JSS University

Clinical Pharmacy

A Newsletter of Drug and Prescribing Information

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ADVERSE DRUG REACTION REPORTS: SEP TO DEC 2013

A total of 1118 adverse drug reactions (ADRs) were reported or detected by the Department of Clinical Pharmacy during September to December 2013. The following are some of the suspected ADRs detected during this period. In most of the cases there was a change in drug therapy e.g. cessation of suspected drug or reduction in dose, and/or either specific or symptomatic treatment for the suspected ADRs.

Bupivacaine	Simple Partial Seizures
Cefixime	Fixed Drug Eruption
Dopamine	Piloerection
Duloxetine	Tremor
Escitalopram	Diaphoresis
Haloperidol	Stoop Posture
Isoniazid	Irrelevant Talking
Ketamine	Vivid Dreams
Lorazepam	Asthenia Arms
Losartan	Psoriasis
Nevirapine	Steven Johnson Syndrome
Piperacillin + Tazobactum	DRESS Syndrome
Risperidone	Acne
Stavudine	Lipodystrophy
Succinylcholine	Hypotension

Isoniazid induced irrelevant talking: Irrelevant talk is one of the manifestations of isoniazid induced psychosis. Isoniazid causes deficiency of vitamin B6 by causing excessive excretion of the vitamin, which in turn leads to a disturbance of normal tryptophan metabolism. It also inhibits the activity of brain pyridoxal-5-phosphate (produced in the body from pyridoxine), which leads to a decrease in brain gamma-amino butyric acid and other synaptic transmitters, resulting in neurologic ill effect. Isoniazid induced-psychosis recovers without specific treatment after the withdrawal of the offending agent.

Ketamine induced vivid dreams: Ketamine can produce vivid dreams or hallucinations which may be intense and terrifying. These dreams and illusions usually disappear on full wakening. The incidence of psychic effects is approximately 5–30%. A higher incidence is associated with factors such as increasing age, female gender, patients who normally dream, rapid intravenous administration, and large doses. When ketamine is given to humans for medical reasons, it is often given in combination with another drug that prevents hallucinations.

Nevirapine induced Steven Johnson Syndrome: Steven Johnson Syndrome or Toxic Epidermal Necrolysis has been reported to occur in 0.3% of patients taking nevirapine within the first 4–6 weeks of treatment. Individual lesions may heal within 1–2 weeks unless secondarily infected.

We encourage you to report all suspected adverse drug reactions to Department of Clinical Pharmacy. Adverse drug reaction reporting forms are available at all nursing stations. Alternatively you may call Department of Clinical Pharmacy on 2548356 or 2548363/4 Extn. 8404 or sms to 07411137840. (Format : ADR/IP or OP Number/Name of the patient/ ward)

Drug-Drug Interaction between Clarithromycin and Calcium-Channel Blocker

Concurrent use of clarithromycin among older adults taking a calcium-channel blocker (CCB) is reported to be associated with a greater 30-day risk of hospitalization with acute kidney injury (AKI).

Clarithromycin and erythromycin are the commonly used macrolide antibiotics and clinically important inhibitors of the CYP3A4. CCBs are a popular class of antihypertensive drugs that are metabolized by the CYP3A4 enzyme. Because azithromycin is only a weak inhibitor of CYP34A, the type of intensification of the CCB that occurs with clarithromycin is not expected. Clarithromycin can increase blood concentrations of CCBs by as much as 500% when administered concurrently. A population-based case-crossover study of older adults found a greater risk of hospitalization with hypotension (enhanced blood pressure lowering) when a CCB was co-prescribed with erythromycin or clarithromycin compared with azithromycin. Currently USFDA warns that "serious hypotension have been reported in patients taking clarithromycin concomitantly with CYP3A4 substrates, which includes CCBs (e.g. nifedipine, amlodipine, verapamil, diltiazem)". When hypotension occurs, the kidney is particularly prone to acute ischemic injury from poor blood perfusion. Yet CCBs and clarithromycin continue to be frequently co-prescribed in routine care especially in elderly, close monitoring is necessary to observe the occurrence of AKI.

In a population-based retrospective cohort study aimed the effect of CCB with clarithromycin or azithromycin observed that patients prescribed with clarithromycin along with CCB are 98% more prone to get AKI than patients with azithromycin (OR, 1.98 [95% CI, 1.68-2.34]). The risk was highest with dihydropyridines, particularly nifedipine. Patients' co-prescribed clarithromycin also had a higher risk of hospitalization for hypotension and all-cause mortality.

