hepatorenal syndrome that may be rapidly fatal if liver transplantation is not possible or available as a treatment option (22,31,35,36).

Moreover, in the first 72 h of intoxication, amatoxins are excreted unchanged in the urine and their concentration rises from 6 to 90 times higher than in the liver (24). This explains the nephrotoxicity of those toxins, while dehydration may also contribute to kidney injury in these patients. Amatoxins can be found for 30 h in plasma or serum, and up to 72 h in urine (25).

The first gastrointestinal symptoms can be seen only 6 to 12 hours after ingesting the mushrooms (1, 11-15, 21). Sometimes the symptoms may appear after a long latency period of 40 hours, and can negatively influence medical intervention because cellular apoptosis and severe hepatic necrosis with fulminant hepatic failure occurs (1,4,5). Bonacini *et al.* also found that women and older patients were more likely to have a poor outcome than men and younger patients (4). Rapid analysis of amatoxins and phallotoxins that are found in body fluids is essential for vital organ recovery (26,27).

Actually, there are no guidelines or current strategies for amatoxin poisoning, and therapies have not been subjected to rigorous efficacy testing in randomized controlled trials because of ethical reasons. Around 10%-20% of cases of *Amanita phalloides* poisoning have fatal outcome or finish with liver transplantation, despite the use of antidotes (11).

The new literature recommendations indicate that prompt contact with regional poison centers is an important factor to provide the best clinical approach in cases of poisoning. Furthermore, supportive therapy for vital functions, including volume replacement and electrolyte and bicarbonate correction is highly important. The rationale of this intervention is to avoid hypovolemic shock and reduce the risk of tubular necrosis (2,29,30).

The next step is toxin binding and decrease in the concentration of amatoxins. The intervention consists of gastrointestinal decontamination with gastric lavage that removes the contaminated meal and the amatoxin concentration from the stomach. Together with

activated charcoal, it has a synergistic effect to avoid the absorption process of toxins from the enteric tract. This intervention interrupts the enterohepatic reabsorption of amatoxins (31-39).

Regarding α-AMA antidote therapy, there are three medications available, i.e., NAC which is an antioxidant, and penicillin G and silibinin, which act by inhibiting the hepatocyte uptake of α-AMA. Several studies recommend the administration of two antidotes with different mechanisms of action to achieve maximum benefit (2,11,13,14,29-38,40-42) (Table 2). NAC has antioxidant and glutathione-regenerating effects. Thus, penicillin G and silibinin inhibit the uptake of amatoxins by hepatocytes, which are mediated by the OATP1B3 transporter (43).

Table 2. *Principal articles available in the literature in the last 20 years on Amanita phalloides poisoning with short description of their main characteristics and relevant intervention and experimental therapies*

