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PARAQUAT POISONING

1-methyl-4-[3-methyl(pyridin-2-ium-4-yl)] (pyridine-2-ium known as PARAQUAT or GRAMOXONE). It is a toxic chemical that mainly and widely used as an herbicide (plant killer). It primarily used to control weeds and grass in plantation. However, it is often misused as a suicidal agents.

Paraquat use has been restricted in US due to its toxicity. It can be used only by people who are commercially licensed applicators. In Malaysia, use of paraquat is banned since 2002 by the Secretary of Malaysia’s Pesticides Control Board. It has been the major concern due to higher number of paraquat poisoning incident reported among the agriculture workers. Therefore, Malaysia classified it as a Class I (extremely hazardous) pesticide.

Paraquat is highly toxic. It enters the body mainly by swallowing, or through damaged skin, but may also be inhaled. Thousands of deaths have occurred from ingestion or dermal exposure to paraquat.

Paraquat is corrosive to the skin and once skin is damaged, it is easily penetrated into the body. One farmer died after just 3.5 hours spraying diluted paraquat with a leaking knapsack. Others have died from spilling the concentrated paraquat on their skin. Thousands more suffered severe, acute and chronic effects from occupational use.
WHY POISONOUS?

THE EXTENT of poisoning caused by paraquat depends on the amount, route, duration of exposures and the person's health condition at the time of exposure.

After paraquat enter the body, it is distributed to all areas which causes toxic chemical reactions to occur, primarily at the lungs, liver and kidneys. (2)

Paraquat-induced toxicity is a manifestation of its ability to undergo redox-cycling and subsequent generation of reactive oxygen species (ROS).

Paraquat is metabolized by several enzyme systems (NADPH-cytochrome P450 reductase, xanthine oxidase, NADH-ubiquinone oxidoreductase and nitric oxide synthase). Its metabolism through these systems generates a paraquat mono-cation radical (PO⁺). Inside the cell, PO⁺ rapidly re-oxidized to PO₂⁺ and it generates superoxide (O₂⁻). O₂⁻ acts as an electron acceptor and NADP as an electron donor in this reaction. This gives rise to formation of the hydroxyl free radical (HO). In the presence of iron via the Fenton reaction, NO⁻ combines with O₂⁻ to generate peroxynitrite (CNOO⁻) which is a very strong oxidant and a nitrating intermediate. NO⁻ is enzymatically produced from L-arginine by NO synthase, and PO₂⁺ also directly or indirectly induces NO synthase-mediated nitric oxide production. Generation of highly reactive oxygen and nitrite species results in toxicity in most organs. However, the toxicity is more severe in the lungs as paraquat is taken up against a concentration gradient in to the lung. (3)

Paraquat can induce lipid peroxidation. Lipid peroxidation compromises cell membrane function and may trigger apoptosis. Lipid peroxidation can be considered to be a key initial pathophysiological process in the cascade of events following paraquat poisoning. From this it could lead to apoptosis, mitochondrial toxicity, and activation of nuclear factor kappa B (NF-kB). (5)

As, paraquat toxicity is most severe in the lungs it could lead to an acute alveolitis. In the lung, paraquat toxicity mainly target on alveolar epithelium. During the acute destructive phase both type I and type II pneumocytes demonstrate swelling, vacuolization and disruption of mitochondria and the endoplasmic reticulum. Sloughing of the alveoli is associated with pulmonary edema. This initial phase is followed by a proliferative phase where the alveolar space is filled with mononuclear fibroblast which mature into fibroblasts within days to weeks. This stage is followed by lung fibrosis. This stage may need immunosuppressant agents to aid.

