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Pharmacy Newsletter provides information regarding the decisions of P & TC, current concepts in drug therapy, warnings and cautions issued by various regulatory agencies, drug interactions, ADRs and matters related to drug usage.

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Drug & Poison Information Centre,
Tel: +92 21 34861504, 1506, 1477, 1479
Email: drug.information@aku.edu
hospital.aku.edu/Karachi/pharmacy

Inside this Issue:

Vancomycin Dosing in ESRD with Intermittent Hemodialysis (IHD)

Bilal Ahmad, DPIC Pharmacist

Due to its poor dialyzibility via low flux membranes, dose adjustment of Vancomycin is complicated in IHD. Prehemodialysis Vancomycin levels are a good predictor to define the maintenance doses, administered preferably after dialysis session. Loading dose (weight based has good clinical outcomes compared to fixed dosing regimen) is followed by post dialysis dose and withdrawal of levels before second dialysis session, subsequent dosing are based on Vancomycin levels. There is no validated guideline for dosing but AJHP recommended the following strategy.

Vancomycin TDM in ESRD with IHD

Dosing in mild-moderate

Loading Dose Algorithm	
Actual body weight, kg	Vancomycin LD (15-20mg/kg)
<65	1000mg IV
65.1 – 85	1250mg IV
85.1 – 100	1500mg IV
>100	1750mg IV
Maintenance dose algorithm	
Serum Vancomycin Conc, mcg/mL	MD after dialysis
<10	1000mg IV
10-15	500-750mg IV
15.1- 20	500mg IV
>20	Hold Vancomycin

Dosing in severe Infections.

Loading Dose Algorithm	
Actual body weight, kg	Vancomycin LD (20mg/kg)
<65	1000mg IV
65.1 – 85	1500mg IV
85.1 – 100	1750mg IV
>100	2000mg IV
Maintenance dose algorithm	
Serum Vancomycin Conc, mcg/mL	MD after dialysis
<10	1gm-1.5gm IV
10-15	750-1000mg IV
15.1- 20	500-750MG IV
>20	500mg IV
>25	Hold Vancomycin

Reference:

Page Crew, Shannon J. Heintz, Brett H. Heintz, Vancomycin dosing and monitoring for patients with end-stage renal disease receiving intermittent hemodialysis, American Journal of Health-System Pharmacy, Volume 72, Issue 21, 1 November 2015, Pages 1856–1864,

Increased Risk of Ventricular Arrhythmias with Domperidone

Muhammad Amir, Specialist

Increased risk of serious ventricular arrhythmias or sudden cardiac death have been associated with the use of Domperidone. Risk is increased particularly with doses >30 mg, geriatrics , children and with drug causing QT elongation and CYP 3A4 interacting drugs. To reduce the risk

1. In adults and children aged ≥ 12 years old weighing ≥ 35 kg, the recommended maximum oral daily dose is 30 mg, given in doses of 10 mg up to three times daily

2. Children aged < 12 years old and those aged ≥ 12 years old weighing < 35 kg, the recommended dose is 0.25 mg/kg orally up to three times daily. For

rectal administration, these patients may also be given 0.75 mg/kg twice daily as suppositories.

3. Use the lowest possible dose for the shortest duration necessary.

4. Avoid drugs causing QT elongation or CYP 3A4 inhibition or induction

References:

[1] *Health Science Authority. New recommendations on the use of domperidone. https://www.hsa.gov.sg/content/hsa/en/Health_Products_Regulation/Safety_Information_and_Product_Recalls/Product_Safety_Alerts/2017/new-recommendationsontheuseofdomperidone.html*

Drug Induced Esinophilic Pneumonia

Nida Abbasi, Clinical Pharmacist

Eosinophilic pneumonia (EP) is a rare and heterogeneous syndrome, also known as pulmonary infiltrates with eosinophilia syndrome. Drugs known to cause eosinophilic pneumonia are gemcitabine, infliximab, ranitidine, sulfasalazine/ mesalamine, venlafaxine As per the hypothesized mechanism, drug increased concentration results in the retention of in the alveoli leading to continuous activation of immune system. Further studies are required to understand this phenomena. In order to treat Drug induced EP, corticosteroids are suggested for use, as they may cause eosinophilic apoptosis. As a common regimen intravenous methylprednisolone is recommended as 60–125 mg every 6 h, with conversion to prednisone 40–60 mg oral daily and taper over 2–6 weeks.