Paper ID	Year	Type of article	Patient(s)	Mushroom	Intervention therapy
Enjalbert *et al.* **(11)**	2002	Retrospective study	2108 patients	*A. phalloides*	Silibinin, NAC, benzylpenicillin
Letschert *et al.* **(14)**	2006	Experimental study	*In vitro* study	*A. phalloides* toxin uptake	Rifampicin, antamadine, MK571, silibinin, dihemisuccinate, cyclosporine A
Ennecker-Jans *et al.* **(40)**	2007	Case report	54-year-old man, 51-year-old woman, 55-year-old woman	*A. phalloides*	High-dose penicillin G, silibinin, and NAC
Thaler *et al.* **(33)**	2008	Letter to the editor	72-year-old man	*A. phalloides*	Activated charcoal, NAC, silibinin
Magdalan *et al.* **(22)**	2010	Comparative study	*in vitro* study on cultured human hepatocytes	*A. phalloides* α-amanitin	Benzylpenicillin, NAC,silibinin
Grabhorn *et al.* **(34)**	2013	Retrospective study	5 children	*A. phalloides*	Intravenous (IV) silibinin, NAC, active charcoal, liver transplantation
Ward *et al.* **(36)**	2013	Case reports	72-year-old woman, 45-year-old son	*Amanita Ocreata*	Activated charcoal , NAC, penicillin (1,000,000 units intramuscular), silibinin, and transfer to a center with liver transplant capabilities
Vanooteghem *et al.* **(42)**	2014	Case series	4 women	*A. phalloides*	NAC, silibinin, liver transplantation
Varvenne *et al.* **(30)**	2015	Illustrative case	9-year-old boy, 11-years-old girl,mother	*Lepiota brunneoincarnata*	IV rehydration, analgesics, oral activated charcoal, IV silibinin, penicillin G, NAC
Chibishev *et al.* **(38)**	2015	Case series	8 patients	*A. verna*	Charcoal, NAC, vitamin therapy, penicillin, H2 blockers, ornicetil
Yilmaz *et al.* **(37)**	2015	Case report	61-year-old man	*A. Phalloides*	Activated charcoal, penicillin G
Garcia *et al.* **(49)**	2015	*In silico* study on animals	intoxicated animals (n=20 male CD-1 mice)	α-amanitin	Polymyxin B
Vo *et al.* **(29)**	2017	Morbidity and Mortality Weekly Report, California Department of Public Health	14cases	*Amatoxin exposure*	Aggressive IV fluid hydration, IV octreotide, IV silibinin, liver transplantation
Bonacini *et al.* **(32)**	2017	Brief Communication	27 patients	*A. phalloides*	Activated charcoal and NAC, penicillin G, silymarin, orthotopic liver transplantation
Li *et al.* **(41)**	2018	Case report	41 and 48- years-old woman	*Amanita fuliginea*	Silibinin, penicillin G, and plasma exchange
Sun *et al.* **(47)**	2019	Case reports	55-year-old male	*Lepiota brunneoincarnata*	Naso-biliary drainage, Legalon silibinin
Wang *et al.* **(35)**	2019	Case series	56-years-old male, 58-years-old female, 58-years-old female	*Amanita fuliginea*	Silibinin, activated charcoal, glutathione, and magnesium isoglycyrrhizinate, fibrinogen and platelets
Garcia *et al.* **(50)**	2019	Short-term study (24 h) and a survival study (30 days) on animals	intoxicated animals (n=40+40 male CD-1 mice)	α-amanitin	Polymyxin B and methylprednisolone
Wennig *et al.* **(39)**	2020	review article	4441 cases in Germany	90% of 32 death was caused by *A. phalloides*	Activated charcoal, silibinin, NAC, hemodialysis/ albumin dialysis, liver transplant as a lifesaving measure
Zuker-Herman *et al.* **(51)**	2021	Short communication	79-year-old man, 72-year-old woman	*A. phalloides*	IV rifampicin, activated charcoal, NAC
Le Daré *et al.* **(48)**	2021	Short communication	*in vitro* study	*A. phalloides*	HEMO2life®

Angioi *et al.* **(2)**	2021	Case report	a 79-year-old man and his wife	*A. phalloides*	NAC, SLEDD-f, hemodialysis
Smędra *et al.* **(10)**	2022	Case report	28-year-old man	*A. phalloides*	Liver transplantation

SLEDD-f= sustained low-efficiency daily diafiltration; MK571 [(3-(3-(2-(7-chloro-2-quinolinyl)ethenyl)phenyl)((3-dimethylamino-3-oxopropyl) thio)methyl)thiopropanoic acid];NAC= N-acetylcysteine; HEMO2life®=extracellular hemoglobin commercialized by Hemarina, Morlaix, France

Treatment for liver failure is the same as for the liver failure of other etiologies. The Clichy criteria (44) and Munich criteria (45) provide a suitable basis for decision-making on whether a liver transplant is indicated. Liver transplantation is limited mainly by the availability of donors.

Impairment of coagulation factor production caused by liver damage may necessitate administration of fresh frozen plasma, and forced diuresis may be indicated in the first 5 days as α-AMA is mainly excreted in the urine.

