A NEWSLETTER BY DEPARTMENT OF PHARMACY—SIH

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Shifa International Hospitals Ltd.
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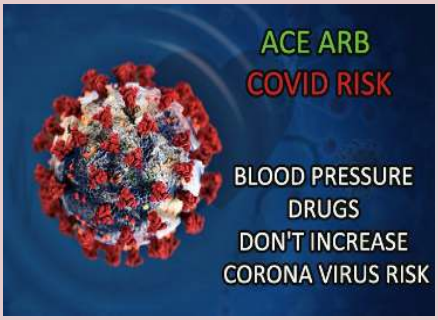
Inside this issue

BLOOD PRESSURE DRUGS DON'T INCREASE COVID-19 RISK

Amna Naeem, Inpatient Staff Pharmacist

Widely prescribed drugs ACE and ARBs for the treatment of high blood pressure do not increase patient's risks for corona virus infection, or for serious illness if they do become infected, according to new research. The findings were published 15th May in the *New England Journal of Medicine*. The study findings are good news for the millions of people who take ACE inhibitors and ARBs. The research also found no risk associated with three other classes of frequently used blood pressure drugs: beta blockers, calcium-channel blockers, and thiazide diuretics. The *NEJM* research involved a review of the records of more than 12,500 patients who were tested for the corona virus, including 5,894 who were infected. Some of the patients also had high blood pressure. After examining the patients' likelihood of being infected, the severity of the illness, and the medications they were taking before being tested for the virus, and using statistical methods to rule out differences in terms of age, smoking history, and other factors, the researchers found no meaningful differences. So there is no increased risk of hypertensive patients using ACE inhibitors or ARBs to become infected with corona virus.



AHA, ACC, HFSA, European Society of Cardiology recommend to continue treatment with RAAS antagonists in those patients who are currently prescribed such agents.

Reference: Reynolds et al. New England Journal of Medicine - 2020

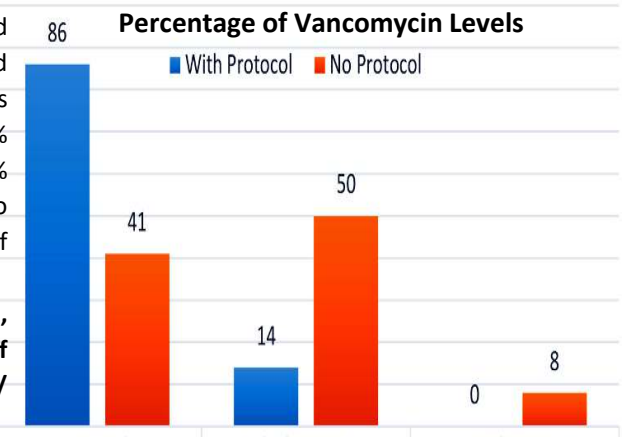
NEW DOSING PROTOCOL FOR VANCOMYCIN

Successfully piloted and implemented in Shifa

Shifa Hospital was facing issue of lots of patients not achieving optimum serum drug levels with Vancomycin. Team of clinical pharmacists at Shifa reviewed literature and came up with modified dosing protocol. It was piloted in ICUs first and after major success (86% patients achieving target levels vs 41% before protocol) it was rolled out to entire hospital. The main features of new protocol include:

Weight based dose, Loading dose, q8hrly dosing and careful monitoring of patients with reduced or high (>100ml/ min) creatinine clearance.

For further information contact Drug & Poison Information Centre, Shifa



	Optimal	Subttherapeutic	Supratherapeutic
With Protocol	86	14	0
No Protocol	41	50	8

Glimpses of New Vancomycin Dosing Protocol

Loading Dose: Indicated in critically ill patients or with invasive infection or those with high trough goals

Loading Dose 25-30 mg/kg (Max 3g)*	
Weight (kg)	**Dose**
45-55	1.25g
56-65	1.5 g
66-75	1.75g
76-85	2g
86-95	2.25 g
95>	2.5g

Indication	Target Trough Ranges
UTI, skin wound /abscess	10-15 mcg/mL
Sepsis, bacteremia , osteomyelitis, Pneumonia, Endocarditis, MRSA	15-20 mcg/mL

