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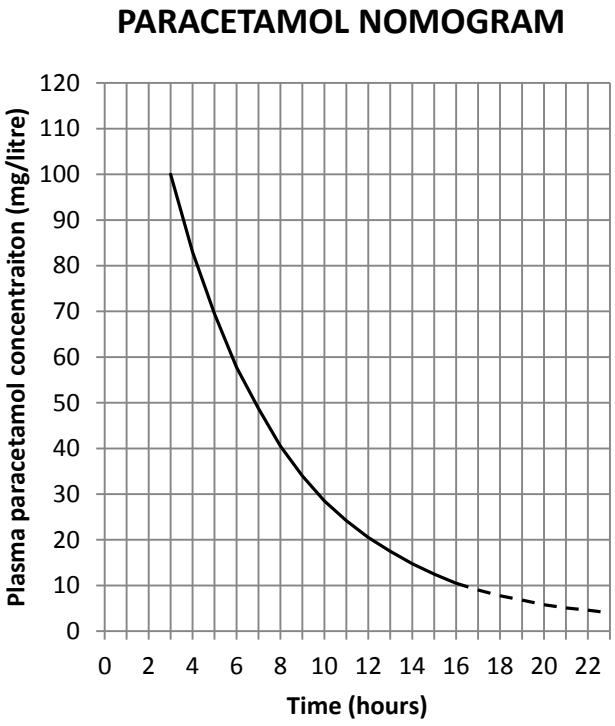
NEWSLETTER

2013 / 1

A new treatment protocol for paracetamol overdose was introduced in Ireland on January 7th 2013. This follows approval by the Irish Medicines Board of a simplified guidance on the treatment of oral paracetamol overdose with **PARVOLEX** (acetylcysteine). The paracetamol nomogram has been updated to include only one treatment line and risk factors are no longer considered.



- Plasma paracetamol levels **can not** be interpreted if blood is taken less than 4 hours post-ingestion.
- Check the units and time of ingestion carefully when using the graph.
- Give acetylcysteine if the paracetamol level is above the treatment line.
- Give acetylcysteine if there is any doubt about the timing of the overdose.
- Do not use the graph if your patient has taken a staggered overdose or chorinc therapeutic excess. Clinical judgement should be used to determine the need for treatment in these patients.

Key Changes:

- Patients who have, or may have, ingested >75mg/kg in an acute overdose will be now referred to hospital for assessment.
- All patients who have taken a staggered paracetamol overdose, chronic therapeutic excess or an overdose with unknown time of ingestion will now be referred to hospital for assessment regardless of ingested dose.
- Risk factors are no longer considered when determining the need for antidotal treatment. Acetylcysteine is indicated for all patients who have a plasma paracetamol level above a line joining **100mg/L a t 4 hours** and **15mg/L at 15 hours** on the paracetamol graph (see above).
- The duration of administration of the 1st dose of acetylcysteine (150mg/kg) has been increased from 15 minutes to **60 minutes** in order to reduce the risk of an anaphylactoid reaction.

METHAEMOGLOBINAEMIA

Ingestion of oxidising agents is an uncommon but potentially a serious cause of methaemoglobinaemia. A range of pharmaceutical and industrial agents including nitrates, nitrites, Dapsone, aniline, and chlorates have the potential to cause methaemoglobinaemia and exposure to these agents can cause prolonged toxicity.

Case Report

A female patient who took an overdose of Dapsone was admitted to the Emergency Department with a GCS of 3/15 and a MetHb concentration of 45%. She received 2mg/Kg of methylene blue and her MetHb concentration quickly fell to 15%. Within 2 hours it rose again to 35% and she appeared cyanotic. Additional bolus doses of methylene blue were administered over the next 72 hours and on each occasion her MetHb concentrations fell and then rose again by ~20% every two hours. On day 3 she was extubated but was desaturating to 80% on room air so she remained on supplemental oxygen for a further 48 hours. Her platelets were low but there was no evidence of haemolysis. She received her last dose of methylene blue on day 4 and methaemoglobinaemia did not recur.