Kidneys exposed to paraquat demonstrate development of large vacuolation in proximal convoluted tubules which leads to necrosis. Congestion and hepatocellular injury associated with rough and smooth endoplasmic reticulum degranulation and mitochondrial damage occur in the liver. These changes can be observed within a few hours to days. (6)

CLINICAL MANIFESTATION (3)

IMMEDIATE SIGNS AND SYMPTOMS OF LARGE AMOUNT OF PARAQUAT EXPOSURE

• Pain and swelling of mouth & throat
• GI symptoms: nausea, vomiting, abdominal pain & bloody diarrhea.
• Severe GI symptoms: dehydration, electrolytes abnormalities & low blood pressure.

SIGNS AND SYMPTOMS OF LARGE AMOUNT OF PARAQUAT EXPOSURE AFTER A FEW DAYS OR WEEKS

• Acute Kidney Failure
• Confusion
• Coma
• Tachycardia
• Liver failure
• Lung scarring
• Respiratory failure
• Pulmonary edema

PHARMACOKINETIC INFO

PARAQUAT volume of distribution: 1.2–1.6 l/kg

Within 12–24 h after ingestion, 90% of the absorbed paraquat is rapidly excreted unchanged in urine.

Graphical presentation of paraquat toxicity and side of antidote actions (6)

Paraquat tongue late lesion, 2 weeks after ingestion with extensive ulceration.
MANAGEMENT OF PARAQUAT TOXICITY

1. CONTAMINATED clothing should be removed immediately. Contaminated skin should be washed with soap and water.
2. Insert nasogastric tube (NG) and stomach washout should be carried out as soon as possible.
3. 300 ml of FULLER’S EARTH (15% suspension) via NG tube as soon as possible, then 20 ml Fuller’s earth every hour until diarrhea and PR passage of Fuller’s earth OR
4. Activated charcoal 50 g STAT and 25 g every 4 hourly for several days.
5. Magnesium sulphate (Mist alba) 30 ml every 4 hourly until diarrhea and passage of Fuller’s earth or Mannitol 20% ml as STAT dose.
6. IV Fluids approximately 4-5 L/day (NS and D5%) for the first 24 hours, then 3 L/day orally or IV subsequently for several days. Maintaining good hydration is important. In established renal failure, IV or oral fluids should be restricted.
7. Potassium supplement either IV or orally depending on BUSE.
8. Frusemide 40mg BD IV or oral for several days.
9. Hemodialysis or charcoal haemoperfusion may be useful if started very early, especially within 5-7 hours of ingestion before the distribution of paraquat into tissues especially the lungs.
10. Oxygen is to be avoided unless P2O2 falls <60mmHg or for palliation in a patient who is severely dyspnea. This is because, oxygen tends to increase toxic effect on the lungs.
11. Allow liquid diet as soon as patient is able to tolerate.

SEVERE INFLAMATION of lungs play a major role in lethal hypoxemia of patients with paraquat toxicity. In selected cases with moderate to severe poisoning, there will be the role of prophylactic immunosuppressant agents: Methylprednisolone 15mg/kg +/- cyclophosphamid 15mg/kg followed by dexamethasone at high dose.

INVESTIGATION AND MONITORING

1) Send gastric lavage/aspirate, urine and blood for toxicology screening.
2) Send gastric lavage/aspirate and urine for paraquat toxicity screening.
3) Urine for paraquat daily for 3 days. Result should be traced immediately as it is one of the prognostic indicators and has implication on subsequent management of patient.
4) If urinary sodium dithionite test which results in dark blue: severe poisoning & poor prognosis, blue: moderately severe poisoning, light blue: mild poisoning.
5) BUSE daily
6) FBC, LFT, RP and CXR once every 3 days.
7) ABG to check for respiratory failure
8) I/O chart monitoring: assess chest and CVS for signs of fluid overload and pulmonary fibrosis regularly.

REFERENCES
1. Paraquat Dichloride, United States Environmental Protection Agency. (2012)
2. Paraquat. (Center for Disease Control and Prevention (CDC)).
6. Medical Management of Paraquat Ingestion, Indira et al. (2014)
7. Paraquat Poisoning, Sarawak Handbook of Medical Emergencies 2nd Edition
World Antibiotic Awareness Week is celebrated annually all over the world in the month of November to raise awareness about the serious health issue that comes with antibiotic resistance including Malaysia with our tagline - “Antibiotik - Perlu ke?”