References:

1. *Higashi Y, Nakamura S, Tsuji Y, et al. Daptomycin-induced Eosinophilic Pneumonia and a Review of the Published Literature. Intern Med. 2018;57(2):253–258. doi:10.2169/internalmedicine.9010-17*
2. *Yang Ye, Zijing Xia, Dan Zhang, et al., "Multifunctional Pharmaceutical Effects of the Antibiotic Daptomycin," BioMed Research International, vol. 2019, Article ID 8609218, 9 pages, 2019. https://doi.org/10.1155/2019/8609218.*
3. *Priyasha Uppal, Kerry L. LaPlante, Melissa M. Gaitanis, Matthew D. Jankowich,Kristina E. Ward, Daptomycin-induced eosinophilic pneumonia - a systematic review, Antimicrobial Resistance & Infection Control, 2016, Volume 5, Number 1, Page 1*

An Insight on aspirin; ASCEND, ARRIVE and ASPREE Trials

Syeda Anum Fatima, IPD Pharmacist.

Up till now meta-analysis on using low-dose-aspirin suggested benefit in preventing cardiovascular events, reducing all-cause mortality and even reduction in colon cancer risk. However, three major RCT's in 2018 have concluded otherwise. The first trial known as the 'ASCEND' evaluated the role of aspirin in 15,480 diabetic patients concluding that there might be some benefit associated with the reduction in CVS events in diabetics but there was increase in the major bleeding events is aspirin groups as compared with the placebo with most patients experiencing gastrointestinal and other extracranial bleeding events. Another important highlight of this trial was that there was no significant difference between the aspirin and placebo groups with respect to G.I or other cancers. The second trial known as the 'ARRIVE' study to evaluated the use of aspirin in patients who were at moderate risk of CVS events, this study published data based on 13000 patients and concluded that aspirin had no effect in reducing all-cause mortality or CVS events as primary endpoints, there was a slight increase in G.I bleeding events in the aspirin groups as compared to the placebo. The third trial known as the 'ASPREE' trial evaluated 20000 patients for aspirin effect on All-cause mortality in healthy elderly patients. The findings of this large RCT was different from the other two as All-cause mortality in the aspirin group was 12.7% while in the placebo group was 11.1% with cancer being the major contributor for death i.e. 3.1% in the aspirin group while 2.3% in the placebo group. With these three major RCTs clinicians need to be careful about using aspirin as primary prevention for CVS events but we must keep in mind that this does not have to do anything with the use of aspirin for secondary prevention as the evidence for latter is definite with benefit outweighing the risks.

Reference:

Kuehn BM. Aspirin for Primary Prevention Takes a Hit With New Trial Results. Circulation. 2018 Dec 4;138(23):2713-2714.

Drugs Administeration Through Nasogastric Tube (Advantages and Its Restrictions)

Saba Jawed, In-patient Pharmacist

Enteral feeding tube is mostly used in those patients that are critically ill and cannot take solid diet. Before administration, following parameters should be considered via enteral tube like drug formulation, type of tube, interaction with feed and site of drug absorption.

FORMULATION TO BE ADMINSTERATED VIA NG TUBE:

Liquid Dosage Form: Many drug formulations available in both solid and liquid form are easily administered but some are not commercially available. But can be prepared. Available liquid preparations should be diluted enough to be used via NG because some are very thick and viscous preparations.
Solid Dosage Form: Some tablets/capsules are used through NG by crushing them or in powder form. Dilute enough to easily administer (mostly 30-50 ml WFI). Sugar coated and film coated can also be used except enteric/ controlled release tablets/capsules/ buccal/sublingual/ cytotoxic drugs because of increase risk of adverse drug reactions.
Parenteral: Some IV preparations given orally can be given through NG tube.
Following drugs have interaction with enteral feed like Carbamazepine, Hydralazine, Ciprofloxacin, Thyroxine, Warfarin and Phenytoin sodium leading to decreased absorption, it may adhere to tubing.
Following drugs are easily administered:

Acetazolamide	Amoxicillin	Amlodipine	Atenolol	Amitriptyline	Amiodarone	Baclofen	
Bromocriptine	Clopidogrel	Valsartan	Septran	Aspirin (non enteric)	Vancomycin	Pyridoxine	Perindopril

References:

American Parkinson's Disease Association, APDA

FDA Box Warning | Opioid- Withdrawal Symptoms

Hafsa Ghalib, Pharmacist

US FOOD AND DRUG ADMINISTRATION, notified about the serious harm in patients physically dependent on opioid pain medicines, with the sudden discontinuation or rapid decrease in their dose. These include serious withdrawal symptoms of uncontrolled pain, psychological distress, and suicide. These symptoms can cause patients to seek other sources of opioid pain medicines, which can be confused with drug seeking for abuse. Patient may attempt to treat their pain and symptoms with illicit opioids, such as heroin, and other substances.