Methaemoglobin is formed when the iron moiety in haemoglobin is oxidised from the ferrous (Fe^{2+}) state to the ferric (Fe^{3+}) state; normal levels in whole blood do not exceed 1-2% but increased oxidant stress can cause methaemoglobinaemia. At high levels, there can be symptoms of cellular hypoxia and cyanosis. Some oxidising agents product cyclical methaemoglobin and have a slow rate of elimination; patients who have been exposed to these agents may have recurring methaemoglobinaemia and will require prolonged treatment. Heinz-body haemolysis can occur 12-24 hours after episodes of methaemoglobinaemia.

SYMPTOMS:

<10% - Frequently asymptomatic
10%-20% - Cyanosis, chocolate brown blood
20%-50% - Dizziness, fatigue, headache, exertional dyspnoea, palpitations
50%-70% - Tachypnea, seizures, cardiac arrhythmias, metabolic acidosis, coma
>70% - Grave hypoxic symptoms, death

DIAGNOSIS:

Generalised cyanosis in the presence of a normal arterial PO_2 suggests methaemoglobinaemia.

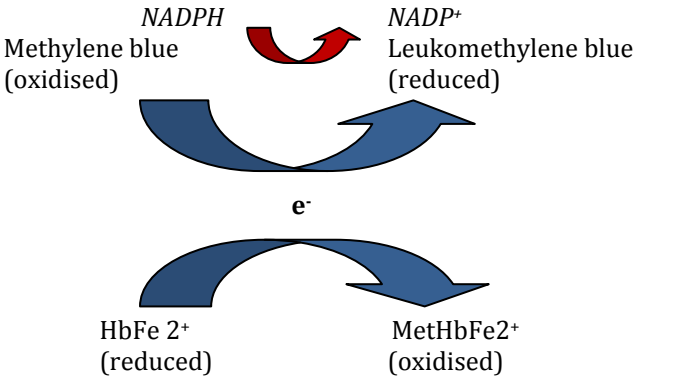
ABGs and pulse oximetry will not accurately diagnose methaemoglobinaemia: •Arterial PO_2 reflects the total dissolved oxygen in plasma and assumes the presence of normal haemoglobin. Calculated oxygen saturation will be falsely elevated in the presence of methaemoglobin. • Pulse oximeters determine oxygen saturation by differentiating between oxyghemoglobin and deoxyhemoglobin; methaemoglobin is not identified and high concentrations will cause unreliable pulse oximeter readings.

If methaemoglobinaemia is suspected, diagnosis should be confirmed using a co-oximeter.

TREATMENT: Symptomatic patients should be given high concentrations of oxygen. Check MetHb levels. Give methylene blue if MetHb levels are >20-30% or if there are signs of tissue hypoxia (seizure, coma, chest pain). Repeat doses may be required for recurring methaemoglobinaemia. Treat seizures conventionally. Monitor for onset of haemolysis; exchange transfusion may be required in life-threatening cases.

Methylene Blue (methylthionium chloride)

- Methylene blue is an oxidising agent which in the presence of NADPH and NADPH methaemoglobin reductase is reduced to leukomethylene blue.
- Leukomethylene blue is then available to reduce the ferric iron in the MetHb molecule back to ferrous iron.



Occupational Methaemoglobinaemia
Bradberry S, Ching AT, Williams N, Vale JA. Occup Environ Med 2001; 58: 611

Adults and Children: 1-2mg/kg of 1% solution (ie 0.1-0.2mls/Kg of a 1% solution)given by slow IV injection over 5 minutes. **Repeat dose in 30-60 minutes if no response.**

Methaemoglobin concentration should be measured and repeated 1-2hours after therapy to assess effectiveness; repeated doses may be required.

Note: High methylene blue concentrations can interfere with metHb concentrations causing a falsely low result. Doses of >15mg/Kg can cause haemolysis and should be avoided.

Adverse effects can include nausea, headache, and blue-green discolouration of the urine.