These findings support current safety warnings regarding concurrent use of CYP3A4 inhibitors and CCBs. By observing the results of this study, it is possible to prevent large number of hospitalizations, deaths and high costs of managing AKI, by avoiding this serious drug-drug interaction.

References:

1. Gandhi S, Fleet JL, Bailey DG, McArthur E, Wald R, Rehman F, Garg AX. Calcium-Channel Blocker–Clarithromycin Drug Interactions and Acute Kidney Injury. JAMA November 9, 2013: doi:10.1001/jama.2013.282426
2. Wright AJ, Gomes T, Mamdani MM, Horn JR, Juurlink DN. The risk of hypotension following coprescription of macrolide antibiotics and calcium-channel blockers. CMAJ 2011;183(3):303-307

Eighth Joint National Committee (JNC 8) Evidence-Based Guidelines for the Management of High Blood Pressure in Adults

Unlike the JNC 7 guidelines, JNC 8 guidelines do not focus on the definition of hypertension and pre hypertension. Instead it aims to define thresholds for pharmacological treatment. Specifically, JNC 7 concluded that all adult patients with hypertension (regardless of their age) should have their Blood Pressure (BP) reduced to a systolic BP (SBP) of lower than 140 mmHg, with even tighter control in patients with diabetes or renal disease (SBP <130 mmHg). In contrast, the current recommendation raises target SBP goals to 150 mmHg or lower in those aged 60 years or older, while eliminating the tighter control recommendations in patients with diabetes and renal disease.

JNC 8 made a strong recommendation to initiate pharmacologic treatment to lower blood pressure to less than 150/90 mmHg in hypertensive patients aged 60 or older and to a diastolic goal of less than 90 mmHg in hypertensive patients aged 30 to 59.

While JNC 7 recommended thiazide-type diuretics for initial therapy in the general population, JNC 8 makes a moderate recommendation for selection of initial treatment from a broader range of medications. A thiazide-type diuretic, calcium channel blocker, angiotensin-converting enzyme inhibitor, or angiotensin receptor blocker is reported as an acceptable choice for the general non-black population, including those with diabetes.

JNC 8 makes a moderate recommendation to utilize an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker for blood pressure treatment in all chronic kidney disease patients, regardless of race or diabetes status.

The following are the recommendations made by JNC 8 based on the systematic evidence review.

Recommendation 1

In the general population aged ≥ 60 years, initiate pharma cological treatment to lower BP at SBP ≥ 150 mmHg or diastolic blood pressure (DBP) ≥90 mmHg and treat to a goal SBP <150 mmHg and goal DBP <90 mmHg.

Corollary Recommendation

In the general population aged ≥60 years, if pharmacological treatment for high BP results in lower achieved SBP (e.g., <140 mmHg) and treatment is well tolerated and without adverse effects on health or quality of life, treatment does not need to be adjusted.

Recommendation 2

In the general population <60 years, initiate pharmacological treatment to lower BP at DBP ≥ 90 mmHg and treat to a goal DBP <90 mmHg.

Recommendation 3

In the general population <60 years, initiate pharmacological treatment to lower BP at SBP ≥ 140 mmHg and treat to a goal SBP <140 mmHg.

Recommendation 4

In the population aged ≥18 years with chronic kidney disease (CKD), initiate pharmacological treatment to lower BP at SBP ≥140 mmHg or DBP ≥90 mmHg and treat to goal SBP <140 mmHg and goal DBP <90 mmHg.

Recommendation 5

In the population aged ≥ 18 years with diabetes, initiate pharmacological treatment to lower BP at SBP ≥140 mmHg or DBP ≥90 mmHg and treat to a goal SBP <140 mmHg and goal DBP <90 mmHg.

Recommendation 6

In the general nonblack population, including those with diabetes, initial antihypertensive treatment should include a thiazide-type diuretic, calcium channel blocker (CCB), angiotensin-converting enzyme inhibitor (ACEI), or angiotensin receptor blocker (ARB).

Recommendation 7

In the general black population, including those with diabetes, initial antihypertensive treatment should include a thiazide-type diuretic or CCB.