*Target rough levels should be **>10 mcg/mL** to avoid resistance*

Maintenance Dose 15-20 mg/kg/dose (Max 2 g)				
eGFR**	**Actual Body Weight**			
	45-55 kg	**56 – 75 kg**	**76 – 90 kg**	**>90 kg**
>90	750 mg q 8hr	1 g q 8hr	1.25 g q 8hr	1.5 g q 8hr
50-90	750 mg q 12hr	1 g q 12hr	1.25 g q 12hr	1 g q 8hr
15-49	750 mg q 24hr	1 g q 24hr	1.25 g q 24hr	1.5 g q24hr
<15	750 mg	1 g	1.25 g	1.5 g

Dose Adjustments Based on Trough Levels:

Trough Levels	Suggested dosage adjustment
< 10mg/L	Increase dosage by shortening the dose interval.
10 to 20 mg/L	Maintain current dosage or increase as per target trough levels.
21 to 25 mg/L	Reduce the dose or withhold dose. (Adjustments may not be necessary)
> 25 mg/L	Withhold dose until trough concentration is less than 20 mg/L.

Solid Organ Transplant and COVID-19 - FAQs

Rehan Anjum, Transplant Clinical Pharmacist

I am a transplant patient, Am I at high risk of getting this infection?

There is not any specific information on whether COVID-19 infection will be more severe in transplant recipients compared to healthy people; however, other **viruses often cause more severe disease in people whose immune system is low**, such as transplant recipients. For this reason, it is important to take precautions to prevent infection.

Is there any travel restriction for transplant patients?

It is best to **postpone nonessential travel.** We also highly suggest that transplant recipients' **immediate household contacts should postpone non-essential travel** to areas that are considered high risk.

Can I stop medications if I am more prone to this infection?

Stopping the medication will not put any difference to the infection , instead it will put you on extra risk of organ rejection. **So don't stop taking transplant medications.** Try to keep a one-month supply available at all times. (Shifa Pharmacy is providing Home Delivery)

Should I take vaccines or treatment for COVID-19 ?

Currently, there are no antivirals or vaccines effective against this virus, although studies to develop these are ongoing. You are advised to take **only influenza vaccine if its been more than a month after transplant.**

How I can protect myself from getting this infection?

- Avoid close contact with anyone who is sick.
- Avoid touching your eyes, nose, and mouth.
- Practice cough etiquette – sneeze and cough into your elbow or a tissue, and wash your hands after coughing/sneezing.
- Clean and disinfect high touch objects and surfaces using a household cleaning spray or wipe.
- Wash your hands frequently with soap and water for 20 seconds, especially after going to the bathroom, before eating, and after blowing your nose, coughing or sneezing. If soap and water are not available, use an alcohol based hand sanitizer that contains at least 60% alcohol.
- Avoid all crowded areas. Stay home as much as possible. Wear mask in public areas incl. hospital/clinics
- If you work, try to work from home as much as you can.
- Determine who can provide you with care if your caregiver gets sick.

My family member just returned from an area with high COVID-19 activity. What should I do?

Avoid contact for 14 days with such individuals. If the individual remains healthy after 14 days, contact can be resumed.

What should I do if a family member/co-worker is diagnosed with COVID-19?

If a close contact is diagnosed with or suspected of having COVID-19, he/she should **avoid all further contact** with the transplant recipient. The transplant recipient should be monitored for symptoms and contact their transplant coordinator if they develop fever, cough or shortness of breath.

Light Protection of Neonatal TPN

Muhammad Gulzaib, Peads Clinical Pharmacist

Light Effects in Neonatal TPN:

The Medicines and Healthcare products Regulatory Agency (MHRA) have agreed a letter (Aug 2019) about the important of protecting parenteral nutrition products from light if they are to be used in neonates and in children below 2 years. Recent studies have confirmed, if these nutritional support solutions containing trace elements/or vitamins are exposed to light, their composition can be altered. Free radicals, peroxides, and aldehydes are commonly found in the bodies of newborn animals and premature infants. A significant exogenous source of these byproducts is administered to the patient via TPN.

Light exposure can produce high levels of harmful hydrogen peroxide, oxidants and oxidizing agents that can dangerously stress the compromised antioxidant systems of preterm infants or serious ill neonates.

