Clini News

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Top five questions:

Q1: is there an interaction between Atorvastatin and Cyclosporin?

Answer: the drug interaction between Atorvastatin and cyclosporine is of major severity, with good documentation and results in increased risk of Myopathy and Rhabdomyolysis. This is most probably due to cyclosporine is an inhibitor of cytochrome P450 (CYP3A4) that metabolizes Atorvastatin. Therefore the CPK level should be monitored during the concomitant use of both drugs as well as any early signs of Myopathy; myalgia, generalized body ache and muscle weakness.

Q2: Can the topical use of Mupirocin (Bactroban) cause systemic side effects?

Answer: the systemic absorption from topical application is minimal, yet about 1.2 – 5.1% absorption may result from the nasal application and it may cause the following side effects; headache and some local effects like taste disorder, rhinitis and pharyngitis.

Q3: Is the use of Immunoglobulins safe in renal transplant patients?

Answer: there are some reports of renal dysfunction and acute renal failure associated with the administration of some IGIV products, during the period between 1985- 1997 there are 52 case reports of renal failure published due to the use of IGIV. It was postulated that this may be due to osmotic injury to the proximal renal tubules induced by the sucrose containing products. However this is not the only cause as there were a lot of disposing factors in these reports like; pre-existing renal dysfunction, old age >65, diabetes, volume depletion and sepsis.

So cautious is recommended when using IGIV in renal transplant patients.

Q4: can Celecoxib (celebrex) induce Steven Johnson Syndrome?

Answer: Steven Johnson Syndrome which is a severe form of erythema multiform in which the lesions may involve the oral and anogenetal mucous membranes and in association with malaise, prostration, headache, arthralgia and conjunctivitis. There are many drugs which can induce this syndrome, the classical example of which is: Sulphonamides, Barbiturates, sulphonyl ureas, phenytoin, NSAIDs and many other drugs. Having a Sulphonamide group in its chemical structure Celeocxib was expected to cause Steven Johnson Syndrome. In the literature there is one case report of Erythema multiform induced by Celecoxib which resolved after discontinuation of the drug but he developed a subsequent reaction when Glibenclamide (another sulfonamide) was added to his treatment.

Q5: Can Plendil be given through Naso - Gastric tube?

Answer: No, as Plendil ® (Felodipine) is an extended release formula it should not be crushed.

Enoxaparin Dose in renal impairment:

The kidney extensively excretes Enoxaparin like all other Low Molecular Weight Heparins and the rate of excretion is dependent on GFR. While the company did not recommend specific dose guidelines for the dose in renal impairment patients, it did recommend that dose adjustment should be considered for patients with only severe renal impairment.

In one study [(1)], which included 111 patients with different degree of renal impairment who had concomitantly Unstable Angina or NSTEMI, Enoxaparin was given in the following dose schedule depending on the Creatinine clearance and the target levels of anti-Xa activity (table 1)

Table 1:

Creatinine clearance	Dose mg / kg Q 12 hours	Anti-Xa level reached	Target anti- Xa
> 60 ml / minute	0.92 mg / kg	1.01 IU / ml	0.5-1.01 IU / ml
30 – 60 ml / minute	0.84 mg / kg	0.95 IU / ml	0.5-1.01 IU / ml
< 30 ml / minute	0.64 mg / kg	0.95 IU / ml	0.5-1.01 IU / ml

It seems that these dose adjustments resulted in reaching the required target of anti- Xa for the patients in this study. However the use of Glycoprotein II b / III a antagonists did not affect anti-Xa activity and Only One patient experienced a major bleeding episode.

Collet et al Enoxaparin in unstable angina patients with renal failure Int J Cardiol 2001;80:81-82

Drug Induced Serotonin syndrome

Serotonin syndrome is a condition of serotonergic hyperstimulation. The most frequent clinical features may include presence of **three** or more of the following:

Signs/symptoms	incidence %
Myoclonus	(58%)
Hyperreflexia	(52%)
Muscle rigidity	(51%)
Confusion	(51%)
Restlessness / hyperactivity	(48%)
Hyper pyrexia	(45%)
Diaphoresis	(45%)
Tremor	(43%)
Ataxia / incoordination	(40%)
Sinus tacchycardia	(36%)
Hypertension /Hypotension	(35%)
Agitation	(34%)
Coma/ unresponsiveness	(29%)
Tachypnea	(26%)
Shivering	(26%)
Nausea	(23%)
Euphoria/ hypomania	(21%)
Unreactive pupil	(20%)
Nystagmus	(15%)
Seizures	(12%)

Classically the Serotonin Syndrome would occur when a MAOI drugs like Phenelzine is combined with seretonergic drugs SSRIs or TCAD

There have been numerous reports in the literature of patients who received various combinations of serotonergic agents that resulted in the serotonin syndrome (see the table 2). The presumed pathophysiology of this syndrome is based on animal studies and case reports of drug interactions. It is proposed that the combinations of certain drugs cause activation of the 1A form of serotonin receptors in brainstem and spinal cord neurons, which enhances overall serotonin neurotransmission.