Extracorporeal purification techniques such as hemodialysis, hemoperfusion, or plasmapheresis have been described, although their effectiveness remains limited (11). In the case of liver transplantation, treatment with high-volume plasma exchange has been shown to increase liver transplant-free survival (46).

Interestingly, Sun *et al.* showed that using biliary drainage to interrupt enterohepatic cycling of amatoxins reduced the intestinal amatoxin reuptake (47).

Some of new and promising therapies for amatoxin poisoning include extracellular hemoglobin called M101 extracted from the marine worm *Arenicola marina*. It has intrinsic Cu/Zn-SOD-like (SOD, superoxide dismutase) activity and can be used as an oxygen carrier. Le Darè *et al.* suggest that M101 might effectively reduce AMA-induced hepatotoxicity and may have the potential for further investigation and therapeutic development (48) (Table 2).

Furthermore, some *in vitro* studies with polymyxin B may reveal it as a promising antidote for the future. It reduces liver necrosis caused by α-AMA and improves survival in intoxicated animals (49,50) (Table 2). It still needs to be approved by clinical trials on humans as an effective treatment for amatoxin poisoning. Also, rifampicin may be effective in the management of α-AMA toxicity (51).

This clinical case of severe poisoning with α-AMA confirmed by laboratory tests underlines the clinical importance of early diagnosis. Close collaboration between the Emergency Unit, ICU, and Apulian Regional Poison Center allowed the patient to recover, especially liver and kidney function compromised by poisoning, and to avoid liver transplantation (Figure 2, Table 1). It is crucial to start rapidly with correct medical procedures when amatoxin poisoning is suspected. The poisoned person must be transported to the hospital, perform toxicologic tests, and start appropriate treatment. The time of admission to the hospital is crucial for treatment options including gastric lavage, large doses of activated charcoal, moderately enhanced diuresis, silibinin, penicillin G, and NAC as single or combined therapy.

Nowadays, for aging and eating wild mushrooms is still popular all over the world, so variable prevention modalities can have an important role in reducing the incidence of this kind of poisoning. Public education, particularly in schools, organizing licensed mushroom collectors, and the sites where the collectors can control the collected mushrooms before ingestion are very important. Nevertheless, institutional information campaigns targeting inexperienced mushroom collectors should invest more effort to make them aware of the presence of such lethal mushrooms.

History of poisoning: Two poisonous mushroom ovules were collected in the forest near Foggia, Italy, by the patient's brother-in-law, an expert licensed mushroom collector. All the mushrooms collected were the edible mushroom *Boletus edulis* consumed by two families on the previous day. The two mushroom ovules mimicked *Boletus edulis* ovules and were present together at the same locus. The fact to be stressed is the high polymorphism of this mushroom, and for this reason, the popular names of the 'angel of death' and 'bastard egg' are justified.

REFERENCES

1. Horowitz BZ, Moss MJ. Amatoxin Mushroom Toxicity. In: StatPearls. Treasure Island (FL): StatPearls Publishing, June 28, 2022.

2. Angioi A, Floris M, Lepori N, Bianco P, Cabiddu G, Pani A. Extensive proximal tubular necrosis without recovery following the ingestion of *Amanita phalloides*: a case report. J Nephrol 2021;34(6):2137-40.

3. Grabhorn E, Nielsen D, Hillebrand G *et al.* Successful outcome of severe *Amanita phalloides* poisoning in children. Pediatr Transplant 2013;17(6):550-5.

4. Faulstich H. Mushroom poisoning. Lancet 1980;Oct 11;2(8198):794-5.

5. Alvarado P, Gasch-Illescas A, Morel S *et al. Amanita* section *Phalloideae* species in the Mediterranean Basin: destroying angels reviewed. Biology (Basel) 2022;11(5):770.

