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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.

Opinions expressed are of authors and does not necessarily represent AKUH's view/recommendations.
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Inside this Issue:

Impact of Pharmacist-lead Antibiotic Stewardship Program in a Pediatric Intensive Care Unit (PICU)

Kashif Hussain, Specialist, Pharmacy Services

Antibiotic Stewardship Program (ASP) has improved the utilization of antibiotics in hospitalized patients. We prospectively conducted a pilot project of pharmacist-lead ASP, with audit and feedback, in a closed multidisciplinary PICU and compared with historical control in utilization of antibiotics for 3 months. The team of ASP is composed of Pharmacist who has expertise in ASP, pediatric intensives and pediatric infectious disease consultants. Antibiotic exposure on daily basis is considered as Day of Therapy (DOT). 135 and 127 patients were in control and intervention group respectively. Patient's characteristics were same in both groups. DOT in control and intervention groups were 1937 & 1074 per 1000 patient days and 651 & 320 per1000 patient days respectively ($p<0.001$). Similar reduction was noted in individual antibiotic except Colistin. Antibiotics were stopped after 2 days in 8 patients in control group versus 57 patients in intervention group. 29 (22.6%) pharmacist intervention were recorded; including dose adjustment (11), selection of antibiotics (15), dose de-escalation (5) and monitoring recommendation (6).
Duration alerts by pharmacist were not included in it. There was about >50% cost saving in ASP period (PKR 2212468/= vs. 92568/=; $p<0.001$). There was no difference in mortality between two groups. Pharmacist-lead ASP in a PICU have a significant impact on decreasing use of antibiotics as well as cost-reducing intervention.

References:

- *De Waele JJ, Schouten J, Dimopoulos G. Understanding antibiotic stewardship for the critically ill. Intensive Care Med. 2016;42:2063-5.*
- *Barlam TF, Cosgrove SE, Abbo LM, MacDougall C, Schuetz AN, Septimus EJ, et al. Implementing an Antibiotic Stewardship Program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. Clin Infect Dis. 2016; 62:e51-77.*

Twice Daily Dose of Levetiracetam and Clinical Pharmacokinetics

Mohd Amir, Specialist, Pharmacy Services

Levetiracetam is a second-generation, anti-epileptic drug, which is commonly used as a mono- or adjunctive therapy for treating patients with partial and generalized epilepsy. It is a highly soluble drug with high volume of distribution (0.7L/kg) and half-life of 07 hours. The dosing regimen recommended is twice daily. Due to its high volume of distribution, twice daily dosing regimen allows steady state concentration to be achieved in two days. Furthermore, however,

throughout the clinical trials evaluation program of Levetiracetam, a highly efficacious and sustainable effect was observed with twice daily administration and indeed this is now the clinically practiced strategy.
Preferable Route of Administration: Oral product has 100 % bioavailability however, it may interact with food resulting in reduction of 20% of maximum concentration and delay in time for peak by 1.5 hours. Cost effective value of oral is much better than IV.

References:

- *Patsalos PN. Clinical pharmacokinetics of levetiracetam. Clin Pharmacokinetic. 2004; 43(11):707-24.*
- *Product Information: KEPPRA(R) oral tablets, solution, levetiracetam oral tablets, solution. UCB Inc., Smyrna, GA, 2008.*

Management of Acute Hyperkalemia in Neonates

Gul Ambreen, Senior Pharmacist

Hyperkalemia is defined as a serum potassium concentration greater than 5.2 mmol/L (as far as neonate is asymptomatic). Complications of hyperkalemia include ECG changes (peaked T waves, broad QRS complexes, and arrhythmias), ventricular tachycardia and impaired AV conduction. Hyperkalemia in the NICU is most commonly associated with non-oliguric hyperkalemia due to immature function of the erythrocyte Na/K – ATPase, Oliguric renal failure and metabolic acidosis.

