A NEWSLETTER BY DEPARTMENT OF PHARMACY—SIH

PHARMACY BULLETIN

Shifa International Hospitals Ltd.
شفا انٹرنیشنل ہسپتال لمیٹڈ

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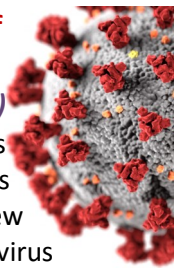
Inside this issue

An excerpt of Surviving Sepsis Campaign Guidelines on the Management of Adults With Coronavirus Disease 2019 (COVID-19) in the ICU:



Rehan Anjum (Clinical Pharmacist ICU)

The Surviving Sepsis Campaign Coronavirus Disease 2019 panel has expanded to include 43 experts from 14 countries. The Surviving Sepsis Campaign Coronavirus Disease 2019 panel issued nine statements (three new and six updated) related to ICU patients with severe or critical coronavirus disease.

Therapy Recommendations	
For adults with severe or critical COVID-19, we recommend **against** using hydroxychloroquine.	**Strong**
For adults with severe or critical COVID-19, we **recommend using** a short course of systemic corticosteroids over not using corticosteroids.	**Strong**
For adults with severe or critical COVID-19 who are considered for systemic corticosteroids, we **suggest using** dexamethasone over other corticosteroids. *Remark*: If dexamethasone is not available, clinicians may use other corticosteroids in doses equivalent to 6 mg daily of dexamethasone for up to 10 days.	**Weak**
For adults with severe COVID-19 who do not require mechanical ventilation, we **suggest using** IV Remdesivir over not using it. *Remark*: Remdesivir should *ideally* be started within 72 hours of positive severe acute respiratory syndrome coronavirus 2 polymerase chain reaction or antigen testing.	**Weak**
For adults undergoing mechanical ventilation for critical COVID-19, we suggest **against** starting IV remdesivir.	**Weak**
For critically ill adults with COVID-19 who develop fever, we **suggest using** acetaminophen/paracetamol for temperature control over no treatment.	**Weak**
In critically ill adults with COVID-19, we **suggest against** the routine use of standard IV immunoglobulin.	**Weak**
For adults with severe or critical COVID-19, we **suggest against** the use convalescent plasma outside clinical trials.	**Weak**
For adults with severe or critical COVID-19, we **recommend using** pharmacologic VTE prophylaxis over not using prophylaxis.	**Strong**
For adults with severe or critical COVID-19 and no evidence of VTE, we **suggest against** the routine use of therapeutic anticoagulation outside of clinical trials.	**Weak**
For adults with COVID-19 and shock, we **recommend against** using dopamine if norepinephrine is available.	**Strong**
For the acute resuscitation of adults with COVID-19 and shock, we **suggest using** buffered/balanced crystalloids over unbalanced crystalloids	**Weak**
For the acute resuscitation of adults with COVID-19 and shock, we recommend **against** using hydroxyethyl starches	**Strong**

For complete details about these guideline please follow the link followed.
https://journals.lww.com/ccmjournal/Fulltext/2021/03000/Surviving_Sepsis_Campaign_ Guidelines_on_the.21.aspx

Is there any Role of Ivermectin in COVID-19?

Sundus Maria, Infectious Diseases (ID) Clinical Pharmacist

Data on Ivermectin for COVID-19 is intriguing and warrants further investigation. **To date, there is a lack of high-quality evidence, from methodologically sound clinical trials that have been peer-reviewed to suggest Ivermectin is a safe and effective therapy for prevention or treatment of COVID-19.**

- IDSA Guidelines do not mention Ivermectin.
- NIH Guidelines recommend against use of Ivermectin, except in the context of a clinical trial.
- Although it has in-vitro efficacy against SARS-Cov -2, but substantially higher doses are needed to achieve viral Inhibition in vivo. The exact dosing in Covid-19 is not known.
- Large doses cross blood-brain barrier which can lead to depression, ataxia, psychosis, confusion, and seizure.