6. Brandenburg WE, Ward KJ. Mushroom poisoning epidemiology in the United States. Mycologia 2018;110(4):637-41.

7. Janatolmakan M, Ganji MR, Ahmadi-Jouybari T, Rezaeian S, Ghowsi M, Khatony A. Demographic, clinical, and laboratory findings of mushroom-poisoned patients in Kermanshah province, west of Iran. BMC Pharmacol Toxicol 2022;23(1):72.

8. Chen Z, Zhang P, Zhang Z. Investigation and analysis of 102 mushroom poisoning cases in Southern China from 1994 to 2012. Fungal Diversity 2014;64:123-31.

9. Jongthun R, Hemachudha P, Wacharapluesadee S, Hemachudha T. Low-cost management of mushroom poisoning in a limited-resource area: a 12-year retrospective study. Trop Doct 2020;50(2):135-8.

10. Smędra A, Wochna K, Zawadzki D, Berent J. Medical error in treatment of *Amanita phalloides* poisoning in pre-hospital care. Scand J Trauma Resusc Emerg Med 2022;30(1):20.

11. Enjalbert F, Rapior S, Nouguier-Soulé J, Guillon S, Amouroux N, Cabot C. Treatment of amatoxin poisoning: 20-year retrospective analysis. J Toxicol Clin Toxicol 2002;40(6):715-57.

12. Berger KJ, Guss DA. Mycotoxins revisited: Part I. J Emerg Med 2005;28(1):53-62.

13. Vetter J. Toxins of *Amanita phalloides*. Toxicon 1998;36(1):13-24.

14. Letschert K, Faulstich H, Keller D, Keppler D. Molecular characterization and inhibition of amanitin uptake into human hepatocytes. Toxicol Sci 2006;91(1):140-9.

15. Diaz JH. Amatoxin-containing mushroom poisonings: species, toxidromes, treatments, and outcomes. Wilderness Environ Med 2018;29(1):111-8.

16. Leist M, Gantner F, Naumann H *et al.* Tumor necrosis factor induced apoptosis during the poisoning of mice with hepatotoxins. Gastroenterology 1997;112:923-4.

17. Magdalan J, Ostrowska A, Podhorska-Okołów M *et al.* Early morphological and functional alterations in canine hepatocytes due to α-amanitin, a major toxin of *Amanita phalloides*. Arch Toxicol 2009;83:55-60.

18. Poucheret P, Fons F, Doré JC, Michelot D, Rapior S. Amatoxin poisoning treatment decision-making: pharmaco-therapeutic clinical strategy assessment using multidimensional multivariate statistic analysis. Toxicon 2010;55(7):1338-45.

19. Surai PF. Silymarin as a natural antioxidant: an overview of the current evidence and perspectives. Antioxidants (Basel) 2015;4(1):204-47.

20. Mengs U, Pohl RT, Mitchell T. Legalon® SIL: the antidote of choice in patients with acute hepatotoxicity from amatoxin poisoning. Curr Pharm Biotechnol 2012;(10):1964-70.

21. Mowry JB, Spyker DA, Brooks DE, McMillan N, Schauben JL. 2014 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 32ndAnnual Report. Clin Toxicol (Phila) 2015;53(10):962-1147.

22. Magdalan J, Ostrowska A, Piotrowska A *et al.* Benzylpenicillin, acetylcysteine and silibinin as antidotes in human hepatocytes intoxicated with alpha-amanitin. Exp Toxicol Pathol 2010;62(4):367-73.

23. Kaya E, Karahan S, Bayram R, Yaykasli KO, Colakoglu S, Saritas A. Amatoxin and phallotoxin concentration in *Amanita phalloides* spores and tissues. Toxicol Ind Health 2015 31(12):1172-7.

24. Jaeger A, Jehl, F, Flesch F, Sauder P, Kopferschmitt J. Kinetics of amatoxins in human poisoning: therapeutic implications. J Toxicol Clin Toxicol 1993;31:63-80.

