MUSHROOM (AMATOXIN-CONTAINING)

GENERAL INFORMATION

- Amatoxins are found in several mushroom species including *Amanita sp.*, *Galerina sp.*, and *Lepiota sp.*. Ingestion of amatoxin-containing mushrooms can lead to fulminant hepatotoxicity and death.
- Despite the severity of outcomes, there are limited treatment options available for amatoxin-exposed patients.
- Amatoxin enters into hepatocytes by a transporter protein (OATP 1B3) located in the liver.
- A potential therapeutic approach for management of amatoxin-exposed patients is inhibition of the OATP 1B3 uptake transporter, preventing entry of the toxin into cells.
- Cyclosporine is a calcineurin inhibitor used in the treatment of organ transplant rejection and autoimmune disorders. Cyclosporine is a potent inhibitor of the OATP 1B3 uptake transporter and available in most hospitals.
- OPC is studying the role of cyclosporine in the treatment of amatoxin-poisoned patients. This is an experimental treatment. The recommendation to use cyclosporine for these patients is at the discretion of the on-call Toxicologist and must include consent from the patient or substitute decision maker.

CLINICAL EFFECTS

- Amatoxin ingestion is characterized by:
  - Delayed GI symptoms 6-12 hours post ingestion including abdominal pain, cramping, nausea, and watery diarrhea, resulting in significant fluid losses.
  - Hepatotoxicity develops after 24-96 hours and may progress to fulminant hepatic failure. Concurrent renal injury may be present.

TRIAGE DECISIONS

- All patients with suspected amatoxin-containing mushroom exposures, as per criteria below, should be referred to a health care facility for SDAC (if appropriate) and observation.

- Initiate consultation with on-call Toxicologist for all suspected amatoxin-containing mushroom ingestions.

- Characteristics of amatoxin-containing mushroom ingestion include:
  - delayed GI symptoms (abdominal pain, cramping, nausea, vomiting, diarrhea) > 6 hours post ingestion
  - liver enzyme elevation post mushroom ingestion
  - mushroom description, pictures or sample suspicious for/or confirmed as an amatoxin-containing mushroom
  - when appropriate, consultation with the OPC on-call mycologist can be initiated through the on-call toxicologist for identification

TREATMENT

- SDAC should be considered in all patients within 12 hours of ingestion if there are no contraindications:
    - Dose activated charcoal: 1 g/kg (pediatric) or 25 g PO/NG as tolerated*
- Patient should be NPO (after SDAC given)
    - Continue NPO until liver enzymes normalize and in consultation with on-call Toxicologist
- Early and aggressive volume resuscitation (3-6 L in adult), with continued IV fluids to maintain a urine output of 2-3cc/kg/hr
- Consider initiation of Cyclosporine Treatment Protocol (see below) only in consultation with on-call Toxicologist
- Multidose activated charcoal is often not tolerated due to gastrointestinal symptoms, but can be considered if no contraindication.

*NOTE that this dose is ½ of our usual recommendations. Large doses are NOT necessary as the amount of amatoxin is small (but highly potent) even with the ingestion of several mushrooms.

SPECIAL CONSIDERATIONS

- Initiate consultation with on-call Toxicologist for all patients with suspected amatoxin-containing mushroom ingestion (see above criteria).
- The Toxicology Staff to speak directly to the attending physician to clarify treatment and to be available to assist with patient consent.

MUSHROOM IDENTIFICATION

- Efforts should be made to confirm the identification of the mushroom.
- If mushroom is available, pictures taken from several angles, including the stem, cap (top & underside), and in comparison to a standard measure, if possible, can be sent to poison.pics@sickkids.ca . These pictures, if available, can be forwarded to the personal email of the Toxicologist on call.
- When possible, a sample of the mushroom should be collected (whole mushroom, including stalk and base). The sample should be placed in a paper bag and then in a container to prevent damage to the mushroom and can be stored in the fridge. (This container should not be airtight.) On-call Toxicologist to make arrangements for identification by OPC Mycologist when required.

CYCLOSPORINE TREATMENT PROTOCOL

Initiation of this treatment protocol to be decided in consultation with on-call toxicologist. Informed consent to be provided by patient or substitute decision maker (SDM) prior to initiation.

TREATMENT

- Patient should be NPO (after SDAC given if deemed appropriate as per OPC Amatoxin-containing mushroom protocol)
    - Continue NPO until liver enzymes normalize and in consultation with on-call Toxicology
- Early and aggressive volume resuscitation (3-6L in adult), with continued IV fluids to maintain a urine output of 2-3cc/kg/h
- Cyclosporine 5mg/kg IV infusion over 6 hours, every 24 hours
    - Continue for 48-96 hours post ingestion until evidence of liver enzyme recovery
    - Longer courses to be considered on case by case basis
    - Measure trough plasma cyclosporine levels q 24 hours, just prior to next dose

LABORATORY TESTS

General Lab Work

- Send to hospital lab as usual
- Baseline CBC, AST, ALT, ALP, bilirubin, albumin, INR, creatinine, lactate, electrolytes including Mg, glucose
- Repeat AST, ALT, ALP, bilirubin, albumin, INR, creatinine, lactate, K & Mg q 6 h
- Repeat CBC daily
- Measure trough plasma cyclosporine levels q 24 hours

NOTE: the treating physician may have to speak to the on-call biochemist to have the AST added to the routine laboratory work.

Study Specific Lab Work

- **Patient/SDM to provide informed consent prior to these samples being collected**
- Send samples to Dr. Rommel Tirona's lab (details below).
- Blood sample x 2 (Lavender tube) for genomics testing to be sent to Dr. Rommel Tirona's lab
- Urine samples for amatoxin detection and clearance
    - Urine collections ARE necessary at presentation and MUST be repeated every 4 hours. It might be best to place a foley catheter to facilitate this.
    - If a foley catheter is inserted, empty the bag and collect this urine (2 x 50cc samples) as the first sample. Repeat urine collections (2 x 50cc samples) q 4 hours. Empty the bag every 4 hours after the collection. Please mark collection time and date on each sample.
    - Samples can be stored in the hospital refrigerator and sent as a single batch to arrive to Dr. Rommel Tirona's lab during business hours Monday-Friday. These samples do NOT need to be sent to the OPC.
    - Urine samples to be sent to Dr. Rommel Tirona's lab. Lab needs to be notified of sample collection prior to sending.

Samples to be sent to:

- Contact Dr. Tirona's lab to notify prior to sending samples.

Dr. Rommel Tirona
rommel.tirona@schulich.uwo.ca (email communication preferred)

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