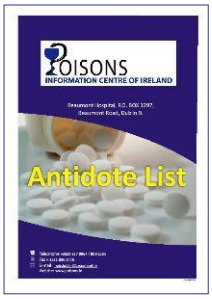
POISONS © INFORMATION CENTRE OF IRELAND

NEWSLETTER

Tel: 01-837 9964 / 01-809 2566

Summer 2011

Welcome to the **Summer 2011** edition of our newsletter, and best wishes to all new NCHD's who are starting their rotation in E.D. this month. When you get a chance, please take the time to familiarize yourself with the poisons database TOXBASE© that should be available in your department, and don't hesitate to call us if you wish to discuss any aspect of poisoning.



Our website www.poisons.ie also contains some useful information including the current Poisons Centre Antidote List which is available in pdf format. This publication provides details about all the antidotes you may need if treating a poisoned patient. In particular, please note the recent replacement of the digoxin-specific antibody ***Digibind*** by a new product called ***Digifab***. This product is equally effective but has a slightly different dosing protocol. There is also some new information about the cyanide antidote hydroxycobalamin which has recently become available in Ireland as the commercial product ***Cyanokit ©.*** Please contact us for further information about its possible use in treating smoke inhalation patients.

Enjoy your Summer!

Early management of poisoned patients-

i) Treat life-threatening conditions first; Airway, Breathing, Circulation.

ii) Assess level of consciousness (GCS), and check vital signs (HR, BP, RR).

iii) Obtain a full history if available. This should include:

- Age and weight of patient.
- Name and quantity of agent involved.
- Time since exposure.
- Intent (ie deliberate or accidental overdose).
- Symptoms prior to admission (e.g. vomiting, drowsiness, seizures).
- Any underlying medical condition and normal medications.

iv) Perform a 12 lead ECG if cardiotoxic drugs have been taken.

v) Request a urine toxicology screen for unconscious patients.

vi) Consider a plasma paracetamol level in unconscious patients and in patients with unexplained liver dysfunction.

vii) Check the relevant TOXBASE © entry and/or contact the Poisons Information Centre for additional information.

The staff in the poisons centre can provide information to assist in the management of poisoned patients, but they are **not** qualified to make clinical decisions regarding admission or discharge of a patient.

METHOTREXATE

- Methotrexate (MTX) is a cytotoxic drug that is used in cancer therapy, rheumatoid arthritis, and severe psoriasis. It acts by inhibiting the enzyme dihydrofolate reductase which aids conversion of folic acid to tetrahydrofolic acid during DNA synthesis. Methotrexate interferes with the reproduction of tissue cells so the effects of toxicity are most noticeable in organ systems that have rapidly dividing cells (e.g. GI tract, bone marrow).

Toxicity can occur after excess oral ingestion, or after inadvertent intrathecal administration. Peak plasma concentrations occur 1-2 hours after oral doses, and 30-60 minutes after IM injection. Patients who take repeated excess therapeutic doses are at increased risk of toxicity (e.g. a weekly dose taken daily).

FEATURES

Oral overdose

- There may be vomiting, diarrhoea, severe stomatitis, oesophagitis, gastrointestinal ulceration and/or bleeding. Elevated liver enzymes have been reported in both acute and chronic cases.
- Bone marrow depression can develop over 6-12 days and can lead to leukopenia, anaemia, thrombocytopenia, and pancytopenia.
- Pulmonary features can occur at any dose and can include interstitial pneumonitis and fibrosis. Pulmonary infiltrates may be seen on a chest x-ray.
- At high doses, methotrexate accumulates and precipitates in renal tubules, causing reversible acute tubular necrosis. Co-ingestion of other nephrotoxic drugs will increase the risk of acute renal failure.

Intrathecal overdose

Any amount above the recommended dose (12mg in an adult) can cause serious symptoms including neurological complications. Features of acute neurotoxicity can develop and may include seizures, motor dysfunction, cerebellar dysfunction, and stroke-like symptoms (aphasia, weakness). An acute toxic syndrome involving headache, fever, and meningismus has been reported. There may also be confusion, agitation, coma, and respiratory failure.

MANAGEMENT

Oral Overdose

Patients who are on methotrexate therapy are at increased risk of developing severe adverse effects.

- In *all* patients- Check full blood count, renal function, and liver function weekly for 4 weeks.
- Do a chest x-ray in patients with respiratory features.
- If >1mg/kg was taken, do a methotrexate level 4-6 hours post ingestion. Repeat every 24-48 hrs.
- Give **LEUCOVORIN ©** (folinic acid) to all patients who have taken more than 3mg/kg. ***See below***
- Urinary alkalinisation can help to prevent accumulation of methotrexate in the kidneys and should be considered in severe cases to enhance elimination. Correct serum potassium before alkalinisation: Adults: 225 mL of 8.4% sodium bicarbonate over 2 hours (or 1.5 L of 1.26%).

Children: 1 mL/kg 8.4% bicarbonate diluted in 0.5 L 5% dextrose or normal saline at 2-3 mL/kg/hour.

- Check for infection in patients with neutropenia. Granulocyte-macrophage-colony-stimulating-factor (GM-CSF) has been used successfully in one case to treat pancytopenia (Steger et al, J Intern Med1993).