25. Rentsch KM. Laboratory diagnostics in acute poisoning: Critical overview. Clin Chem Lab Med 2010;48:1381-7.

26. Abbott NL, Hill KL, Garrett A, Carter MD, Hamelin EI, Johnson RC. Detection of α-, β-, and γ-amanitin in urine by LC-MS/MS using 15N10-α-amanitin as the internal standard. Toxicon 2018;152:71-7.

27. Zhang S, Zhao Y, Li H *et al.* A simple and high-throughput analysis of amatoxins and phallotoxins in human plasma, serum and urine using UPLC-MS/MS combined with PRiME HLB μElution platform. Toxins (Basel) 2016;8(5):128.

28. Le Daré B, Ferron PJ, Gicquel T. Toxic effects of amanitins: repurposing toxicities toward new therapeutics. Toxins (Basel). 2021;13(6):417.

29. Vo KT, Montgomery ME, Mitchell ST *et al. Amanita phalloides*mushroom poisonings – Northern California, December 2016. MMWR Morb Mortal Wkly Rep 2017;66(21):549-53.

30. Varvenne D, Retornaz K, Metge P, De Haro L, Minodier P. Amatoxin-containing mushroom (*Lepiota brunneo incarnata*) familial poisoning. Pediatr Emerg Care 2015;31(4):277-8.

31. Zellner T, Prasa D, Färber E *et al.* The use of activated charcoal to treat intoxications. Dtsch Arztebl Int 2019;116:311-7.

32. Bonacini M, Shetler K, Yu I, Osorio RC, Osorio RW. Features of patients with severe hepatitis due to mushroom poisoning and factors associated with outcome. Clin Gastroenterol Hepatol 2017;15(5):776-9.

33. Thaler T, Aceto L, Kupferschmidt H, Mullhaupt B, Greutmann M. First intoxication with freshly picked *Amanita phalloides* in winter time in central Europe. J Gastrointest Liver Dis 2008;17(1):111.

34. Grabhorn E, Nielsen D, Hillebrand G *et al.* Successful outcome of severe *Amanita phalloides* poisoning in children. Pediatr Transplant 2013;17(6):550-5.

35. Wang Q, Sun M, Lv H*et al.Amanita fuliginea* poisoning with thrombocytopenia: acase series. Toxicon 2020;174:43-7.

36. Ward J, Kapadia K, Brush E, Salhanick SD. Amatoxin poisoning: case reports and review of current therapies. J Emerg Med 2013;44(1):116-21. doi: 10.1016/j.jemermed.2012.02.020. Epub 2012 May 1. PMID: 22555054.

37. Yilmaz I, Ermis F, Akata I, Kaya E. A case study: what doses of *Amanita phalloides* and amatoxins are lethal to humans? Wilderness Environ Med 2015;26(4):491-6.

38. Chibishev A, Perevska Z, Simonovska N, Petkovska L, Miletic M, Shikole E. Severe mushroom poisoning in one Macedonian family. Int J Artif Organs 2015;38(8):425-32.

39. Wennig R, Eyer F, Schaper A, Zilker T, Andresen-Streichert H. Mushroom poisoning. Dtsch Arztebl Int 2020;117(42):701-8.

40. Ennecker-Jans SA, van Daele PL, Blonk MI, Varin DS, van Laar JA. Amatoxine-intoxicatie door soep van zelfgeplukte groene knolamaniet (*Amanita phalloides*) [Amatoxin poisoning due to soup from personally picked deathcap mushrooms (*Amanita phalloides*)]. Ned Tijdschr Geneeskd 2007;151(13):764-8.

41. Li Y, Mu M, Yuan L, Zeng B, Lin S. Challenges in the early diagnosis of patients with acute liver failure induced by amatoxin poisoning: two case reports. Medicine (Baltimore) 2018;97(27):e11288.

42. Vanooteghem S, Arts J, Decock S *et al.* Four patients with *Amanita phalloides* poisoning. Acta Gastroenterol Belg 2014;77(3):353-6.

