Shaukat Khanum Memorial Cancer Hospital and Research Center

Pharmacy Newsletter

Volume X, Issue # 3, 2020

Issued By:

Drug Information Centre, SKMCH & RC

P&TC Updates:

Following drugs are approved by Pharmacy & Therapeutics Committee (P&TC) during 2020 SKMCH&RC:

For COVID-19 (Restricted by Services – ICU / IM & ID)

1. **Hydroxychloroquine Tab.**
2. **Chloroquine Tab.**
3. **Tocilizumab Inj**.
4. **Montelukast Tab.**
5. **Ascorbic acid (Vit C) Tab.**
6. **Remdesivir Inj.**

Others

7. **Valacyclovir Tab** – Approved as regular formulary item.
8. **Mometasone Nasal Spray** – Approved as regular formulary item.
9. **Sorafenib Tab** – 4 indigent patients / year (FLT3-ITD Mutated acute myeloid leukemia prior to allogenic transplant)
10. **Plerixafor Inj** – 6 Indigent patients / year (Patients with stem cell harvest failure)
11. **Pentoxifylline Tabs.** – Approved as regular formulary item.
12. **Tocopherol (Vitamin E) Caps.** – Approved as regular formulary item.
13. **Rasburiucase Inj.** – Effective 2021, the slots for adult patients have been increased from 10 to 30 per year with following distribution,
    a. Therapeutic dose 0.2mg/kg = 05 Slots/Year
    b. Prophylactic flat dose 3mg = 25 Slots/Year

New Approvals:

BIG News: First Point-of-care Antibody test for COVID-19

First serology (antibody) point-of-care (POC) test for COVID-19 has been issued emergency use authorization by FDA on September 23, 2020. The Assure COVID-19 IgG/IgM rapid test device is the only FDA approved COVID-19 POC serology test and is available by prescription only, which is authorized for use with venous whole blood, serum, plasma and finger stick whole blood. This serology POC test, unlike POC COVID-19 diagnostic tests, uses a blood sample obtained from the fingertip. FDA warns patients that the results of this test, or any other serology test, should not be used as an indication to stop taking COVID-19 precautions. Until now, a central lab was the only place where serology tests could be evaluated, which was time consuming and required additional resources for transporting samples and proceeding the test. Hence, the introduction of this test has led to the profound conservation of resources and time as compared to the previously available COVID-19 tests.

Ref: *https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-first-point-care-antibody-test-covid-19*

Risk of Non-Melanoma Skin Cancer: Updates in Hydrochlorothiazide (HCTZ) Label

FDA has approved the updates to label of hydrochlorothiazide (HCTZ) use to be associated with a small increased risk of non-melanoma skin cancer (basal cell skin cancer or squamous cell skin cancer). The purpose of this change is to encourage patients to protect their skin from the sun. Following changes in the labeling sections have been made.

- Adverse Reactions, Post marketing Experience: information has been added regarding the increased risk of non-melanoma skin cancer associated with HCTZ.
- Patient Counseling Information: information has been added instructing patients to protect their skin from the sun and undergo regular skin cancer screenings.

The risk increases with the individuals age and as they spend more time in the sun. In a study, the increased risk was mostly for squamous cell carcinoma (SCC), and it was approximately one additional case per 16,000 patients per year. Patients are advised to continue the use of HCTZ and to take protective skin care measures to reduce their risk of non-melanoma skin cancer, unless directed otherwise from their health care provider. Measures to protect sun exposure include using broad-spectrum sunscreens with a sun protection factor value of at least 15, reapplying sunscreen regularly, and limiting time in the sun. Protective clothing, sunglasses and broad-brimmed hats are other ways to avoid sun exposure.

Ref: *https://www.fda.gov/drugs/drug-safety-and-availability/fda-approves-label-changes-hydrochlorothiazide-describe-small-risk-non-melanoma-skin-cancer#:~:text=%5B8%2F20%2F2020%5D,HCTZ%20use%20and%20to%20encourage*

Fostemsavir: A New Antiviral for HIV Patients with Limited Treatment Options

A new type of antiviral fostemsavir (Rukobia) has been granted approval for adults who have tried multiple HIV medications and whose infection cannot be successfully treated with other therapies. FDA approval is based on a clinical trial in which three hundred and seventy one heavily pre-treated adult patients with high levels of virus (HIV-RNA) in their blood participated for the purpose of safety and efficacy. Main trial arm treated two hundred seventy-two participants, and an additional 99 participants received fostemsavir in a different arm of the trial.