RECOMMENDATIONS FOR HEALTH CARE PROFESSIONALS:

i. Health care professionals should not abruptly discontinue opioids in physically dependent patients.
ii. Dose of opioids analgesics should be tapered based on factors, including the dose of the drug, the duration of treatment, the type of pain being treated, and the physical and psychological attributes of the patient.
iii. No standard opioid tapering schedule exists that is suitable for all patients.
iv. Create a patient-specific plan to gradually taper the dose and ensure ongoing monitoring and support to avoid serious withdrawal effects.

Reference:

FDA Drug Safety Communication (April 9, 2019)
https://www.fda.gov/drugs/fda-drug-safety-podcasts/fda-identifies-harm-reported-sudden-discontinuation-opioid-pain-medicines-and-requires-label-changes

Warning | Fluoroquinolone use Associated with Aortic Aneurysm

Nida Abbasi, Clinical Pharmacist

Recently FDA has issued warning that fluoroquinolones use is associated with aortic aneurysm. It was identified after a review of cases reported in FDA adverse event reporting system. The findings from the observational studies confirm the positive association between fluoroquinolone and the development of aortic aneurysm/ dissection, hence suggested to avoid fluoroquinolone in patients with known aortic aneurysms or those with risk factors for aneurysm such as Marfan's syndrome, Ehlers-Danlos syndrome, peripheral atherosclerotic vascular diseases, hypertension, and/or advanced age. Although exact mechanism is unknown, but there are several possibilities. Fluoroquinolone destroy the collagen and connective tissue along the aortic wall causing aortic aneurysm and dissection as they do on tendon and cornea. Moreover, some risk factors may appear to prevail including prolonged fluoroquinolone treatment and older age.
The FDA offers the following advice for the physicians:

- Do not prescribe fluoroquinolone to those patients who are with aortic aneurysm or are at the risk of developing it, except if there is no any alternative.
- Advice all patients to seek immediate medical attention if they develop symptoms of aortic aneurysm.
- Stop fluoroquinolone immediately if patients have symptoms of aortic aneurysm or dissection.

References:

US Food and Drug Administration. Fluoroquinolone Antibiotics: Safety Communication - Increased Risk of Ruptures or Tears in the Aorta Blood Vessel in Certain Patients.

Medications to Be Avoided or Used with Caution in Parkinson's Disease |APDA

Bilal Ahmad, DPIC Pharmacist

Medications to be avoided or used with caution in combination with Selegiline & Rasagiline.

Medication Type	Medication Name
Narcotics/Analgesics	Meperidine Tramadol Methadone Propoxyphene
Antidepressants	St. John's Wort
Muscle Relaxants	Cyclobenzaprine
Cough Suppressants	Dextromethorphan
Decongestants/Stimulants	Pseudoephedrine Phenylephrine Ephedrine
Other medications that inhibit Monoamine oxidase	Linezolid (antibiotic) Phenelzine Tranylcypromine Isocarboxazid
Medications to be avoided or used with caution in all patients with Parkinson's disease	
Typical Antipsychotics	Chlorpromazine Fluphenazine Haloperidol Trifluoperazine (Block D2 (dopamine) receptors in the brain, which can worsen Parkinson's)symptoms
Atypical Antipsychotics	Risperidone Olanzapine Ziprasidone Aripiprazole Lurasidone Paliperidone (Block dopamine receptors, but dissociate from the recep- tor more quickly than typical antipsychotics. They also tend to block serotonin receptors in addition to dopamine recep- tors. The result is less parkin- sonism than that caused by the typical antipsychotics).
Antiemetic (used to treat nausea or vomiting)	Chlorpromazine Droperidol Metoclopramide Prochlorperazine Promethazine (Block D2 (dopamine) receptors in the brain, which can worsen Parkinson's symptoms).
Drugs to treat hyperkinetic movements such as chorea and tardive dyskinesia	Tetrabenazine Deutetrabenazine Valbenazine (Decrease dopamine stores)
Antihypertensives	Reserpine (Decreases dopamine stores)
	Methyldopa (Inhibits an enzyme which converts L-dopa into dopamine in the brain)
Antidepressants	Phenelzine Tranylcypromine Isocarboxazid (Block monoamine oxidase non-selectively. If taken in combination with certain classes of PD meds, these medications could result in dangerous increases in blood pressure and agitation).
	Amoxapine (Although classified as a tricyclic anti-depressant, it can also block dopamine receptors)

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Thank you in advance for your feedback!
Link: *https://goo.gl/forms/Ghh1Nc2KY2jEkiUL2*