Note: Currently 39 trials are currently registered on ClinicalTrials.gov (Ivermectin & SARS-CoV-2)

https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/

https://www.covid19treatmentguidelines.nih.gov/antiviral-therapy/

Simulation Based Pharmacist Training

Shifa Pharmacy is committed to providing best pharmaceutical care to the population it serves, and this is not possible without highly trained and skilled pharmacists! Traditionally tools like Continuing Education (CE) sessions and on the job training have been used for competency development of pharmacists. Shifa took it a step further with 'Simulation based Training'

How it works:

⇒ We started with inpatient including oncology and compounding staff.

⇒ A simulation package was designed that included prescription scenarios for 'Appropriateness Review' (dose/route/frequency/duplications/hospital approved criteria for use etc.) and scenarios for correct medication filling and checking, with known and built-in errors. Pharmacists had to review and identify errors in time constrained manner resembling actual workload and pressures.

⇒ Baseline scores were assessed to see that what % of errors pharmacists were able (or not able) to catch.

Results:

There were few areas as follows, which needed improvement (as depicted by baseline scores): Checking Therapeutic duplications (esp. for antibiotics), hepatic dose adjustment and checking prescription against hospital approved criteria for use etc.

Action on baseline scores:

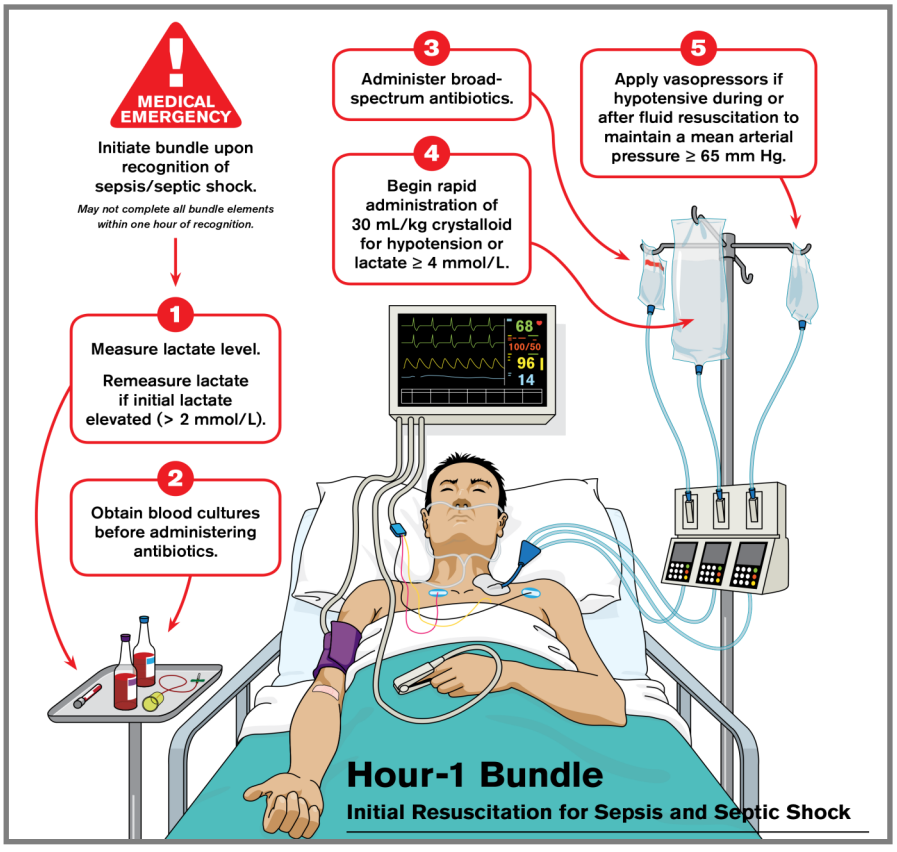
Training sessions on each topic were conducted which were mandatory to be attended by all pharmacists, followed by a brief test to ensure all staff understood the concepts.

Few days after this test, a repeat simulation (Post-Test) was conducted to assess the practical application of knowledge in areas for which specific trainings were conducted.