Table 2:

Some selected drug combinations that are currently prescribed and reported to induce Serotonin Syndrome

Drug	When combined with
Alprazolam (Xanax)	Clomipramine (Anafranil)
Amitriptyline (Triptyzole)	Dihydroergotamine (Cafergot) Sertraline (Zoloft)
Bromocriptine (Parlodel)	Levodopa / carbidopa (Sinemet)
Buspirone (Buspar)	SSRIs TCADs Trazodone (Molipaxin)
Carbamazepine (Tegretol)	Fluoxetine (Prozac)
Dextromethorphan (Riopan) the cough sedative	SSRIs
Dihydroergotamine (Cafergot)	SSRIs TCADs
Fentanyl	SSRIs
Linzolid the new antibiotic for resistant gm+ve cocci	SSRIs Tramadol (Tramal) TCADs
Lithium	TCADs SSRIs
Metoclopramide	Sertraline (Zoloft) Venlafaxine (Effexor)
Serotonin agonists (Imigran, and others)	MAOIs SSRIs TCADs Tramadol (Tramal)
SSRIs	TCADs Tramadol (Tramal) MAOIs
St John's wort	TCADs MAOIs SSRIs
Sympathomimetics	TCADs

Key words

- Tricyclic antidepressants TCADs (Clomipramine, Imipramine, Amitriptyline)
- Selective serotonin reuptake inhibitors SSRIs eg Sertraline, Fluoxetine, Paroxitine, Citalopram, and the new Venlafaxine which also has Noradrenalin reuptake inhibition effect
- Monoamino-oxidase inhibitors MAOIs

Guidelines for the management of serotonin syndrome:

1. Supportive treatment, crystalloid solution for hypotension and cooling blankets for hyperthermia.
2. If hyperthermia is severe chlorpromazine to control fevers may be used.
3. Nor epinephrine is the preferable vassopressor for the management of hypotension
4. Benzodiazepines are used for rigors, while Clonazepam may be useful for treating myoclonus
5. Endotracheal intubations may be needed in certain conditions.
6. Beta blocking agents are used to control the tachycardia, and tremors.
7. Cyprohetadine (Periactin) which has serotonin receptor blocking effect as well as antihistamine has been used with appreciable efficacy in a dose up to a maximum of 32 mg / day on divided doses.

While the recovery has been seen within 1 day in 70% of cases the mortality rate is about 11%.

SARS: Is it Coronavirus or Chlamydia?

The puzzle of the frightening respiratory illness that is spreading worldwide is still waiting for an answer!!
WHO Experts are suspecting the etiology to be something that has not been described before in humans or animals and the prime suspect is a **Coronavirus** that probably originated in animals, while in China where the disease was early addressed as atypical pneumonia, they suspect a **Chlamydia- like agent.**
The first outbreak of the disease was in November 2002 at Guangdong (China) and spread around the globe in March 2003.
While the number of people killed by the disease is 100, the numbers of infected people are increasing worldwide “3000 cases” reported till now.

Risk of life threatening asthma induced by Salmeterol

The FDA announced that UK GlaxoSmithKline has halted a large-scale study of the long acting B2 agonist (Salmeterol Xinofoate) due to concerns that the drug may be associated with an increased risk of life threatening episodes of asthma.
The study, which begun in 1996 was designed to investigate post- marketing reports of several asthma deaths associated with the use of Servent inhalation and other B2 agonists.
While the analysis of the study did not demonstrate that the drug was associated with significant increase in the comorbid endpoint of respiratory related deaths or intubation, it did show a trend towards a greater increase in asthma deaths and serious asthma episodes prevalent in African-American patients.
Further analysis showed that patients taking inhaled corticosteroids at the study entry appeared to be at lower risk than those who were not taking inhaled corticosteroids.
The FDA is planning to meet the drug-maker in the near future to obtain more details about the interim analyses and determine what steps are warranted to address this new risk information.

All refrences are available upon request at “Drug Information Center”, Al- Jazeira Hospital, Abudhabi. Ext.518.