What is Antibiotic Resistance? Antibiotic resistance occurs when bacteria start to change and improve themselves to protect against the antibiotic making the infections much harder to treat. The prevalence of misuse and overuse of antibiotics is causing the increment of antibiotic resistance in an alarming trend.

Do you know?

❖ Just because symptoms last for a long time, doesn’t mean your children need antibiotics. Most children get better in 2 weeks.
❖ Regular hand washing (using soap and running water) can help to prevent the spreading of antibiotic resistance.
❖ Animal husbandry is a source of antibiotic resistance.
❖ Antibiotics are not to be shared, not even within your family.
❖ Antibiotics do not treat viral infections like cold and flu.
❖ Antibiotics resistance can affect people of any age and in any country.
On 3rd of October 2017, our department had conducted Quality of Use Medication program (QUMC) in Sekolah Kebangsaan Sungai Seluang, Lunas Kedah. It was participated by 50 to 60 students of Standard 5 and 6 and five teachers. The objectives for this program are to:

- outline the differences between dosage forms and types of medication that available in our hospital or in market,
- increase awareness on a proper use of medication,
- educate on the right way of medication storage,
- educate students and teachers on how to practice 5 R in handling their medication.

During this program, our pharmacist, Mr. Low Chia Ren delivered a talk on “Know Your Medication”, followed by an exhibition on medicines & medication related devices.
Aerobic

Healthy Diet “Bento” Competition

Walkaton

“Kenali Ubat Anda” Booth

Medical check-up

Heath Talk

QUIZ

“Quit Smoking” Booth
SPIRIVA RESPIMAT* Inhaler

INDICATION
SPIRIVA RESPIMAT* (tiotropium bromide) Inhalation Spray is a prescription medicine used once daily (a maintenance medicine) to control symptoms of chronic obstructive pulmonary disease (COPD) by relaxing your airways and keeping them open. COPD includes chronic bronchitis and emphysema.

SPIRIVA RESPIMAT also reduces the likelihood of COPD flare-ups (COPD exacerbations).

GET TO KNOW YOUR SPIRIVA RESPIMAT INHALER

PREPARE FOR FIRST-TIME USE
1. With the aqua cap closed, press the safety catch while pulling off the clear base.
   Be careful not to touch the piercing element located inside the bottom of the clear base.
2. Write the discard by date on the label of the SPIRIVA RESPIMAT Inhaler.
   The discard by date is 3 months from the date the cartridge is inserted into the inhaler.
3. Take your SPIRIVA RESPIMAT cartridge out of the box.
   Do not turn the clear base before inserting the cartridge.
   Push the narrow end of the cartridge into the inhaler. The base of the cartridge will not sit flush with the inhaler. About 3/4 of an inch will remain visible when the cartridge is correctly inserted.
   The cartridge can be pushed against a firm surface to ensure that it is correctly inserted.
   Do not remove the cartridge once it has been inserted into the inhaler.
4. Put the clear base back into place.
   Do not remove the clear base again.
   Your SPIRIVA RESPIMAT inhaler should not be taken apart after you have inserted the cartridge and reattached the clear base.
PRIME FOR FIRST-TIME USE

The following steps are needed to fill the dosing system the first time you use it and will not affect the number of doses available. After preparation and initial priming, your SPIRIVA RESPIMAT inhaler will be able to deliver the labeled number of doses.

Proper priming of the inhaler is important to make sure the correct amount of medicine is delivered.

5. Hold the inhaler upright, with the aqua cap closed, to avoid accidental release of dose.
   Turn the clear base in the direction of the black arrows on the label until it clicks (half a turn).

6. Flip the aqua cap until it snaps fully open.

7. Point your SPIRIVA RESPIMAT inhaler toward the ground (away from your face). Press the dose-release button. Close the aqua cap.