Results:

It was heartening to see that a substantial improvement in knowledge and skills was evident in all weak areas and average 40% cumulative improvement from baseline was observed, while highest improvement was seen in duplication of therapy (44%)

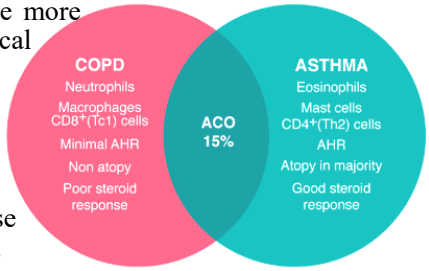
Way forward: I t was decided to run this for every new joiner + every 6 months so that pharmacists are capable of doing accurate prescription review and dispensing. The same procedure for outpatient pharmacists is also underway.



Management of side effects related to Inhaled Corticosteroids:

Sehrish Saeed, Resident Pharmacist

Inhaled corticosteroids (ICS) are the FDA-indicated treatment of choice in preventing asthma exacerbation in patients with persistent asthma and chronic obstructive pulmonary disease (COPD), which affects the alveoli and pulmonary blood vessels. A national review of asthma deaths in the UK in 2014 found that patients with asthma who did not use an ICS were at significantly greater risk of death. In contrast, the place of an ICS in COPD is more uncertain. A clinical review of the risk-to-benefit ratio of ICSs in patients with COPD concluded that their use (particularly at high dose) in a typically older cohort, frequently with co-morbidities, put COPD patients at increased risk of ICS-associated side-effects.
The reason for this difference in efficacy may be related to the mechanism of action of ICS. In asthma, inflammation is primarily caused by eosinophils, while in stable COPD neutrophils are predominant. Corticosteroids are more effective in reducing eosinophilic inflammation, which may explain this difference in clinical response.



High dose Inhaled corticosteroid (ICS): A high dose of ICS is defined as ≥1,000mcg beclometasone dipropionate (BDP) equivalent per day. Fluticasone propionate, mometasone and the newer ultrafine BDP hydrofluoroalkane (HFA) inhalers are considered twice as potent as standard BDP inhalers. However, dose equivalents are approximate, and the dose delivered will depend on other factors such as inhaler technique. Patients who require prolonged high-dose ICS are at risk of systemic side effects, particularly immunosuppression and adrenal suppression.

Reference: *National Institute for Health and Care Excellence. Chronic obstructive pulmonary disease: Management of chronic obstructive pulmonary disease in adults in primary and secondary care. London: NICE 2010 .*

Local Side of Effects of inhaled Corticosteroids
Sore throat, hoarseness, Oral candidiasis (white patches in mouth)
Management
• Advice the patient to rinse out their mouth with water (spitting out the rinse) • Brush their teeth after using the device • Using a spacer device with meter dose inhaler • Treatment with topical antifungal (nilstatin drops or amphotericin lozenges)
Systemic Side Effects
• Are dose-related, or more evident in patients with diabetes, osteopenia or COPD etc. • Patients with COPD are at a higher risk of developing pneumonia • High-dose ICS may increase the risk of fractures in COPD
Management
• All COPD patients to be offered a pneumococcal and the annual influenza vaccination. • Bone mineral density monitoring and treatment only for adults on long-term or frequent courses of corticosteroid tablets, and not those on ICS. • Tapering of Dose

Bevacizumab plus chemotherapy for initially unresectable liver-limited metastatic RAS-mutant metastatic colorectal cancer

Anum Farooq Butt (Clinical Pharmacist Oncology)

Bevacizumab has only modestly improved resectability rates when added to an oxaliplatin-containing chemotherapy backbone, and whether the benefits outweigh the risks in patients undergoing conversion therapy for potentially resectable colorectal cancer (CRC) liver metastases has been controversial.

In the **BECOME randomized trial** of patients with *RAS* mutant initially unresectable but liver-limited, metastatic CRC, the addition of bevacizumab to oxaliplatin plus leucovorin and short term infusional fluorouracil (FOLFOX) was associated with **higher rates of objective response and a nearly four-fold increase in the complete (R0) resection rate (22 versus 6%)**.
Bevacizumab plus an oxaliplatin-containing regimen is an option for conversion therapy in those with *RAS* mutant CRC liver metastases. For most other patients, we prefer an oxaliplatin-containing combination regimen without bevacizumab, or an irinotecan-containing regimen in combination with an agent targeting the epidermal growth factor receptor (for *RAS/BRAF* wild-type disease).