Rukobia 600 mg twice daily by mouth or a placebo twice daily for eight days, were administered to participants in the main cohort of the trial in addition to their failing antiretroviral regimen. On the eighth day, a significantly greater decrease in levels of HIV-RNA in the blood of participants treated with fostemsavir was found as compared to those taking the placebo.

After the eighth day, all participants received Rukobia with other antiretroviral drugs. After 24 weeks of Rukobia plus other antiretroviral drugs, 53 percent of participants achieved HIV-RNA suppression, where levels of HIV were low enough to be considered undetectable. After 96 weeks, 60 percent of participants continued to have HIV-RNA suppression.

Elevations in liver enzymes among participants also infected with hepatitis B or C virus, and changes in the immune system (immune reconstitution syndrome), are some severe adverse reactions of using fostemsavir.

Ref: https://www.fda.gov/news-events/press-announcements/fda-approves-new-hiv-treatment-patients-limited-treatment-options

Policy updates:

BSA Capping Revoked *- For Adults Patients Only*

As per recommendations from medical oncologist, and with approval of P&TC, the capping of body surface area (BSA) at 2.0 has been revoked. For individual drugs like vincristine or any other drug requiring capping or maximum dose limit as per the chemotherapy protocol guidelines, will remain the same.

Rituximab Approval Guidelines

For indigent patients of SKMCH & RC, the approval criteria for Rituximab has been revised. The newly added diagnosis for Rituximab slots for indigent patients are as following.

1. Non-Hodgkin's lymphoma (diffuse large B cell, previously untreated) in combination with 1st line chemotherapy for up to 8 cycles.
2. Hodgkin’s lymphoma, nodular lymphocyte-predominant, with or without chemotherapy, up to 8 cycles.
3. Non-Hodgkin’s lymphoma (diffuse large B-cell; relapsed or refractory) not previously treated with a Rituximab containing regimen for up to 6 cycles.
4. Non-Hodgkin’s lymphoma (low grade or follicular, CD20-positive B-cell, previously untreated with rituximab) in combination with chemotherapy for up to 8 cycles.

5. Chronic lymphocytic leukemia, previously untreated with rituximab, relapsed/refractory, with or without chemotherapy.
6. Non-Hodgkin's lymphoma (diffuse large B-cell; relapsed at least after > 12months from end of treatment) previously treated with a Rituximab containing regimen for up to 6 cycles.
7. Non-Hodgkin's lymphoma (low grade or follicular, CD 20-positive, B-cell) maintenance therapy (as a single agent, in patients with partial or complete response to rituximab plus chemotherapy; for 12 cycles).

Sharing is caring:

Organizing webinar on 'ASHP Global: Advancing Pharmacy Practice Together – Pakistan' with collaboration of ASHP Global Initiative