Treatment Strategies	Doses
10% Calcium Gluconate	• 0.5 ml/kg IV over 10-30 min. The dose of calcium gluconate may be repeated.
IV Dextrose and Insulin	• Dextrose: 3-4 ml/kg/hr 25% dextrose in addition to maintenance fluid, aim for blood glucose concentration (BGC) > 12 mmol/l. When BGC >12 mmol/L, start insulin infusion (0.1-0.6 units/kg/hr).
Salbutamol	• Nebulize: 400 micrograms/dose (made up to a total of 4 ml with normal saline) up to 2 hrly.
Sodium bicarbonate Correction of an existing metabolic acidosis can be considered	• Sodium bicarbonate dose (ml) = base deficit x 0.6 x weight (kg).
Polystyrene Sodium Sulfonate (should be avoided in preterm infants)	• 0.5 – 1 g/kg rectally

Table 01: Treatment Strategies of Acute Hyperkalemia in Neonates

References:

- *Vemgal P, Ohlsson A. Interventions for non-oliguric hyperkalaemia in preterm neonates. Cochrane database Syst Rev. 2012;5:CD005257.*
- *Hu PS, Su BH, Peng CT, Tsai CH. Glucose and insulin infusion versus kayexalate for the early treatment of non-oliguric hyperkalemia in very-low-birth-weight infants. Acta Paediatr Taiwan;40:314–8.*
- *Singh BS, Sadiq HF, Noguchi A, Keenan WJ. Efficacy of albuterol inhalation in treatment of hyperkalemia in premature neonates. J Pediatr. 2002 ;141:16–20.*

Influenza Oral Tablet Vaccine Shows Promise in Phase 2 Trial

Hafsah M. Ashfaq- Clinical Pharmacist

A tablet vaccine for flu could significantly change the way we administer vaccines,"
An investigational H1 influenza oral tablet vaccine was found to provide comparable defense against influenza as an injectable quadrivalent influenza vaccine (QIV) in a Phase 2 clinical trial.
The study results showed that the tablet vaccine has a good safety profile and it has provided a 39% reduction in clinical disease relative to placebo, compared to a 27% reduction with injectable QIV.

This oral vaccine is delivered to the epithelium of small intestine where they activate the local immune system of the gut, and this in turn generates a broad local and systemic immune response. This vaccine does not enter the bloodstream and prevents neutralization by blood or muscle tissue-based immune system. This effective way of administering the vaccine in a tablet form will significantly increase the compliance and will provide health benefits for high risk population.

Reference:

- *Influenza Oral Tablet Vaccine Shows Promise in Phase 2 Trial; http://www.empr.com/drug (Accessed 24/11/2017)*

Drug Induced Neuroleptic Malignant Syndrome (NMS)

Mahreen Sohail, Trainee Pharmacist

The use of antipsychotic drugs can cause a rare, life-threatening, idiosyncratic condition known as Neuroleptic malignant syndrome. NMS is characterized by hyperthermia, muscles rigidity, dysautonomia and mental status changes. NMS mostly occur within 2 weeks of therapeutic initiation. Treatment involves immediate withdrawal of causative agent and supportive care, which includes, volume resuscitation, correction of electrolyte abnormalities, IV fluids and parenteral nutrition are recommended for patients in respiratory distress or those unable to tolerate oral intake. Treatment includes, direct acting skeletal muscles relaxant, centrally acting dopamine agonist (bromocriptine and amantadine) and benzodiazepines are reserved for patients who do not respond to withdrawal of medication and supportive care.

Pharmacists play a crucial role in counseling the patient or the caregivers about the possible side effects and measures taken in case of emergency, advising physicians on recognition of early symptoms and therapeutic options or alternatives in NMS treatment.

Typical antipsychotics	Atypical antipsychotics	Antiemetic	Dopaminergic	Others
• Chlorpromazine • Chlorprothixene • Haloperidol • Pimozide • Fluphenazine • Thioridazine • Trifluoperazine	• Clozapine • Olanzapine • Quetiapine • Resperidone • Ziprasidone • Aripiprazole	• Dropiredol • Metoclopramide • Prochlorperazine • Promethazine	• Amantidine • Bromocriptine • Carbidopa • Levodopa • Tolcapone	• Desipramine • Dosulpine • Lithium • Phenelzine • Reserpine • Tetrabenazine • Trimipramine

Table 02: List of Drug Associated with NMS

References:

- *Oruch R, Pryme IF, Engelsen BA, Lund A. Neuroleptic malignant syndrome: an easily overlooked neurologic emergency. Neuropsychiatric disease and treatment. 2017; 13:161.*
- *Buckley PF, Hutchinson M. Neuroleptic malignant syndrome. J Neurol Neurosurg Psychiatr. 1995; 58(3):271-273.*

Drug-Drug Interaction – QT Interval Prolongation

Sumaira Khan, Specialist, Pharmacy Services

An elderly woman of 67 years old with history of stroke and diabetes mellitus (DM) was on multiple drugs including Fluoxetine and Donepezil. Her heart monitoring showed prolonged QT waves. Pharmacist on clinical rounds identified drug –drug interaction between Fluoxetine and Donepezil. Donepezil has been associated with QT-interval prolongation. Studies suggest to use caution when administering donepezil concomitantly with other drugs that cause QT-interval prolongation like Fluoxetine as it may result in increased risk of QT-interval prolongation and torsade de pointes. Health care team agreed with scientific evidence and discontinued the Fluoxetine.