Reference: https://www.uptodate.com/contents/management-of-potentially-resectable-colorectal-cancer-liver-metastases regimen

Following drugs are added in Shifa High Alert Medication List
Refer to usage guidelines for details (intranet)

RIVAROXABAN **APIXABAN**

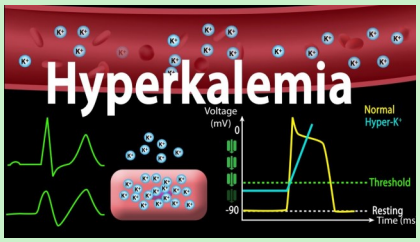
Do You Know How to Switch Warfarin to Apixaban?
Ans: Discontinue Warfarin and start Apixaban when the INR is < 2

(see guidelines for details)

Potassium Binding agents in management of hyperkalemia

Ayesha Mubeen, Resident Pharmacist

Hyperkalemia (serum potassium [K+] >5.0 or >5.5 mEq/L) is a potentially life-threatening complication of chronic kidney disease (CKD). Its management in patients with CKD can be challenging because specific CKD treatments may exacerbate the potential for hyperkalemia. Hyperkalemia is associated with alteration in neuromuscular and cardiac function. Treatment strategies for treating hyperkalemia involve **use of IV calcium, insulin, sodium bicarbonate, Beta 2 agonist, diuretics and cation exchange polymer.**



Potassium-binding drugs reduce serum K+ levels via ion exchange mechanisms in the GI tract, drugs included are:

- Sodium polystyrene sulfonate (**SPS**)
- Calcium polystyrene sulfonate (**CPS**)
- Patiromer
- Sodium zirconium cyclosilicate (**ZS-9**)

Sodium zirconium cyclosilicate is a non-polymer compound that exchanges K+ for sodium and hydrogen ions. In contrast, **Patiromer** is a polymer that exchanges K+ for calcium ions. **SPS**, a nonspecific sodium–cation exchange resin, exchanges sodium with potassium ions from the intestinal cells .

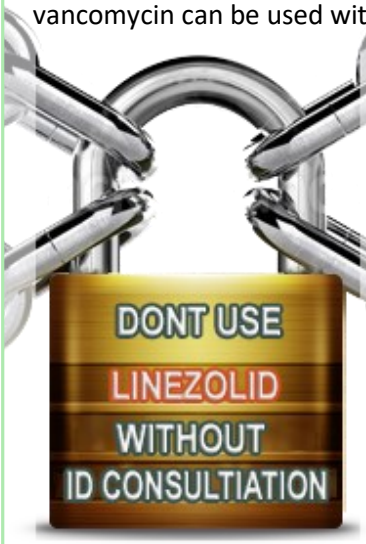
The use of SPS, however, is limited by its GI adverse effects, In randomized controlled studies of patients with hyperkalemia, ZS-9 and Patiromer effectively reduced serum K+ and were generally well tolerated. ZS-9 is associated with dose-related mild to moderate edema that can be managed with dose reductions or with diuretic therapy. GI adverse effects are the most common adverse effects associated with Patiromer .

	SPS	ZS-9	Patiromer
Cation selectivity	Lesser specificity causing significant electrolyte disturbance	Greater selectivity for potassium over other monovalent and divalent cations.	More selectively exchange potassium by calcium thus suitable for patients sensitive to exogenous sodium delivery including cirrhosis or heart failure
Onset of action	Onset is within 1-2 hrs	Fastest onset of action (within 1 hr at dose of 10mg)	Reduces baseline serum potassium within 7 hrs, reduction maintains for 48 hrs
Administration and safety	Oral suspension 1-4 times daily depending upon dose Can be used as enema	OD dosing improves patient adherence. Typically administer 3 times daily for initial lowering of potassium over 48 hr	Twice daily for maintenance therapy (clinical trials)