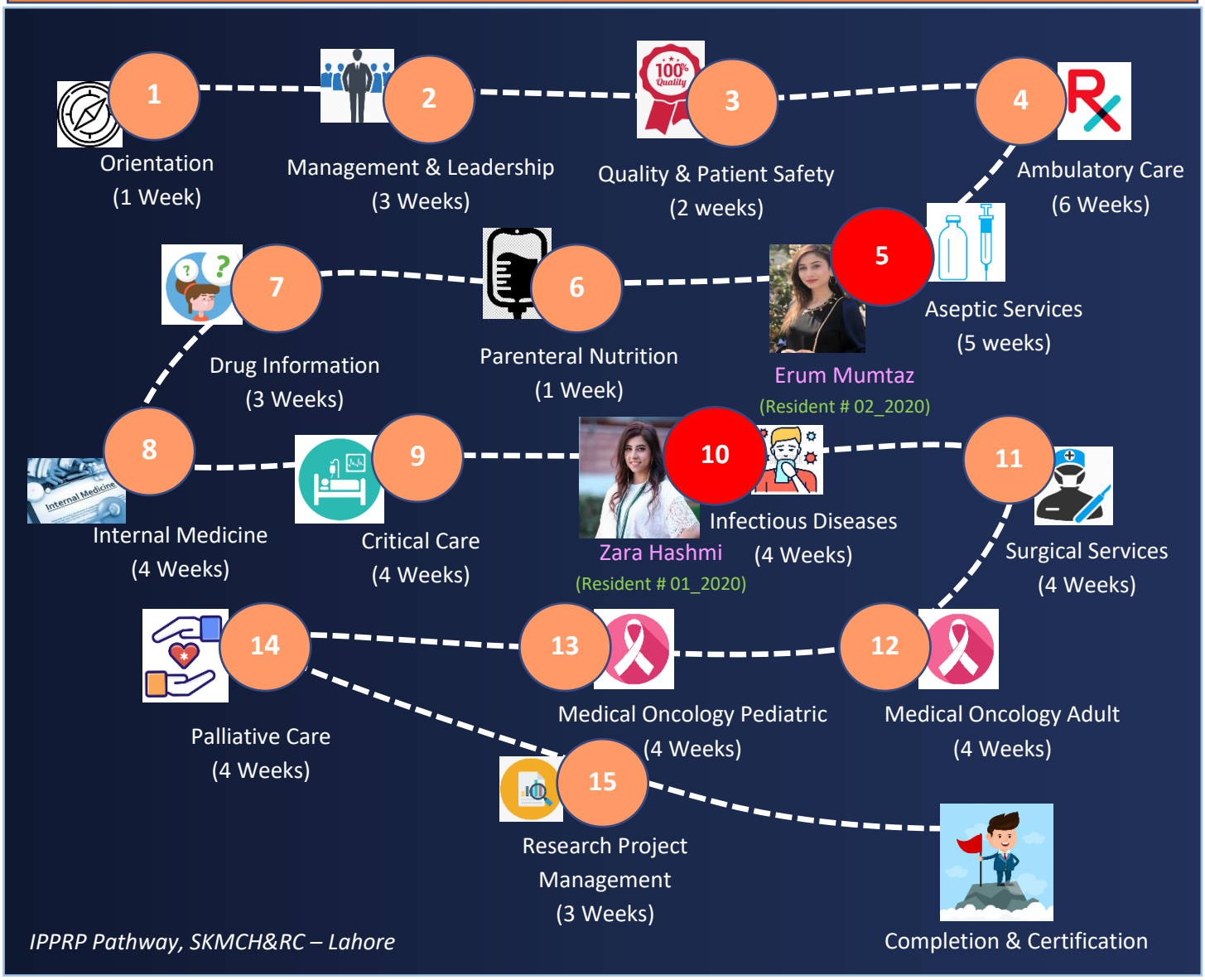
Shaukat Khanum Memorial Cancer Hospital & Research Center is the first institution in the region, which is successfully conducting the International Pharmacy Practice Residency Program (IPPRP) accredited by American Society of Health System Pharmacists (ASHP).
*On August 27, ASHP organized an online webinar on, '**ASHP Global: Advancing Pharmacy Practice Together – Pakistan'.***

The topics included were advancing pharmacy practice, hospital pharmacy accreditation, pharmacy residency accreditation and accreditation preparation and training. The webinar was advertised productively on social media and hence, received a good response from the pharmacists of Pakistan. We plan to continue contributing and organizing such events in the future.

Investigational Drugs & Trials: (Update)

In SKMCH&RC, Lahore currently three trails are in process which include RIFASHOT, WHO Solidarity trial & Recombinant Novel Corona Virus Vaccine trial. One is related to estimation of toxicity and efficacy of anti-tuberculosis drugs, whereas the other two are involved in finding effective vaccination and treatment against COVID-19. Department of pharmaceutical services SKMCH & RC is responsible for keeping and maintaining the stock inventory, preparation and dispensing of the investigational drugs.

International Pharmacy Practice Residency Program (IPPRP) - ASHP



Zahra Hashmi – Pharm D (Pharmacy Resident 01_2020)

"Hi! I am Zara; currently going through the ID rotation of the second quarter of my ASHP accredited residency program. I am also in the data collection phase of my research project. So far, it has been a significantly invaluable journey. Although the learning experience has been academically challenging but through practical exposure and persistent guidance and feedback of my incredible preceptors, my professional skills and knowledge have been considerably polished. I expect that, the rest of the residency program will prove to contribute to not only to my professional value as a pharmacist but also to my personal growth."