Repeat steps 5, 6, and 7 until a spray is visible.

Once the spray is visible, you must repeat steps 5, 6, and 7 three more times to make sure the inhaler is prepared for use.

Your inhaler is now ready to use.

These steps will not affect the number of doses available. After preparation and initial priming, your SPIRIVA RESPIMAT inhaler will be able to deliver the labeled number of doses.

A helpful way to remember how to use your inhaler for daily dosing is

T.O.P.: TURN, OPEN, PRESS.

SPIRIVA RESPIMAT must be prepared and primed before first use.

TURN the clear base until you hear a click.

OPEN the cap and close your lips around the mouthpiece.

PRESS the dose-release button and inhale the mist.

These steps should be performed two times to receive the proper dose of medicine.
LASA (Look Alike, Sound Alike)

LASA (Look Alike/ Sound Alike) has major contribution in medication error. This event can lead to confusing medication names that can cause harm or death to patients. Medication errors also happen due to poor handwriting, limited knowledge regarding medication names, new manufactured products, similar labeling and packaging appearances, similar indications, similar strength, frequency and route of administration. In 2011, the Pharmaceutical Services Division, Ministry of Health Malaysia received a total of 5,003 reports on near misses and medication errors through its Medication Error Reporting System. Approximately 6% of the reports were associated with look like or sound alike medications.

Strategies to avoid errors with Look Alike Sound Alike Medications minimise the availability of multiple medicines strengths. Whenever possible, avoid purchase of medicines with similar packaging and appearance. As new products or packages are introduced, compare them with existing packaging.

Store LASA medications separately from their LASA pair. Identify medicines based on its name and strength and not by its appearance or location. Check the appropriateness of dose for the medicines dispensed. READ medication labels carefully at all dispensing stages and perform triangle check. Triangle check is to check actual medicines against the medicines’ labels and against the prescription. Double checking should be conducted during the dispensing and supply process. Highlight changes in medication appearances to patients upon dispensing.

(Tall man Lettering)

One in every 1,000 medication orders in a hospital, and one in every 1,000 prescriptions in a pharmacy, have been associated with selecting the wrong drug while prescribing, transcribing, dispensing, or administering medications. One of the key causes of these errors is drug name similarity. Other risk factors that increase the risk of confusion between similar drug names include similarities in strength, dosing, route of administration, dosage forms, indication, the environment in which the drugs are used, the frequency of use, and product labelling.

Tall man lettering is one technique to differentiate look-alike drug names. Tall man lettering, a term coined by the Institute for Safe Medication Practices (ISMP), describes a method for differentiating the unique letter characters of similar drug names known to have been confused with one another. Starting with a drug name printed in lowercase letters, tall man lettering highlights the differences between similar drug names by capitalizing dissimilar letters. Accentuating a unique portion of a drug name with uppercase letters along with other means, such as color, bolding, or contrast, can draw attention to the dissimilarities between look-alike drug names as well as alert healthcare providers that the drug name can be confused with another drug name.

(Excerpt from ISMP newsletter, 2016)

A survey was done by ISMP to evaluate the scope and effectiveness of Tall man lettering to differentiate products with look alike names. Two-thirds to three-quarters of respondents who use tall man letters with look-alike drug name pairs felt this strategy was effective in reducing the risk of errors. Use on computer-generated pharmacy labels and pharmacy drug selection screens was the most prevalent and considered to be the most effective. (Medscape Pharmacist)
### List of Drug Name Pairs with Tall Man Letters