PREGABALIN

Pregabalin (Lyrica) is an antiepileptic drug used in the treatment of partial seizures. It is also used to treat generalised anxiety disorder, neuropathic pain, and fibromyalgia. Enquiries to the Poisons Centre about pregabalin overdose have increased steadily over the past 5 years with a 10-fold increase for 2008 to 2012. In most cases, pregabalin was co-ingested with other drugs and drowsiness was the most common symptoms.

The mechanism of action of pregabalin is uncertain; it is thought to bind to subunits of calcium channels and decrease the release of several neurotransmitters including glutamate and noradrenaline. Pregabalin is rapidly absorbed after oral doses and peak plasma concentrations occur within 1.5 hours; the mean elimination half-life is 6.3 hours.

Common adverse effects following therapeutic use include dizziness and somnolence. In overdose severe CNS depression and coma have been reported. There can also be non-specific gastrointestinal and musculoskeletal symptoms, cerebella features, and less commonly syncope, congestive heart failure, elevated creatine kinase, rhabdomyolysis and reversible renal failure. Myoclonus has also been reported in a patient with underlying chronic renal failure (Yoo et al, Am J Kidney Dis 2009). No fatalities have been reported.

Treatment is supportive with airway management as required. Symptoms usually develop within 6 hours after ingestion. In symptomatic patients, check U&E's and creatinine. Haemodialysis can enhance the elimination of pregabalin with a clearance of approximately 50% in 4 hours but case reports of patients with normal renal function reported good outcomes with supportive care alone (Wood et al, Je Med Toxicol 2010).

GIFTINFORMATIONSCENTRALEN

In November 2012, we welcomed two colleagues from the Swedish Poisons Inforamtion Centre in Karolinska Hospital, Stockholm. Their visit provided a useful opportunity to compare recent trends in poisoning in our two coutries and discuss ongoing research projects in both centres.

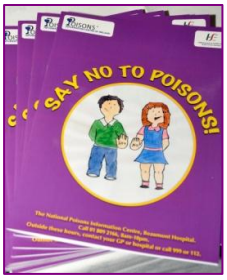
Of note in Sweden is a rise in the use of two new drugs of abuse: **Benzo Fury (benzofuans)** and **5-IT (aminorpropylindole).** Both of these drugs cause hallucinations and stimulant effects and symptoms can persist for a number of days. Benzo Fury is structurally related to the amphetamines and has potent serotonergic activity. 5_IT is structurally related to the hallucinogenic tryptamines (e.g. LSD) and has been implicated in a number of fatalities in Sweden. Stimulant effects are common and there can be severe anxiety, hallucinations and psychosis.

Pictured from left: Matilda Backberg, Elaine Donohoe, Dr Edel Duggan Katarina Luhr

Hyperthermia, rhabdomyolysis and DIC have occurred.

Diazepam or haloperidol may be used to treat agitation caused by these stimulant drugs; in severe cases, sedation, intubation and ventilation has been required. Serotonin syndrome may develop so monitor temperature closely and treat with conventional cooling measures. Cyproheptadine may be useful to treat serotonin syndrome; if this is being considered, discuss these cases with the Poisons Information Centre.

SAY NO TO POISONS!



Following the launch of the "Say No to Poisons" activity pack last year, we were delighted when all the hardwork undertaken by our colleague Nicola Cassidy was acknowledged with commendations at both the 2012 Irish Healthcare Awards (Patient Lifestyle Education category), and the Astellas Changing Tomorrow Awards (Innovation category). These awards recognise creativity and excellence in healthcare initiatives and we would like to say congratulations to everyone involved in this project.

"Say No To Poisons" was the result of a successful collaboration between the NPIC, the HSE, Co. Carlow VEC and Early Childhood Ireland. The project aims to provide healthcare workers, childcare professionals, parents and caregivers with simple, easy to follow poison prevention techniques. The "Say No to Poisons" storybook teaches pre-school children that they should always ask an adult if something is safe to eat or drink; to date over 4000 books have been distributed to childcare organisations around the country.

The storybook and resources can be downloaded from the "Public-Educational Resources" section on www.poisons.ie.

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