Erum Mumtaz – Pharm D (Pharmacy Resident 02_2020)

"Hi! I am Erum. It is an amazing and inspiring to be an ASHP resident pharmacist at SKMCH & RC. The journey started from understanding the management and leadership, and quality and patient safety objectives. After that, I moved to ambulatory care pharmacy services, which requires conscientiousness and where the job is really challenging at times. The extremely cooperative and congenial working environment by the preceptor in ambulatory care, always keeps me motivated and thus, I enjoy interacting with patients at the counter. It is just the start of one-year journey and I am looking forward to many more learning experiences in the coming days."

World Pharmacists Day

World Pharmacist Day – 25th September 2020

"**Transforming global health**" is the theme of this year's World Pharmacists Day: 25 September 2020.

Hazardous Drugs

Hazardous drug definition: Hazardous drugs (HDs) are those drugs that exhibits one or more of the characteristics of carcinogenicity, teratogenicity or other developmental toxicity, reproductive toxicity, organ toxicity at low doses, genotoxicity, structure and toxicity that mimics existing hazardous chemotherapy drugs.[1]

Types Hazardous Drugs

Group 1: Antineoplastic drugs. Many of these drugs may also pose a reproductive risk for susceptible populations.

Group 2: Non-antineoplastic drugs that meet one or more of the NIOSH criteria for an HD. Some of these drugs may also pose a reproductive risk for susceptible populations.

Group 3: Drugs that primarily pose a reproductive risk to men and women who are actively trying to conceive and women who are pregnant or breast-feeding.

Reference – Policy on Safe Handling of Hazardous Drugs (MMU Ref # 13)

Flu Vaccine

Get the Flu Shot
Before the flu gets you

Flu vaccine is your first line of defence against influenza

Who should get vaccinated this season?

Flu Viruses are most common during the fall and winter months, seasonal flu viruses can be detected year–round, however, seasonal flu activity can begin as early as October and continue to occur as late as May.

- ✓ Everyone 6 months of age and older
- ✓ Pregnant Women
- ✓ Residents of nursing homes

People who have medical conditions including:

- ✓ Asthma
- ✓ Neurological disorder
- ✓ Chronic lung disease
- ✓ Heart disease & stroke
- ✓ Blood disorders
- ✓ Kidney disorders
- ✓ Liver disorders
- ✓ Metabolic disorders
- ✓ Weakened immune system due to disease or medication
- ✓ HIV/ AIDS
- ✓ Long term aspirin therapy

Recommended Dose

Age Group	Dose	No. of Doses
6 to 35 months	0.25 ml	1* or 2 **
3 to 8 years	0.5 ml	
≥ 9 years		1

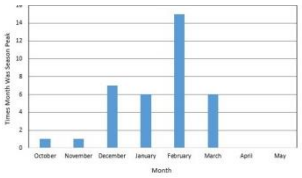
**Children 6 to 35 months of age receive 0.25 ml dose*

***Previously unvaccinated children 6month to < 9years of age require 2 doses of seasonal influenza vaccine with an interval of 4 weeks*

Note: Should not be administered to anyone with a history of severe allergic reaction to egg protein or any component of the vaccine

Fight the Flu
It starts with you

Peak Month of Flu Activity
1982-1983 through 2017-2018



For further information:
Drug Information Centre ¦ Call @ Ext; 3260
druginfo@skm.org.pk

How Flu Spreads:

1- Person to Person
People with flu can spread it to others up to about 6 feet away. Most experts think that flu viruses spread mainly by droplets made when people with flu cough, sneeze or talk

2- When Flu Spread
People with flu are most contagious in the first three to four days after their illness begins
Most healthy adults may be able to infect others beginning 1 day **before** symptoms develop and up to 5 to 7 days **after** becoming sick
Symptoms can begin about 2 days (but can range from 1 to 4 days) after the virus enters the body.

Ref: https://www.cdc.gov/

Extravasation

Extravasation injury is defined as the damage caused by the efflux of solutions from a vessel into surrounding tissue spaces during intravenous infusion. The damage can extend to involve nerves, tendons, and joints and can continue for months after the initial insult.

