Clinical Pharmacology & Toxicology Pearl of the Week

~ Salicylate poisoning ~

- ✓ Salicylate toxicity can be life threatening and results from either acute ingestion or excessive therapeutic use.

- ✓ Toxic effects are the result of direct toxicity to the CNS, uncoupling of oxidative phosphorylation, and interference with glucose/fatty acid metabolism and platelet function.

- ✓ Toxicity can be delayed and prolonged due to several factors: enteric coated (EC) formulation, formation of bezoars (concretions), erratic intestinal absorption, and enzyme saturation.

- ✓ Concentrations may continue to rise for 12 hours or more post ingestion, especially with ingestions of EC products.

- ✓ Acute toxicity = vomiting, tachypnea, tinnitus, diaphoresis, and lethargy. This may progress to seizures, hypoglycemia, hyperthermia, coma, and pulmonary edema. Blood gas usually reveals a mixed respiratory alkalosis and metabolic acidosis.

- ✓ Chronic toxicity = delirium, dehydration, and tachypnea. Cerebral and pulmonary edema occurs more frequently than with acute toxicity. Severe poisoning occurs at lower salicylate concentrations, and the mortality rate is higher than in acute poisoning.

- ✓ After the diagnosis has been made, the following management plan is recommended:

- ✓ Decontamination:
    - All patients should receive a single dose of activated charcoal 1 g/kg PO unless contraindicated (i.e., unable to protect airway, bowel obstruction, GCS less than 15).
    - Note that charcoal may be administered up to and beyond 6 hours post ingestion to help decrease absorption.
    - Additional doses of activated charcoal (0.5 g/kg PO q2h) should follow the initial dose of charcoal if salicylate concentrations are increasing. This should be limited to three doses. Further doses may be considered in discussion with the medical toxicologist on call.
    - Whole bowel irrigation is not recommended for salicylate ingestions.

- ✓ Urine alkalinization:
    - Indication: Urinary alkalinization is indicated in patients with clinical features of salicylate toxicity (tinnitus, tachypnea, respiratory alkalosis, metabolic acidosis), or a salicylate concentration greater than 2.1 mmol/L.
    - Preparation of infusion: Add 150 mmol (“3 amps”) of sodium bicarbonate 8.4% solution to 850 ml D5W for a final bicarb concentration of 0.15 mmol/mL.
    - Infusion dosing: Administer sodium bicarbonate 0.15 mmol/mL IV at twice the maintenance fluid rate.
    - Mandatory Potassium Supplementation: Must include potassium supplementation to ensure successful urinary alkalinization. Target serum K+ 4.0 to 5.0 mmol/L.
    - Potassium chloride should be administered intravenously. Options for administration can include:
        - Addition of 40 meq KCl to the 1L sodium bicarbonate/D5W infusion
        - KCl via a mini bag
    - Oral potassium may be required in addition to IV supplementation.

- Note: Patients in oliguric or anuric renal failure should not receive supplemental potassium until the renal failure is corrected.

✓ Ongoing tests:
- Urine pH q2h (urine dipstick is sufficient)
  - Goal urine pH is 7.5 to 8
- Salicylate concentrations q2h
- Electrolytes (Na, K, Cl, CO2) q2h
- Blood gases (venous or arterial) as needed
  - Do not exceed serum pH of 7.55 or serum Na 155 mmol/L.

✓ When to stop urine alkalinization:
- Two salicylate concentrations declining over at least 4 hours. At least one concentration must be less than 1.4 mmol/L (therapeutic range 0.7 to 1.8 mmol/L)
- Normal anion gap
- Clinically well (no tinnitus, tachypnea, nausea, vomiting, abdominal pain, mental status changes)

✓ Hemodialysis can be considered based on the extracorporeal treatments in poisoning (EXTRIP) workgroup recommendations: https://www.extrip-workgroup.org/salicylates
- If salicylate concentration is greater than 6.5 to 7.2 mmol/L
- If salicylate concentration is greater than 5.8 to 6.5 mmol/L in the presence of impaired kidney function
- pH is less than 7.2
- In the presence of altered mental status
- In the presence of new hypoxemia requiring supplemental oxygen
- If standard therapy (supportive measures, bicarbonate, etc.) fails

✓ Pearls and pitfalls of salicylate poisoning:
- Airway – Respiratory alkalosis due to tachypnea is a compensatory mechanism with severe salicylate toxicity. Intubation of such patients is a high-risk event and should be performed by the most skilled person available. Any respiratory acidosis during intubation may suddenly increase salicylate distribution into the CNS and result in acute deterioration. Patients who are intubated require frequent monitoring of ventilator settings and blood gases to ensure their minute ventilation matches their pre-intubation state. Such patients should be considered for hemodialysis post-intubation.

- Fluid resuscitation – Patients may be volume deplete by several litres on presentation because of vomiting and increased respiratory and metabolic rate. Resuscitate to euvolemia with isotonic crystalloids if required. Target urine output of 1 mL/kg/hour. Forced diuresis with excess fluids is not recommended. If pulmonary edema is present, intravenous fluids should be restricted and hemodialysis should be considered.

- Glucose – Administer supplemental dextrose as needed for hypoglycemia. Altered mental status or seizures may be due to neuroglycopenia despite a normal serum glucose and should also be treated empirically with supplemental dextrose.

- Imaging – An abdominal x-ray may show radio-opaque material, but a negative x-ray does not rule out salicylate ingestion.

The Clinical Pharmacology physician consultation service is available Mon-Fri, 8am-5pm. The on-call physician is listed in ROCA on the AHS Insite page. Clinical Pharmacology consultations are also available through the Netcare e-referral process and through Calgary Zone Specialist Link. Click HERE for more details.

The Poison and Drug Information Service (PADIS) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414 (AB and NWT) or 1-866-454-1212 (SK).