Shaukat Khanum Memorial Cancer Hospital and Research Center

Pharmacy Newsletter

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TaLL mAn leTTer Technique

Tall man lettering is an ISMP recommended practice of writing part of a drug's name in upper case letters to help distinguish look-alike sound-alike drugs. The confusion over Levetiracetam and Levofloxacin (sound-alike drugs) has been a concern at our institute. For example, once a prescription order read Levetiracetam 500mg OD. You can guess something is wrong with the order and when you review it, patient is a case of pneumonia. Using tall-man letter technique, levofloxacin showed as 'LEVOfloxacin' and levetiracetam showed as 'LevETIRAcetam' in HIS at SKMCH&RC. Presumably the spellings are noticeable enough and that is what was expected as well until last week when we received an in-patient order of Levofloxacin 1250mg BID. Fortunately, dosing recommendations of the two drugs are different to identify in case of error. In light of 3 cases of the kind in past 40 days, we have now revised the tall-man letters to make it even more peculiar. You view 'Levo - FLOXAcin' and 'Leve TIRACETAM' now. There is no bigger pearl, however, than being a bit more cautious while prescribing and dispensing these medications to avoid any error.

GUIDE FOR DRUG LEVEL MONITORING OF COMMONLY USED MEDICATIONS

DRUGS	SAMPLE TIMING	REF. RANGE	REMARKS
PENYTOIN	0-60 min. prior to 6th dose	10-20mg/L "free" phenytoin: 1-2.5 µg/mL	Initial: 1 hr. Post IV load. Wait 7days after each oral dosing change to measure levels. Maintenance: Only if patient still has seizures. If toxicity is suspected, take level at time of symptoms.
DIGOXIN	0-60 min. prior to next dose (Must be AT **LEAST 6 hours** post dose	0.7–2.0 ng/mL	Normal renal function: at least 4 half lives since Start of therapy (i.e. at least 6 days)
VANCOMYCIN	0-30 min. prior to 4th dose	10-20 mg/L	Trough monitoring is recommended for patients receiving aggressive dosing (i.e., to achieve sustained trough levels of 15–20 mg/L) and all patients at high risk of nephrotoxicity (e.g., patients receiving concurrent nephrotoxins).
DIVALPROATE	Within 30 minutes before 5th or 6th dose	50-100 µg/mL	Maintenance: Only if patient still has seizures.
GENTAMICIN	Extended interval with 18-24 hr after 2nd dose. Serum conc. <1mg/L Maintain once weekly levels	<2mg/L(1.5m g/L optimal)	Traditional dosing: 0-30 min prior to next dose. Serum Conc. 0.6-2mg/L. Usually after 3rd dose and repeated weekly levels for maintenance
METHOTREXATE	Clinically relevant concentration-toxicity response. Administration of an antidote (Leucovorin)	standard dosing until serum MTX≤0.2uM	Standard protocols are run at rescue doses depending on MTX serum concentration
CARBAMAZEPINE	0-60 min. prior to next dose	4-12 mg/L	Initial: 3-7 days after final dosing alteration. Maintenance: Only if patient still has seizures. If toxicity is suspected, take sample at time of symptoms, or 3 hours after the dose

SPECIAL CONSIDERATIONS

GENTAMICIN

- Peak therapeutic ranges vary depending on the severity of infection i.e higher peaks for more severe infections (e.g. cystic fibrosis) For
- HD patients target Pre HD or Post HD level will depend on severity of infection. Provider will determine if redosing needed.
- Pre or Post (HD)1-3 mg/L: Pre HD or 1 hour Post HD level before a dose to determine if redosing needed

VANCOMYCIN

- Obtain trough in patients with unstable renal function, renal replacement therapy, when serum Cr may not accurately reflect GFR i.e. patients > 70, reduced muscle mass, severely altered volumes of distribution, or for CNS infections, endocarditis, ventilator-associated pneumonia, bacteremia or osteomyelitis caused by MRSA
- Random vancomycin concentrations may be appropriate for patients with CrCl <10 ml/min not on renal replacement therapy to assess appropriateness of redosing

PHENYTOIN

- Check albumin level concurrently with phenytoin level. Albumin-adjusted phenytoin level may be higher than reported i.e. levels that are at target (10-20) may actually be greater than 20 with hypoalbuminemia.