Minimization and Prevention of Extravasation

Correct Site	Correct Cannulation	Correct Technique	Correct Knowledge

For further details, please see MMU Policy on Chemotherapy Extravasation (Ref # 22)

Trigger Tool Method (TTM): A Strategy to Improve ADR Reporting

Over the last couple of years, different methods have been tried and tested to improve the reporting of adverse drug reactions (ADR) like education of staff, ADR reporting alert in HIS, and patient's chart review. However, retrospective review of patient's chart has shown not much improvement in the reporting. Therefore, to prevent under reporting, a new method named trigger tool method has been developed. Through this method when any of the specific drugs, is prescribed to the patients, an alert of prescribing is generated for clinical pharmacists' team. The designated clinical pharmacy staff then reviews the patient's notes to check the rational of prescribing and whether there is an ADR. Specific drugs include Flumazenil, Naloxone, Hydrocortisone & Pheniramine and Acetylcysteine. Although current list of trigger drugs is limited and not all kinds of ADRs involve treatment with an antidote, but this method of identifying ADR is helpful for documenting missed potential ADRs.

A PDCA to Minimize Delay of Antibiotic in Emergency Patients

A PDCA- "Time to Antibiotic (TTA) in Pediatric Patients with Fever in the setting of Neutropenia" started to overcome the problem of intravenous antibiotic (Piperacillin/Tazobactam) delay in patients visiting emergency room. PDCA started on 10th July 2020 and different dose bands were designed in consensus with pediatric physicians according to Lexicomp utilizing specific weight ranges of patients.

Patient weight	Dose (mg) of Piperacillin/Tazobactum
0-10.49 kg	Individualized to 90 mg/kg
10.5 – 13.9 kg	1260 mg
14.0 – 17.9 kg	1680 mg
18.0 – 24.9 kg	2160 mg
25.0 – 32.9 kg	3000 mg
33.0 – 43.9 kg	3960 mg
44.0 kg plus	4500 mg

Based on prescribing trends, it was identified that 1260 mg and 1680 mg were the most prescribed doses, therefore these fixed doses preparation were started on 29th July. The check phase of PDCA showed no delay in antibiotic dispensing till by today. This PDCA has the advantages of timely dispensing of antibiotic, dose accuracy, reduced work burden and minimized errors.

Appropriateness Review: JCI Recommendations' Refresher

Appropriateness review; the process where a health professional reviews the patient, the illness, and the drug treatment (Standard MMU.5.1). The complete appropriateness review is performed by clinical pharmacists; however, the JCI standards identify that it is acceptable for other licensed, trained healthcare individuals to perform the review when clinical pharmacists are not available.

Pharmacy department SKMCH & RC has recently conducted training sessions for nursing staff about how to conduct appropriateness review of drugs.

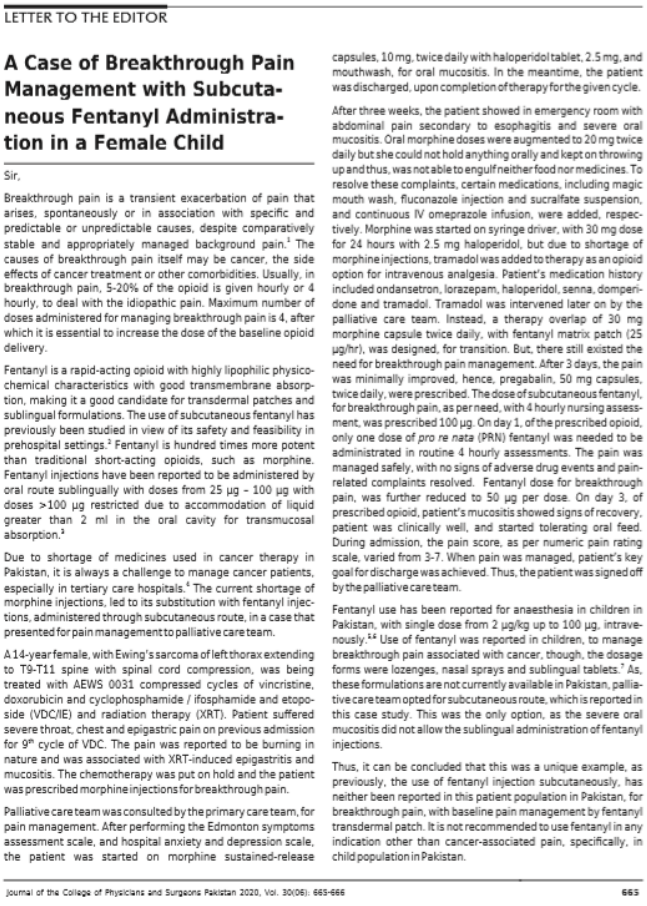
Publications

1. **A Case of Breakthrough Pain Management with Subcutaneous Fentanyl Administration in a Female Child**