Reference: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4699486/

Restricted Use of Linezolid

Linezolid has a potentially important role in the treatment of MDR Gram-positive infections. Linezolid remains one of the few active drugs for treating vancomycin-resistant enterococci (VRE) and Vancomycin resistant staphylococcal infections. To decrease the potential for emergence of linezolid-resistant VRE, linezolid should not be used routinely to treat vancomycin-susceptible isolates. It is frequently misused especially in **CKD/AKI** patients as it has no renal dose adjustment, whereas vancomycin can be used with adjusted doses in such patients. Unless patient has developed AKI secondary to vancomycin or experienced true allergy to vancomycin (Not **Red-Man syndrome**). Vancomycin should always be preferred over linezolid as it is a bactericidal agent whereas linezolid is bacteriostatic and achieves suboptimal levels in **MRSA** bacteremia .Another common reason for use of linezolid is the Excellent **oral bioavailability** of linezolid which allows convenient IV to Oral switching upon discharge. However, there are other **oral options available for MRSA** such as co-trimoxazole, doxycycline and clindamycin. **Linezolid use should be reserved only for VRE and VRSA.** Physicians should prescribe this agent judiciously so as to minimize antimicrobial resistance.



!!!!!!! GOOD NEWS !!!!!!!

Caspofungin is now Available in Pakistan

Caspofungin is a parenteral fungicidal agent that belongs with the class of echinocandins. It has approved indications for the treatment of candidemia, invasive aspergillosis in patients refractory or intolerant to other therapies, empiric therapy for febrile neutropenic patients, candidial intra-abdominal abscesses, peritonitis and pleural space infections.

Process of Medication Reconciliation

Saliha Sayyab, Ambulatory Care Pharmacist

The process of comparing a patient's medication orders to all of the medications that the patient has been taking. This reconciliation is done to avoid medication errors such as omissions, duplications, dosing errors, or drug interactions. It should be done at every transition of care in which new medications are ordered or existing orders are rewritten. Transitions in care include changes in setting, service, practitioner, or level of care.

Factors associated with medication discrepancies

- Medication discrepancies are defined as any difference between the discharge medication list and the medications a patient actually takes once at home) and the need for vigilance in medication reconciliation.
- Certain patient risk factors – such as language barriers, hearing and visual impairment, and cultural differences – are associated with medication discrepancies.
- These risk factors are particularly prevalent among the elderly, as well as patients with low health literacy, cognitive impairment, or polypharmacy.

Process of Medication Reconciliation

Collect information from available sources

- Patient/caregiver verbal history
- Any written medication lists from the patient
- Medical records from the provider, discharge lists, or admission lists
- A **brown bag checkup** : requires patients to gather all of their current medications, including OTC, mail order, or herbal products, into a "brown bag" The patient can then review these medications with the pharmacist

Identify discrepancies

Check for the following:

- **Completeness**: All prescription, OTC, and PRN medications and supplements
- **Clear instructions**: For example, dose, route, frequency, therapy duration
- **Currency**: See all new orders, dosage changes; delete all discontinued medications
- **Duplicate therapy**: Same drug or in same drug class (e.g., brand names or combination products)

◊ Medication deleted but still in list could lead to duplicate therapy or drug interactions.
◊ Family members or caregivers to be included to compare/verify information
◊ Also check with community pharmacies medication profile(s), Prescriber records

Resolve discrepancies

Identify the cause/reason for the discrepancy

- E.g.: New order with dosage change, or for new drug, or for discontinuing a drug
- Formulary substitutions (hospital drug formulary, insurance coverage, etc.)
- Patient misunderstanding or confusion
- Changes in patient status (e.g., renal function, worsening disease, lab values, vitals etc)
- Make recommendations according to the cause of the discrepancy
- Obtain prescriber approval

Teach-back method can be used to explain information to patients and caregivers

Used to make sure patients understand what you have just taught

◊ Ask patients in a caring way to show or explain in their own words what they need to know or do. Avoid simply asking patients if they understand.
◊ Use open-ended questions instead of closed-ended questions that can be answered with "yes" or "no."

Provides opportunity to re-explain in a different way if misunderstood

Communicate changes

- Properly following up with pending discrepancies until ultimately resolved
- Document order changes in the medical record
- Update the medication list
- Transmit the updated list to other providers as needed
- Educate ambulatory patients on the reconciled regimen, emphasizing any changes
- Provide the reconciled list to ambulatory patients; a chart organizing the medications by administration times may be preferred
- Encourage patient to maintain complete and up-to-date list and to bring it to for each visit.