Reference:

- *Takaya T, Okamoto M, Yodoi K et al: Torsades de Pointes with QT prolongation related to donepezil use. J Cardiol Dec, 2009; 54(3):507-511.*
- *Tanaka A: Donepezil-induced adverse side effects of cardiac rhythm: 2 cases report of atrioventricular block and Torsade de Pointes. Intern Med 2009; 48(14):1219-1223.*

Influenza and Influenza Vaccine Myths and Reality

Drug & Poison Information Team

Acknowledge: This table has been accessed on 29th December, 2017, retrieved from https://www.jointcommission.org/assets/1/6/JC_influenza_myths.pdf

Myth	Reality
• **The flu vaccine can cause influenza.**	• The injectable flu vaccine does not contain the live virus so it is impossible to get influenza from the vaccine. Side effects may occur in some people, such as mild soreness, redness, or swelling at the injection site, head ache, or a low-grade fever. The nasal spray flu vaccine contains live, attenuated (weakened) viruses that can cause mild signs or symptoms such as runny nose, fever, sore throat, and nasal congestion. This vaccine, however, cannot cause influenza infection in the lower respiratory tract. Vaccination is safe and effective, and the best way to help prevent influenza and its complications.
• **The flu shot doesn't work.**	• The influenza vaccine will prevent influenza most of the time. In scientific studies, the effectiveness of the vaccine ranges from 70 to 90 percent, depending on how well the circulating viruses match those in the vaccine. In populations in which the vaccine is less effective in preventing influenza, such as the elderly, the vaccine reduces the severity of the disease and the incidence of complications by 50 to 60 percent and the incidence of death by approximately 80 percent. Getting vaccinated is the most effective way to protect against influenza and its serious outcomes.
• **Our staff follows Standard Precautions, with good hand hygiene practices and appropriate glove and mask use – so vaccination is not necessary.**	• Influenza is spread by respiratory droplets generated when talking, coughing or sneezing. Adults shed influenza virus at least one day before any signs or symptoms of the disease, so health care personnel can unknowingly infect patients or other staff. 50 percent of influenza infections can be asymptomatic, and both symptomatic and asymptomatic individuals can shed the virus and infect others.
• **Our staff stays at home if they are sick - so vaccination is not necessary.**	• Since unvaccinated individuals are contagious at least one day before any signs or symptoms of influenza appear, they can still shed the virus and infect patients and other staff. Unvaccinated health care personnel can become infected with influenza and not have any symptoms, and both symptomatic and asymptomatic individuals can shed the virus and infect others.
• **There is no evidence to support that influenza vaccination of staff im proves patient outcomes.**	• Health care personnel can acquire influenza from the community or their patients and can transmit it to patients or other staff. Influenza transmission and outbreaks in health care organizations have been recognized for many years and have been associated with substantial morbidity, mortality, and costs. Influenza's short incubation period and ease of transmission through respiratory droplets from person to person can result in explosive outbreaks of febrile respiratory illness. Health care settings are favorable environments for such transmission. Increased rates of staff vaccination result in decreased rates of health care-associated influenza. In fact, one group of researchers concluded that the reduction in morbidity, mortality, and use of health service resources associated with vaccinating their long term care facility was "equivalent to preventing five deaths, two admissions to hospitals with influenza-like illness, seven general practitioner consultations for influenza-like illness, and nine cases of influenza-like illness per 100 residents during the period of influenza activity."
• **Influenza vaccinations for staff will be too costly.**	• The cost savings associated with health care personnel influenza vaccination programs generally outweigh the costs associated with providing the vaccine, and vaccinating ultimately results in a safer environment for patients.

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Thank you in advance for your feedback!

Link:

https://goo.gl/forms/Ghh1Nc2KY2jEkiUL2