Intrathecal Overdose

- Sit the patient up to delay the flow of methotrexate to the brain.
- Cerebrospinal fluid drainage should be done as soon as possible. Up to 95% of the methotrexate dose can be removed if 30mls is drained **within 15 minutes**. A delay in drainage will significantly reduce the amount of methotrexate that can be removed. For large overdoses (>100mg), it is recommended that a ventriculostomy is performed to allow perfusion of isotonic fluid at the lumbar site.
- Do a methotrexate level and give Leucovorin © as indicated. **DO NOT give Leucovorin intrathecally.**

LEUCOVORIN (folinic acid)

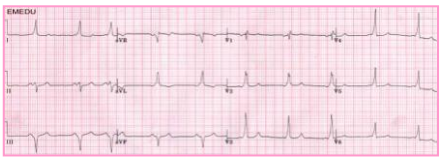
- If the ingested dose of methotrexate is known, give at least the equivalent dose of folinic acid. Repeat the dose every 6 hours while waiting for a plasma level.
- If the ingested dose is unknown, give 1000mg/m^2 every 6 hours.
- If plasma MTX is**: > 50 micromol/L,** give **1000mg/m^2** every **6** hours (IV).
  5-50micromol/L, give **100mg/m^2** every **3** hours (IV).
  0.5–5 mircomol/L, give **30mg/m^2** every **6** hours (PO / IV).
  <0.5 micromol/L, give **10mg/m^2** every **3** hours (PO / IV).

Continue giving folinic acid until the plasma methotrexate is < 0.05micromol/L. Reports of adverse reactions to folinic acid are rare but the calcium content of Leucovorin © warrants a slow infusion rate (160mg/min).

Note: An alternative antidote called ***Voraxaze*** is available on a named patient basis and may be useful in patients with renal failure or severe toxicity. *Please discuss with the Poisons Information Centre.*

AMITRIPYTLINE

Over the past 18 months, we have noticed a significant increase in the number of enquiries about amitriptyline. The combination of sodium channel blockade and anticholinergic effects caused by amitriptyline results in wide-complex tachyarrhythmias with severe hypotension. Severe agitation and seizures can also occur. Patients who take > 5mg/kg are at risk of toxicity and should be observed for at least 6 hours.



Summary of treatment points :

⇒ Correct hypoxia and check arterial blood gases.

⇒ Do a 12-lead ECG and check QRS duration. **N.B.** A QRS of >160msec suggests severe cardiotoxicity.

⇒ Treat wide complexes with sodium bicarbonate. Dose: 50mmol. Repeat to maintain a pH of 7.5.

⇒ Correct metabolic acidosis with fluid resuscitation and sodium bicarbonate if required.

⇒ Consider the use of Intralipid © (lipid emulsion) if cardiotoxicity is unresponsive to other treatments.

Amitriptyline poisoning is potentially life-threatening. All serious cases should be discussed with the NPIC.

A global shortage of **HEROIN** over the past few years has resulted in poor quality, low strength heroin being sold on the streets. As a result, long-term users started to inject larger doses and/or take their heroin with other drugs of abuse.

According to recent information from the NACD Early Warning & Emerging Trends committee, this heroin "drought" now appears to be over. The resulting surge in high grade heroin, together with a reduced tolerance in users, has increased the likelihood of overdose and subsequent respiratory arrest.

Treatment:

Naloxone is an effective opioid antagonist and should be given to all patients with coma and respiratory depression. Give an initial dose of 0.4mg to 2mg IV and repeat if no response is seen within 2 minutes. An intravenous infusion may be required in severe cases; 60% of the initial dose per hour is usually recommended. The half-life of naloxone is quite short so patients should be monitored closely for recurrence of CNS depression. Monitor blood pressure, respiratory rate, and oxygen saturation for at least 6 hours after the infusion.

Intramuscular administration of naloxone has a slower onset and longer duration of action. It may be useful in patients who want to self-discharge but who are at risk of recurring CNS depression.

GIANT HOGWEED *(Heracleum mantegazzianum)*

This common plant grows to heights of 10-12 feet and is seen growing wildly in hedgerows or along river-banks. It is easily recognisable by its numerous large white umbrella shaped flowers that appear from early spring to late summer.

Toxicity: Giant Hogweed sap contains furocoumarin, a phototoxic agent that causes phytophotodermatitis. Skin contact with the sap followed by exposure to sunlight leads to a severe inflammatory eruption on the skin. Initial symptoms occur within 24 hours and can include skin discolouration, rash and painful lesions. Large fluid-filled blisters may develop over the following 24 hours. One patient, who developed blisters 2 days after exposure, went on to develop a full thickness cutaneous burn two weeks later (Chan et al 2011). Hyperpigmentation of the area can persist for several months.

Treatment: Irrigate the exposed skin with soap and water to remove all residue of sap. Cover the area and prevent exposure to sunlight for at least 48 hours. Further treatment is determined by clinical condition; cold compresses and topical steroids may provide some relief. Give analgesics as required and treat blisters conventionally. In severe cases, it may be necessary to refer the patient to a burns specialist. Photosensitivity can persist for months so patients should be advised to use sunscreen and to avoid excessive sun exposure.

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