DEPARTMENT OF PHARMACOLOGY
ARMED FORCES MEDICAL COLLEGE, PUNE-40

The Pill Box

Issue: First, Jan-Mar 2021

Dear Readers,
The purpose of this bulletin is to disseminate some important information related to drugs and medical devices likely to be of interest to everyone, involved directly or indirectly in patient care. The current issue highlights recent drug approvals , drug safety alerts of some commonly used drugs and what to do in case of levothyroxine overdose/ poisoning. Feedback and suggestions, if any, may be sent at email Id: thepillboxafmc@gmail.com .

Adverse Drug Reactions: Be Aware to Take Care

SGLT2 inhibitors

Sodium-glucose co-transporter 2 (SGLT2) inhibitors like canagliflozin, dapagliflozin, empagliflozin and ertugliflozin etc. are indicated to treat adults with diabetes to improve glycaemic control. Although, a detailed European review in 2016 confirmed diabetic ketoacidosis as a rare risk for the SGLT2 inhibitors, few drug regulatory bodies recently have advised health-care professionals to interrupt sodium-glucose co-transporter 2 (SGLT2) inhibitor treatment in patients who are hospitalised for major surgical procedures or acute serious medical illnesses, and to monitor ketones during the period. Testing of ketones in blood is recommended rather than measuring ketone bodies in urine because SGLT2 inhibitors may diminish the excretion of ketone bodies in urine. SGLT2 inhibitor can be restarted once ketone values are normal and the patient's condition has stabilized.

Fournier's gangrene is necrotising fasciitis of the genitalia or perineum. Although diabetes mellitus is a risk factor for the development of Fournier's gangrene, some of the EU post-marketing reports suggest this condition to be related to the use of SGLT2 inhibitors. Patients taking SGLT2 inhibitors must be advised to seek urgent medical attention if they experience: severe pain, tenderness, erythema, and swelling in the genital or perineal area accompanied by fever or malaise. If Fournier's gangrene is suspected, SGLT2 inhibitor treatment should be stopped and urgent alternative treatment started as appropriate.

References: Drug Safety Update, MHRA, 18 March 2020 and WHO Pharmaceuticals Newsletter No.1, 2020

New Drugs Corner

Evinacumab-dgnb
MOA: Blocks angiopoietin-like protein 3 (ANGPTL3)
Indication: Homozygous familial hypercholesterolemia

Tepotinib
MOA: Mesenchymal-epithelial transition (MET) tyrosine kinase inhibitor
Indication: Non-small cell lung cancer

Voclosporin
MOA: Calcineurin-inhibitor immunosuppressant
Indication: Lupus nephritis

Vericiguat
MOA: Soluble guanylate cyclase stimulator
Indication: Chronic Heart Failure

Reference: USFDA

Have you ever wondered what would happen if the entire autonomic nervous system was blocked? It can indeed be done pharmacologically by using ganglion blockers like hexamethonium. Lets hear the story of 'hexamethonium man' as described by Paton: He is a pink-complexioned person, except when he has stood in a queue for a long time, when he may get pale and faint. His handshake is warm and dry. He is a placid and relaxed companion; for instance he may laugh but he can't cry because the tears cannot come. Your rudest story will not make him blush, and the most unpleasant circumstances will fail to make him turn pale. His collars and socks stay very clean and sweet. He wears corsets and may, if you meet him out, be rather fidgety (corsets to compress his splanchnic vascular pool, fidgety to keep the venous return going from his legs). He dislikes speaking much unless helped with something to moisten his dry mouth and throat. He is long-sighted and easily blinded by bright light. The redness of his eyeballs may suggest irregular habits and in fact his head is rather weak. But he always behaves like a gentleman and never belches or hiccups. He tends to get cold and keeps well wrapped up. But his health is good; he does not have chilblains and those diseases of modern civilisation, hypertension and peptic ulcer, pass him by. He gets thin because his appetite is modest; he never feels hunger pains and his stomach never rumbles. He gets rather constipated so that his intake of liquid paraffin is high. As old age comes on, he will suffer from retention of urine and impotence, but frequency, precipitancy and strangury (i.e. an intensely painful sensation of needing to pass urine coupled with an inability to do so) will not worry him. One is uncertain how he will end, but perhaps if he is not careful, by eating less and less and getting colder and colder, he will sink into a symptomless, hypoglycaemic coma and die, as was proposed for the universe, a sort of entropy death.