DOSE RELATED ADRs OF PHENYTOIN	
Phenytoin level	**ADRs**
> 20 mg/l:	Far lateral nystagmus
> 30 mg/l:	lateral gaze nystagmus and ataxia
> 40 mg/l:	Decreased mentation
> 100 mg/l	Death

PHENYTOIN SERUM CONCENTRATION ESTIMATION

Change in albumin	Renal failure	Renal failure with change in albumin
$Cp = Cp'/(0.2X\ albumin) + 0.1$	$Cp = Cp'/0.5$	$Cp = Cp'/(0.1X\ albumin) + 0.1$

HD= Hemodialysis; Cp=Corrected phenytoin Level; Cp'=phenytoin Level measured from Lab

News & Updates

Metronidazole-Associated Encephalopathy

NEJM reports a case of 58-year-old man with cryptogenic cirrhosis who was admitted to the intensive care unit with confusion after an event of fall at home. He had been taking a prolonged course of metronidazole (500 mg three times per day for >3 weeks) for *Clostridium difficile* infection. Discontinuation of metronidazole resulted in resolution of the imaging findings. One month later neurologic assessment was difficult, and the patient never regained his baseline mental status Encephalopathy associated with metronidazole use is an uncommon side effect of the medication. It typically manifests as dysarthria and gait instability. Risk factors include liver dysfunction and a prolonged course of metronidazole (typical cumulative dose >20 g). MRI of the brain is usually diagnostic and typically reveals a symmetric, enhanced FLAIR signal in the dentate nuclei of the cerebellum.

Piperacillin and tazobactam combination - Risk of bronchospasm and hypokalaemia

The Central Drugs Standard Control Organization (CDSCO), India has requested that bronchospasm and hypokalaemia be included as adverse reactions in the package insert for combination products of piperacillin and tazobactam. The request follows the recommendation received from the Pharmacovigilance Programme of India - Indian Pharmacopoeia Commission (PvPI-IPC). Based on available evidence and advice of the subject expert committee, CDSCO/PvPI has decided that it was necessary to revise the package insert to add hypokalaemia and bronchospasm as clinically significant adverse reactions.

Life Threatening Arrhythmias with Loperamide – FDA Warning

Loperamide – an opioid antidiarrheal has maximal approved dose of 16mg per day. FDA has issued a recent warning that taking higher than recommended doses of loperamide including through abuse or misuse of the product, can cause serious life-threatening arrhythmias including QT interval prolongation, Torsades de Pointes or other ventricular arrhythmias, syncope, and cardiac arrest. Patients with pre-existing cardiac conduction conditions may be at increased risk. Drugs like cytochrome P450 3A4 (CYP3A4) inhibitors (e.g., itraconazole, clarithromycin), CYP2C8 inhibitors (e.g., gemfibrozil), and P-glycoprotein inhibitors (e.g., quinidine), can increase serum loperamide levels enhancing the cardiac risk potential. Health-care professional awareness and patient education are keys to safe use of loperamide.

FDA advises cautious prescribing of oral fluconazole in pregnancy

FDA is evaluating the results of a Danish study that concludes there is a possible increased risk of miscarriage with the use of oral fluconazole for yeast infections. The current FDA drug label states that data available from studies in people do not suggest an increased risk of problems during pregnancy or abnormalities in developing babies when women are exposed to a single 150 mg dose of oral fluconazole to treat vaginal yeast infections. However, high doses of oral fluconazole (400-800 mg/day) taken by pregnant women for much longer than a single dose have resulted in reports of abnormalities at birth. In the Danish study, most of the oral fluconazole use appeared to be one or two doses of 150 mg. Until FDA's review is complete and more is understood about this study and other available data, FDA advises cautious prescribing of oral fluconazole in pregnancy.