Administration of TPN Recomendations:

- **During administration to neonates and children below 2 years of age, parenteral nutrition products containing amino acids lipids, should be protected from light (containers and administration sets).**
- Light exposed TPN can cause hepatic damage, steatosis, cholestasis, and pulmonary oxidant challenge, remodeling, apoptosis, and an increased marker for pulmonary fibrosis.

Premature neonates are considered at high risk of oxidative stress related to multiple risk factors including oxygen therapy, phototherapy, weak immune system and inflammatory response with reduced oxidant defense. Preterm infants are more vulnerable to oxidative stress, owing to having lower levels of plasma antioxidants, plasma metal-binding proteins, and reduced activity of erythrocyte superoxide dismutase. Peroxides result in oxidative stress, with significant damage to cell integrity. Peroxides and free radicals have been implicated in the pathogenesis of various complications associated with prematurity, such as bronchopulmonary dysplasia, necrotizing enter colitis, and retinopathy of prematurity.

Reference: *https://www.bapm.org/posts/69-warning-to-protect-pn-products-from-light*

Myths and Facts about Medicines

Zeeshan Ali, Emergency Pharmacist

I don't need to tell my doctor about the OTC drugs/ supplements I take: Such medicines don't require a prescription, but can alter the effectiveness of some other prescription medications. So always use them after discussion with your physician or pharmacist.

I feel OK, so I don't need to take my medication: You are feeling OK because you are taking medicine! therefore complete the prescribed course. Don't stop taking medications without your doctor's advice.

Taking pills are the only answer: Many ailments can go away (or managed well) with slight change in life style, i.e. the way we work, sleep, eat and rest.

If I still have symptoms, I can take extra dose: Medicines work well when taken as prescribed, with defined intervals. Taking extra dose can lead to adverse effects or toxicity. Never increase dose or take extra without consulting your doctors/pharmacist

I missed the dose, so I should take 2 doses: Never make up for the missed dose. If this is almost time for next dose, skip the previous one and only take next due dose. If you have missed the doses in a row inform your doctor/ pharmacist

Antibiotics are the answer for every illness: No - Antibiotics only work against illness caused by bacteria. Stop taking Antibiotics for common colds, simple diarrhea etc as or which antibiotics will NOT work.

Cool Facts:

Shifa Ambulatory Care pharmacies have successfully implemented Therapeutic Drug Monitoring program for 2 high alert drugs **Warfarin and MTX** (Oral). All prescriptions of these 2 drugs are assessed on standard checklist of intervention and patients are counselled.

On an average we review 200 Rxs of MTX and 90 Rxs of Warfarin per month and counsel patients!