   Contributors: Irum Ghafoor, *Adeel Siddiqui*, Haroon Hafeez, *Hafiz Muhammad Usman*
   Journal: Journal of the College of Physicians and Surgeons Pakistan (JCPSP)
   Impact factor 0.426

2. **Analgesics Prescribing Trends in Emergency and Outpatients at Tertiary Care Hospital – A Cross Sectional Study**

   Contributors: *Shahbaz Ahmad Khan, Omar Akhlaq Bhutta,* Ateeq-ur-Rehman Ghafoor, *Saad Bin Zulfiqar*
   Journal: Journal of Cancer and Oncology Research



LETTER TO THE EDITOR

A Case of Breakthrough Pain Management with Subcutaneous Fentanyl Administration in a Female Child

Sir,

Breakthrough pain is a transient exacerbation of pain that arises, spontaneously or in association with specific and predictable or unpredictable causes, despite comparatively stable and appropriately managed background pain.[1] The causes of breakthrough pain itself may be cancer, the side effects of cancer treatment or other comorbidities. Usually, in breakthrough pain, 5-20% of the opioid is given hourly or 4 hourly, to deal with the idiopathic pain. Maximum number of doses administered for managing breakthrough pain is 4, after which it is essential to increase the dose of the baseline opioid delivery.

Fentanyl is a rapid-acting opioid with highly lipophilic physicochemical characteristics with good transmembrane absorption, making it a good candidate for transdermal patches and sublingual formulations. The use of subcutaneous fentanyl has previously been studied in view of its safety and feasibility in prehospital settings.[2] Fentanyl is hundred times more potent than traditional short-acting opioids, such as morphine. Fentanyl injections have been reported to be administered by oral route sublingually with doses from 25 µg - 100 µg with doses >100 µg restricted due to accommodation of liquid greater than 2 ml in the oral cavity for transmucosal absorption.[3]

Due to shortage of medicines used in cancer therapy in Pakistan, it is always a challenge to manage cancer patients, especially in tertiary care hospitals.[4] The current shortage of morphine injections, led to its substitution with fentanyl injections, administered through subcutaneous route, in a case that presented for pain management to palliative care team.

A 14-year female, with Ewing's sarcoma of left thorax extending to T9-T11 spine with spinal cord compression, was being treated with AEWS 0031 compressed cycles of vincristine, doxorubicin and cyclophosphamide / ifosphamide and etoposide (VDC/IE) and radiation therapy (XRT). Patient suffered severe throat, chest and epigastric pain on previous admission for 9th cycle of VDC. The pain was reported to be burning in nature and was associated with XRT-induced epigastritis and mucositis. The chemotherapy was put on hold and the patient was prescribed morphine injections for breakthrough pain.

Palliative care team was consulted by the primary care team, for pain management. After performing the Edmonton symptoms assessment scale, and hospital anxiety and depression scale, the patient was started on morphine sustained-release capsules, 10 mg, twice daily with haloperidol tablet, 2.5 mg, and mouthwash, for oral mucositis. In the meantime, the patient was discharged, upon completion of therapy for the given cycle.

After three weeks, the patient showed in emergency room with abdominal pain secondary to esophagitis and severe oral mucositis. Oral morphine doses were augmented to 20 mg twice daily but she could not hold anything orally and kept on throwing up and thus, was not able to engulf neither food nor medicines. To resolve these complaints, certain medications, including magic mouth wash, fluconazole injection and sucralfate suspension, and continuous IV omeprazole infusion, were added, respectively. Morphine was started on syringe driver, with 30 mg dose for 24 hours with 2.5 mg haloperidol, but due to shortage of morphine injections, tramadol was added to therapy as an opioid option for intravenous analgesia. Patient's medication history included ondansetron, lorazepam, haloperidol, senna, domperidone and tramadol. Tramadol was intervened later on by the palliative care team. Instead, a therapy overlap of 30 mg morphine capsule twice daily, with fentanyl matrix patch (25 µg/hr), was designed, for transition. But, there still existed the need for breakthrough pain management. After 3 days, the pain was minimally improved, hence, pregabalin, 50 mg capsules, twice daily, were prescribed. The dose of subcutaneous fentanyl, for breakthrough pain, as per need, with 4 hourly nursing assessment, was prescribed 100 µg. On day 1, of the prescribed opioid, only one dose of *pro re nata* (PRN) fentanyl was needed to be administrated in routine 4 hourly assessments. The pain was managed safely, with no signs of adverse drug events and pain-related complaints resolved. Fentanyl dose for breakthrough pain, was further reduced to 50 µg per dose. On day 3, of prescribed opioid, patient's mucositis showed signs of recovery, patient was clinically well, and started tolerating oral feed. During admission, the pain score, as per numeric pain rating scale, varied from 3-7. When pain was managed, patient's key goal for discharge was achieved. Thus, the patient was signed off by the palliative care team.