JCIA Standards for Hospitals — 7th Edition is Out Now!

Key Medication Related changes:

MMU 1: Added medication error and adverse reporting to the list of processes that must be addressed in the organization's medication management system

MMU 3.1: Added new points on emergency medicines access, replacement, risk based approach for monitoring

MMU 3.2: process for identifying, retrieving, and returning or destroying recalled medications including compounded drugs

MMU 4: Added requirement on how to conduct medication reconciliation

MMU 4.1: all medication orders and prescriptions contain the required listed elements

MMU 5: requirement for training, competency for staff preparing/ compounding sterile products. Add guidelines for the use of single-use and multidose vials. Plus medications stored, prepared, and dispensed outside the pharmacy comply with the same cleanliness measures as the pharmacy

MMU 6.2: conduct risk assessment for medications brought by patients and sample medications

MMU 7: standardized reporting process for adverse medication effects in patient record and as part of the hospital quality program

IPSG 3.1: Annual review of high alert and LASA medicines list

Only trained staff access concentrated electrolytes, follow standardized protocols for electrolyte replacement therapy

ADVERSE DRUG REACTIONS QUARTER 4, 2020

Muhammad Gulzaib, Clinical Pharmacist

Total ADRs reported: 44
Reported by pharmacists: 32 (73%)
Identified via Trigger Tool: 2 (4.5%)
Allergic Reactions: 8 (18%)
Top Drugs involved:

1. **Vancomycin**
2. **Radiology Contrasts**
3. **Chemotherapy**

Proud to Announce!

Ms Sundus Maria, ***Clinical Pharmacist ICU*** **has been Certified as "Infectious Diseases (ID) Pharmacist" from Society of Infectious Diseases Pharmacist (SIDP) — USA. She is also an active member of Antimicrobial Stewardship Subcommittee of Shifa**

Ms Salwa Ahsan, ***Chief of Pharmacy Shifa*** **has been appointed as member Expert Panel for the revision of Joint Commission International (JCI) standards for Home Care, 2nd Edition**

Did You Know?

- Agatha Christie (novelist) was a Pharmacy Assistant
- Benjamin Franklin (Founding father of USA) and Hubert Humphrey (US Vice President) were Pharmacists!

DRAP Alerts

- DRAP launched 'MED safety mobile app' to report drug reaction cases
- DRAP has bound companies to report gluten and lactose contents on primary and secondary packs of drugs
- Application process of NOC for import of drugs by patients has been made online

Pharmacist Intervention Pearls

Bushra Anjum, Principal Oncology Pharmacist

Rituximab 100 mg Injection was prescribed to patient without premedications, pharmacist called the physician and informed about **black box warning of Rituximab;** "Rituximab administration can result in serious, including fatal, infusion-related reactions. Deaths within 24 hours of rituximab infusion have occurred. Approximately 80% of fatal infusion-related reactions occurred in association with the first infusion. Monitor patients closely. Discontinue rituximab infusion for severe reactions and provide medical treatment for grade 3 or 4 infusion-related reactions". Physician agreed and added as premedication Acetaminophen and diphenhydramine with proper doses and appropriate gap before chemo.

Formulary Updates

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

Brand	Generic	Class	Indications
Apiban 5 mg	Apixaban tab	DOAC	DVT, PE
Caspofungin	Caspofungin inj	Echinocandins	Fungal Infection
Toujeo 300u/ml	Insulin Glargine inj	Basal Insulin	Diabetes
L-Pam	Lorazepam tab	Benzodiazepine	Anxiety, Seizure
Lextran Sachet 5g	Cholestyramine sachet	Quaternary ammonium anion exchange resin	Dyslipidemia, Jaundice induced pruritus etc.
Influenza Vaccine	Influenza Vaccine	Quadrivalent Flu	Prevention of influenza
Etovel Capsule 50mg	Etoposide cap.	Topoisomerase II inhibitor	Cancers like breast, Ovarian, Prostate
Doxulip Injection 20mg	Liposomal Doxorubicin inj.	Anthracycline	Antineoplastic
Olonase Nasal Spray	Olpatadine 0.6% n/s	Anti-Histamine	Seasonal allergic rhinitis

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.