Reference: Rang & Dale's Pharmacology, 8th Edition

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Levothyroxine overdose/ poisoning: What to do?

A 2-year-old girl child presents to emergency department with her parents after ingesting an unknown quantity of her mother's levothyroxine five days ago. The child was fine until today when he became agitated , was sweating profusely and had 4 –6 episodes of vomiting and diarrhea in last 4 hours. On examination, temperature 101* F, HR: 170 bpm, RR: 28 breaths per minute, BP: 72/40 mmHg. Child looks agitated and was not sitting still.

Levothyroxine overdose/ poisoning: Things to know

Potential Toxic dose: > 20 mcg/kg

Symptoms & signs:

Mild poisoning: Subtle tremor, anxiety, insomnia, mild sinus tachycardia, hypertension

Moderate to severe poisoning: Altered mental status, headache, vomiting, diarrhoea, palpitations, anxiety, headache, flushing, agitation, confusion, hallucinations, delirium, hyperactivity, excitability, irritability, sweating, hyperpyrexia, tremor, muscle cramps, muscle weakness, tachypnoea, tachycardia and hypertension. May lead to coma, convulsions, angina and cardiac arrhythmias.

Rarely, features of hyperthyroidism may develop after 3-6 days. Chronic overdose may cause pronounced weight loss, anxiety, accelerated osteoporosis, myocarditis, cardiac dysrhythmias, tachycardia, cardiac failure, psychosis and thyroid storm.

Monitoring: Vitals, Blood glucose, electrolytes, CBC, ABG, RFT

Continuous cardiac monitoring in patients with symptoms and signs of cardiac toxicity.

No role of serial measurements of T3 & T4 levels as they do not correlate with clinical symptoms

Management:

-Do not induce vomiting.

-Perform endotracheal intubation, assist ventilation and administer humidified oxygen if needed.

-Gastric lavage: In case of large ingestion (>3 mg)

-Activated Charcoal: In case of large ingestion (>3 mg)

-Antidote: None

-Consider use of beta blockers in symptomatic patients.

Propranolol : Adults- Oral (10-40 mg TDS); IV (1 mg over 1 min); Repeat doses if no clinical response (Max 10mg); Children- Oral (250-500 mcg/kg TDS); IV (25-50 mcg/kg IV TDS) (Max 5 mg)

Use esmolol or diltiazem in patients of bronchial asthma or COPD.

-In case of excessive ingestion, to block peripheral conversion of T3 to T4, IV hydrocortisone can be given.

-Treat seizures, hyperthermia, hypotension, arrhythmias if present.

Observation period (if asymptomatic): 12 hours. Providing adequate discharge instructions is of paramount importance for levothyroxine ingestions. Follow-up period of 14 days in initially asymptomatic patients.

mRNA vaccines: Fast & Furious

Successive epidemics/pandemics during last 10-12 years have underlined the importance of faster vaccine development. RNA based vaccine platform is one promising technology that hastens vaccine development many folds. Indeed, SARS CoV-2 mRNA vaccine was ready for testing in just 66 days after viral genome sequencing. RNA vaccines exhibit self-adjuvanticity and induces both a humoral and cellular immune response against the encoded protein, spike protein in case of COVID. An important feature of mRNA vaccines is faster and scalable manufacturing process that can be quickly tailored to any ongoing outbreak. RNA being intrinsically unstable , these vaccines are required to be stored between –80° C to –20°C , a major limitation for public use deployment. Evolving advances in technology of lyophilisation/ freeze drying or formulating thermostable RNA are likely to ameliorate this limitation. Vaccinology is certainly going through an exciting phase and we may not be very far from the day when we shall never be far from a vaccine against a novel infective agent, natural or fabricated.

The Pill Box Crossword: 01

Instructions:

1. Scan the QR code or click on the below link to get the crossword.
https://crosswordlabs.com/view/the-pill-box-crossword1-2
2. Click on the given hint.
3. Enter your answers in highlighted space.
4. Correct answers will be indicated by "✓" sign.

For correct answers, scan the QR code or click on the link: https://ibb.co/jHzCXMG

Prescribe medicines as if every patient was your own.
Be safety minded and not safety blinded while prescribing medicines.