Fentanyl use has been reported for anaesthesia in children in Pakistan, with single dose from 2 µg/kg up to 100 µg, intravenously.[5,6] Use of fentanyl was reported in children, to manage breakthrough pain associated with cancer, though, the dosage forms were lozenges, nasal sprays and sublingual tablets.[7] As, these formulations are not currently available in Pakistan, palliative care team opted for subcutaneous route, which is reported in this case study. This was the only option, as the severe oral mucositis did not allow the sublingual administration of fentanyl injections.

Thus, it can be concluded that this was a unique example, as previously, the use of fentanyl injection subcutaneously, has neither been reported in this patient population in Pakistan, for breakthrough pain, with baseline pain management by fentanyl transdermal patch. It is not recommended to use fentanyl in any indication other than cancer-associated pain, specifically, in child population in Pakistan.

Analgesics Prescribing Trends in Emergency and Out Patients at Tertiary Care Hospital – A Cross Sectional Study

Journal of Cancer and Oncology Research Short Article

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Abstract

Unnecessary or inappropriate prescription of analgesics specifically in emergency is a major concern. Sometimes inappropriate drugs are selected, as if opioid use in first place may cause serious side effects but also waste of precious drug in a country where availability of opioids is already in scarcity. Limited studies have examined the impact of analgesics prescribing trend in developing countries. In our setting, we examined the 5675 patients who visited emergency assessment room (EAR) or out-patient department (OPD) during the last 12 months and received different types of analgesics for their pain management. Out of 5675 patient's prescription, there were only 105 prescriptions for morphine. This constitutes only 1.85 % of total prescriptions order out of 5675. Moreover, 3941 patients out of 5675 were managed with paracetmol plus tramadol combination. Nevertheless only 1629 patients received paracetmol & ibuprofen combination for their pain management. So from the above given prescription trend, we can say that if we evaluate the patients efficiently and prescribe analgesics according to pain scale, we can manage most of our patients without opioids. Proper analgesic prescribing will not only decrease opioids use but also decrease the suffering of patients.

Key Words: Analgesic Prescribing; Emergency; Morphine

Aims and Objectives

The aim of the study was to review the rational use of analgesic prescribed in EAR and OPD during of the hospital over one year period.

Methods

Retrospective, cohort study reviewing 5675 patients who were evaluated during the last one year during their visit in EAR or OPD for pain management. The date was collected through hospital information system and Microsoft excel was used to quantify the data.

Results

Only 105 prescription having morphine as opioids prescribed to manage pain. Out of 5675 prescriptions orders, only 1.85 % prescribed morphine, while 3941 patients were managed with paracetmol plus tramadol combination. Nevertheless only 1629 patients received paracetmol & ibuprofen combination for their pain management. Efficient use of analgesic prescribing will not only decrease opioids use but also decrease the suffering of patients.

Conclusion

Despite an oncology setup, the proportions of prescriptions having morphine were very small. Our findings support the need to further standardize and improve adherence to analgesic treatment guidelines. It will lead to better use of opioids drugs whose availability and misuse is always a concern worldwide.

Acknowledgments

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P&TC Update – 27th August 2020

MMU Policies Updated:

- MMU Manual
- Policy on Continual Quality Improvement
- Policy on Chemotherapy Associated Hypersensitivity.
- Policy on **Safe Handling of Hazardous Drugs**
- Policy on Medication Reconciliation and Patient Own Medication Use
- Policy on High Alert Medications
- Policy on Drug Product Recall

Feedback

To keep the Pharmacy Newsletter updated, Please contact at druginfo@skm.org.pk