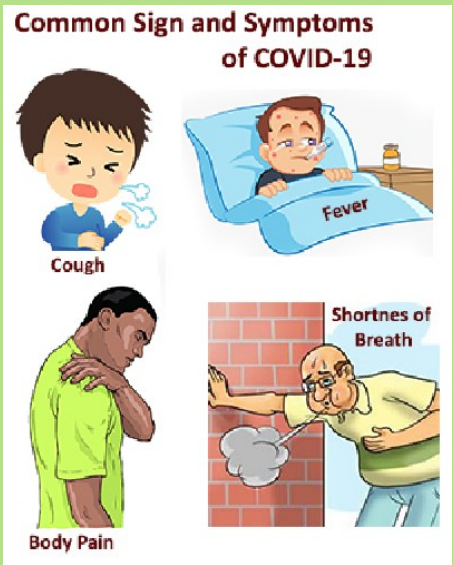


Photo courtesy By : Sara Yahya Ambulatory Care pharmacist

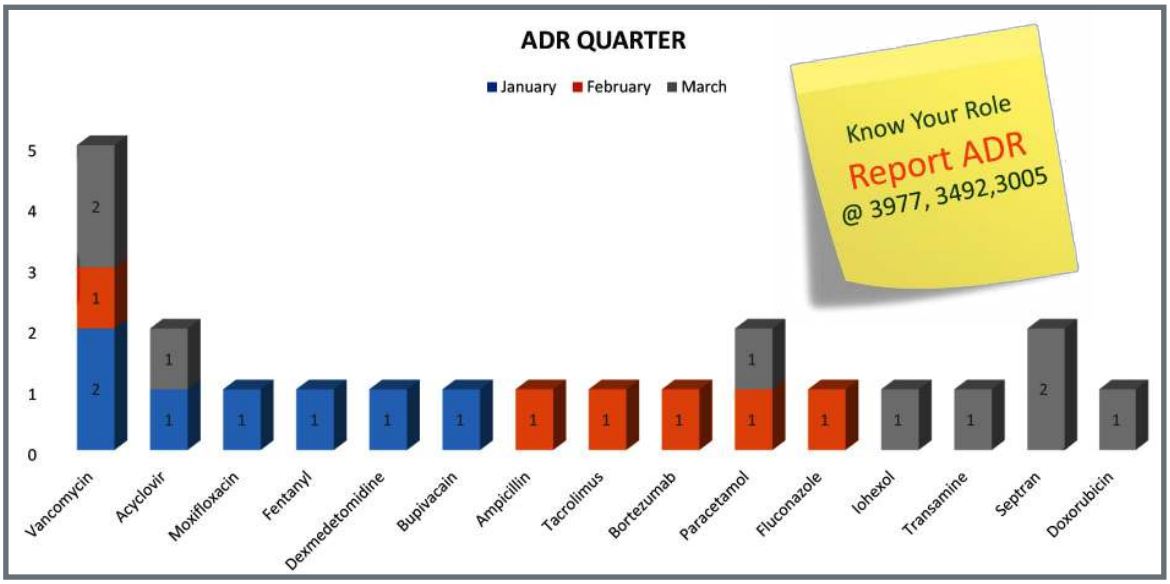
Iron protects childhood ALL cells from Methotrexate Cytotoxicity

Bushra Anjum Principal Oncology Pharmacist

Acute lymphoblastic leukemia (ALL) is a blood cancer in which the immature lymphoid progenitors are neoplastic and show deregulated proliferation. This malignancy is the most common type of leukemia in children under 15 years of age. Drug resistance is a fundamental clinical concern in pediatric acute lymphoblastic leukemia (pALL), and methotrexate (MTX) is an essential chemotherapy drug administered for the treatment. In a study, the effect of iron in response to methotrexate and its underlying mechanisms were investigated in pALL cells. CCRF-CEM and Nalm6 cell lines were selected as T and B-ALL subtypes. Cells were pretreated with ferric ammonium citrate, exposed to the IC50 concentration of MTX and cell viability was assessed using MTT assay, colony formation, and flow cytometry assays. Iron-loaded cells were strongly resistant to MTX cytotoxicity. The inhibitory effect of N-acetyl cysteine to reverse the acquired MTX resistance was greater than that of the iron chelator, Deferasirox, highlighting the importance of iron-mediated ROS in MTX resistance. Subsequently, the upregulation of BCL2 , SOD2 , NRF2 , and MRP1 was confirmed using quantitative RT-PCR. Moreover, a positive correlation was demonstrated between the MRP1 expression levels and bone marrow iron storage in pALL patients. Further supporting findings were the hematoxylin and eosin-stained histological sections showing that iron-treated nude mice xenografts demonstrated significantly more liver damage than those unexposed to iron. Overall, iron is introduced as a player with a novel role contributing to methotrexate resistance in pALL. **The study suggest that the patients' bone marrow iron stores are necessary to be assessed during the chemotherapy, and transfusions should be carefully administrated.** Reference: Abedi et al. - Cancer Medicine - 2020

Formulary Updates (Visit Shifa Intranet Home Page—click Medication Updates for details)

Brand	Generic	Class	Indications
Neudopa 25/250	Levodopa/Carbidopa	Combination product	Parkinson's Disease
Pre-NAN HMF	Human Milk Fortifier	Nutritional Supplement	Premature infant nutrition
Hydrovate cream	Hydrocortisone 1%	Corticosteroid	Inflammatory skin diseases
Synalgo	Flurbiprofen100 mg	NSAID	Arthritis, Pain
Glandin E2	Dinoprostone	Prostaglandin	Cervical ripening
Deston Syrup	Ondansetron	Anti Emetic	Nausea, Vomiting



Stay Safe From Corona

Looking for Your Valuable Feedback

We want to bring to you valuable, updated and interesting information via Pharmacy Newsletter, so please spare some time to provide your valuable feedback in the form of comments or suggestions. Its your newsletter and with your help we'll make it better!

*Kindly send us your **comments/suggestions** via email at : **drug.information@shifa.com.pk***

Thank you , we are looking forward for your valuable feedback.