**EM Basic- Acetaminophen (APAP) Overdose**

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**Background**

Acetaminophen is a component of hundreds of OTC and prescription medications

**Mechanism**

Therapeutic doses - 90% metabolized in liver by sulfation and glucoronidation to harmless conjugates, then excreted in urine-remaining 10% metabolized by hepatic P450 pathway into NAPQI, which is detoxified by hepatic glutathione

Toxic doses – more APAP down P450 pathway🡪more NAPQI and not enough glutathione to keep up🡪liver injury

**History**

Acute or chronic exposure?

Ask for ALL poisonings:

 What did you take?

Dosage – dose per tablet and how many tablets?

TIME of ingestion?

 Suicide attempt?

Single ingestion or repeated ones?

 Any coingestants?

Any comorbid conditions? (EtOH use, anticonvulsants, Gilbert’s)

**EtOH use** – chronic use is a risk factors in those who have ingested multiple supratherapeutic doses of APAP

**Medications that worsen outcome**

CYP inducers – anticonvulsants (carbamezapine, Phenobarbital), anti-TB drugs (INH, rifampin)

Others – TMP-SMX (bactrim), zidovudine, herbal supplements

**Pearl** – ask the patient if they have taken any other pain medications such as Percocet, vicodin, etc, which also contain APAP

**Signs/Symptoms, Physical Exam, and Lab Findings by stage**

**Vital signs** – nonspecific

**Stage I (30 min to 24 hrs post-ingestion)** – some patients asymptomatic, some have N/V, diaphoresis, lethargy

**Labs** - Normal LFTs.

**Stage II (24 to 72 hrs)** – stage I symptoms resolve, pt appears better clinically. As time passes, may develop RUQ pain/tenderness and hepatomegaly

**Labs** - ↑ PT, ↑ total bilirubin, possible oliguria.

**Stage III (72 to 96 hrs)** – jaundice, confusion d/t hepatic encephalopathy, cerebral edema, bleeding diathesis, multiorgan failure, possible ARF

**Labs** – ↑ AST and ALT, often > 10,000 IU/L, hyperammonemia, ↑ PT/INR, hypoglycemia, lactic acidosis, total bilirubin >4.0 mg/dL

**Stage IV (begins anytime 4 days to 2 wks post-ingestion)** – complete clinical recovery, and eventually complete hepatic histologic recovery

**Workup**

**Serum APAP concentration** – obtain 4 hrs after ingestion or ASAP if ingestion was > 4 hrs ago

**BMP** (electrolyte, glucose, renal function)

**ABG/VBG** (APAP ingestion and hepatic failure can lead to acidosis)

**Coags, LFTs, Ammonia level** (signs of hepatotoxicity)

**CBC** (baseline)

**Urine hCG** (women of childbearing age)

**ECG, ETOH, and ASA level** (coingestions)

**PEARL** – in patients with chronic APAP ingestion who have any signs/symptoms of hepatotoxicty, order a serum APAP concentration and AST regardless of when the ingestion occurred (risk of hepatoxicity greater in chronic ingestion than for a single, acute OD)

**Management**

**ABCs**

O2 and fluids as necessary

Cardiac monitor (coingestions)

**Activated Charcoal** – 1g/kg up to 50 g PO within 4 hrs of ingestion

**N-acetylcysteine (NAC)**

Indications

 Serum APAP concentration above tx line on nomogram (Fig. 1)

Single APAP ingestion > 150 mg/kg or 7.5 g total in a patient for whom we can’t obtain an APAP concentration until >8 hrs post-ingestion

Patient with unknown time of ingestion and serum APAP > 10mcg/mL

Patient with hx APAP ingestion and ANY evidence of liver injury

Patients who present > 24 hrs post-ingestion with lab signs of liver injury

**PEARL** – the nomogram is the most important way to determine the need for NAC therapy in an acute APAP OD

**72-hour PO protocol** – loading dose 140 mg/kg PO, then 70 mg/kg PO every 4 hrs for 17 total doses

**21-hour IV protocol** – loading dose 150 mg/kg over 1 hr, then 4-hr infusion of 12.5mg/kg/hr, then 16-hr infusion at 6.25 mg/kg/hr

**PEARL** – NAC is safe and effective in pregnant women. Crosses the placenta and thus IV form preferred.

**Disposition**

Patient treated with NAC🡪admitted

Patient asymptomatic/mild symptoms🡪admit to medicine or obs unit

Patient had evidence severe heaptotoxicity/hepatic failure🡪admit to medical ICU

**PEARL** – consult a medical toxicologist/regional poison control center as needed and obtain a psychiatric consult for intentional overdoses

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Figure 1



http://www.mdcalc.com/acetaminophen-overdose-and-iv-nac-dosing/