43. Popp T, Balszuweit F, Schmidt A, Eyer F, Thiermann H, Steinritz D. Assessment of α-amanitin toxicity and effects of silibinin and penicillin in different *in vitro* models. Toxicol In Vitro 2020;67:104921.

44. Escudié L, Francoz C, Vinel JP *et al. Amanita phalloides* poisoning: reassessment of prognostic factors and indications for emergency liver transplantation. J Hepatol 2007;46:466-73.

45. Ganzert M, Felgenhauer N, Zilker T. Indication of liver transplantation following amatoxin intoxication. J Hepatol 2005;42:202-9.

46. Larsen, FS, Schmidt IE, Bernsmeier C. *et al.* High-volume plasma exchange in patients with acute liver failure: an open randomised controlled trial. J Hepatol 2016;64: 69-78.

47. Sun J, Zhang HS, Li HJ. A case study of *Lepiota brunneo incarnata* poisoning with endoscopic nasobiliary drainage in Shandong, China. Toxicon 2019;161:12-6.

48. Le Daré B, Ferron PJ, Bellamri N *et al.* A therapeutic oxygen carrier isolated from *Arenicola marina* decreases amanitin-induced hepatotoxicity. Toxicon 2021;200:87-91.

49. Garcia J, Costa VM, Carvalho AT *et al.* A breakthrough on *Amanita phalloides* poisoning: an effective antidotal effect by polymyxin B. Arch Toxicol 2015;89(12):2305-23.

50. Garcia J, Costa VM, Bovolini A *et al.* An effective antidotal combination of polymyxin B and methylprednisolone for α-amanitin intoxication. Arch Toxicol 2019;93(5):1449-63.

51. Zuker-Herman R, Tong R, Wong A. Intravenous rifampicin use in the management of *Amanita phalloides* toxicity. Clin Toxicol (Phila) 2021;59(9):843-5.

SAŽETAK

OTROVANJE GLJIVOM *AMANITA PHALLOIDES* – RANO LIJEČENJE AKTIVNIM UGLJENOM I N-ACETIL CISTEINOM: PRIKAZ BOLESNIKA I KRATAK PREGLED LITERATURE

L. M. AL-HUSINAT[1‡], G. FERRARA[2], A. ALSABBAH[3], A. COTOIA[2], R. BECK[2‡]

[1]Odjel za kliničke medicinske znanosti, Medicinski fakultet, Sveučilište Yarmouk, Yarmouk, Jordan; [2]Odjel za anesteziju i jedinica za intenzivno liječenje, Sveučilište u Foggiai, Foggia, Italija; [3]Medicinski fakultet, Sveučilište Yarmouk, Yarmouk, Jordan

Jedenje divljih otrovnih gljiva može dovesti do ozbiljnog otrovanja i smrti. Prikaz bolesnika i pregled najnovije literature opisuje otrovanje gljivama *Amanita phalloides* te moguće načine liječenja ovoga hitnog stanja. Poslije 12 sati nakon što je pojeo jajašce otrovne gljive, koje je zabunom zamijenio za jajašce jestive gljive vrganj *(Boletus edulis)*, 54-godišnji muškarac je došao na hitni prijam Kliničke bolnice u Foggiai, Italija, s kliničkom slikom velike slabosti, mučninom, povraćanjem i proljevom. Prikupljene gljive bile su ubrane u šumi blizu grada Foggia. Hitan pregled mokraće je pokazao prisutnost otrova alfa-amanitina. Nakon šest dana liječenja na intenzivnoj njezi aktivnim ugljenom i N-acetil cisteinom pacijent je bio prebačen na odjel interne medicine bez komplikacija na organima te je nakon 10 dana bio otpušten iz bolnice. Rano prepoznavanje otrovanja gljivama i rano intenzivno liječenje s potporom životnih funkcija daje dobre izglede za preživljavanje ovoga opasnog otrovanja.

Ključne riječi: **aktivni ugljen, *Amanita phalloides*, amatoksini, gljive, N-acetil cistein**