<table>
<thead>
<tr>
<th>Drug Name with Tall Man Letters</th>
<th>Name Confused With</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARIPiprazole</td>
<td>RABEprazole</td>
</tr>
<tr>
<td>cefoTetan</td>
<td>cefOXitin – cefTAZidime – cefTRIAXone</td>
</tr>
<tr>
<td>cefOXitin</td>
<td>cefAZolin - cefoTetan – cefTAZidime - cefTRIAXone</td>
</tr>
<tr>
<td>cefTAZidime</td>
<td>cefAZolin - cefoTetan – cefOXitin – cefTRIAXone</td>
</tr>
<tr>
<td>cloZAPine</td>
<td>clonapePAM - cloNIDine</td>
</tr>
<tr>
<td>DOCEtaxel</td>
<td>PACLitaxel</td>
</tr>
<tr>
<td>flavoxATE</td>
<td>fluvoxaMINE</td>
</tr>
<tr>
<td>fluPHENAZine</td>
<td>fluvoxaMINE</td>
</tr>
<tr>
<td>fluvoxaMINE - flavoxATE</td>
<td>fluPHENAZine</td>
</tr>
<tr>
<td>levETIRAcetam</td>
<td>levOCARNitine</td>
</tr>
<tr>
<td>levOCARNitine</td>
<td>levETIRAcetam</td>
</tr>
<tr>
<td>niCARdipine</td>
<td>niMODipine – NIFEdipine</td>
</tr>
<tr>
<td>PACLitaxel</td>
<td>DOCEtaxel</td>
</tr>
<tr>
<td>PEMEtrexed</td>
<td>PRALAtrexate</td>
</tr>
<tr>
<td>PRALAtrexate</td>
<td>PEMEtrexed</td>
</tr>
<tr>
<td>RABEprazole</td>
<td>ARIPiprazole</td>
</tr>
<tr>
<td>RisperDAL*</td>
<td>rOPINIRole</td>
</tr>
<tr>
<td>risperIDONE</td>
<td>rOPINIRole</td>
</tr>
<tr>
<td>romiDEPsin</td>
<td>romiPLOStim</td>
</tr>
<tr>
<td>romiPLOStim</td>
<td>romiDEPsin</td>
</tr>
<tr>
<td>rOPINIRole</td>
<td>RisperDAL - risperIDONE</td>
</tr>
<tr>
<td>SORafenib</td>
<td>SUNIt nib</td>
</tr>
<tr>
<td>sulfADIAZINE</td>
<td>sulfasaLAlazine</td>
</tr>
<tr>
<td>sulfasaLAlazine</td>
<td>sulfADIAZINE</td>
</tr>
<tr>
<td>SUNIt nib</td>
<td>SORafenib</td>
</tr>
<tr>
<td>valACYclovir</td>
<td>valGANciclovir</td>
</tr>
<tr>
<td>valGANciclovir</td>
<td>valACYclovir</td>
</tr>
<tr>
<td>ZOLMitriptan</td>
<td>SUMAtriptan</td>
</tr>
</tbody>
</table>
TAHUNAH ENCIK METFORMIN, ANDA CEPATAN BEKERJA... JADITUGAS ANAK ANDA MEMBANTU CIK INSULIN MEMBRIKAN GULA KE DALAM SELU BADAN TE ...

TERIMA KASIH TUA... SAYA JAKII ALIH-JALIHAN TUGAS DENGAN BAIK...

DAHI AMIODORTINE EMA, JOM BAJU... AKU DEMAK MU DHAN AMIODOR TONGS MENOSTTTIKNAN CIK KERIA KIJIANG TUA... DANCI JAWI ONOK MACA DANGAN UANG KELAS CEKART SAJAI... TUA... TUA...

MAK TAKIZINKAN KAU KEPAL DENGAN SITI DICOFENAC SORTUM TU... CAN INCREASE RISK OF GASTRIC ULCER YOU KNOW...HA, KAN MAH DA SPEAKING NI...

AJAP DIA CINTA PERTAMA SARA MAK...

KO KENANGENDAR CARIAP AKU, AKU NI MAKAN DARIAN UBSIH DARI KO TAU AKU... SALAH CABA KO MAH MAHLI KEKETU...

AKT. KARI TEHAN ORI'S MATEU SONAM UDEE BILI PON DA... COOLSENKIP KAJAK MILLISPIRIN KE KEN...

TU PERTRANJISA KIJIU KUJJE KAMAFAS...