Recommendation 8

In the population aged ≥18 years with CKD, initial (or add-on) antihypertensive treatment should include an ACEI or ARB to improve kidney outcomes. This applies to all CKD patients with hypertension regardless of race or diabetes status.

Recommendation 9

The main objective of hypertension treatment is to attain and maintain goal BP. If goal BP is not reached within a month of treatment, increase the dose of the initial drug or add a second drug from one of the classes in recommendation 6 (Thiazide-type diuretic, CCB, ACEI, or ARB). The clinician should continue to assess BP and adjust the treatment regimen until goal BP is reached. If goal BP cannot be reached with 2 drugs, add and titrate a third drug from the list provided. Do not use an ACEI and an ARB together in the same patient. If goal BP cannot be reached using only the drugs in recommendation 6 because of a contraindication or the need to use more than 3 drugs to reach goal BP, antihypertensive drugs from other classes can be used. Referral to a hypertension specialist may be indicated for patients in whom goal BP cannot be attained using the above strategy or for the management of complicated patients for whom additional clinical consultation is needed.

Reference:

James PA, Oparil S, Carter BL. 2014 Evidence-Based Guidelines for the Management of High Blood Pressure in Adults: Report from the Panel Members Appointed to the Eighth Joint National Committee (JNC 8). JAMA 2013 Dec 18. doi: 10.1001/jama.2013.284427

Quadrivalent Influenza Vaccine in Children

In a recent phase 3 trial**, Quadrivalent Influenza Vaccine (QIV)** was found to be approximately 60% effective against influenza infection of any severity, and more than 70% effective against moderate-to-severe influenza infections, thus highlighting the efficacy in reducing clinically significant events. This study included more than 5000 children enrolled from three global regions and demonstrated the safety and efficacy of QIV in children 3 to 8 years old. Unlike commonly used trivalent vaccines, quadrivalent vaccines contain two influenza B strains, with the aim of improving protection by targeting both of the common B lineages. In an immunogenicity analysis, seroprotection rates against each strain were more than 95% after vaccination. At six months post immunization, seroprotection rates were higher than 90% against A/H3N2 and B/Yamagata, and higher than 80% against A/H1N1 and B/Victoria. Safety end points did not differ between the QIV group and the control group. However, it is important to note that this study was sponsored by GlaxoSmithKline and the sponsor was involved in conducting all stages of the study and analysis of the data.

Reference: Jain VK, et al. Vaccine for prevention of mild and moderate- to- severe Influenza in children. N Eng J Med 2013;369:2481-2491

Vitamin-D Deficiency Linked to Fatal Cardio Vascular Disease

Result of a large prospective study reveals that Vitamin-D deficiency is much more strongly linked to fatal than nonfatal Cardio vascular events. Previous observational and randomized trials linking serum 25-hydroxyvitamin D [25(OH)D] concentrations with increased cardio vascular disease (CVD) risk have typically used only a single vitamin-D measurement and did not separately examine fatal and nonfatal outcomes. The current population-based cohort study confirm an approximately 27% increased total CVD risk and a 62% increased risk for fatal CVD in subjects with vitamin D deficiency. A possible explanation for the stronger association between 25(OH)D and CVD mortality than nonfatal CVD end points is that low vitamin-D levels could lead to more severe events and perhaps also reduce capacity to cope with the events. Alternatively, the association of 25(OH)D with mortality may be more strongly affected by confounders linking to both low vitamin D and poor health status, such as diabetes or chronic kidney disease.

However, there was no association between vitamin-D deficiency and nonfatal CVD events. Overall, the proportion of individuals who had no events was significantly lower among those with vitamin-D deficiency.

Reference: Perna L, Schottker B, Holleczek B, Brenner H. Serum 25-Hydroxyvitamin D and Incidence of Fatal and Nonfatal Cardiovascular Events: A Prospective Study With Repeated Measurements. J Clin Endocrinol Metab 2013;98(12):4908-4915

Drug Information Query of this Quarter

Q: Ms. AK, a 46 year old female (Quetelet Index: 31.2 kg/m^2) visited neurology OPD with complaints of involuntary grinding of the teeth during sleep which caused the destruction of tooth structure, temporo-mandibular joint dysfunction, myofascial pain, and severe sleep disturbances. Her past history revealed that she was on Hormone Replacement Therapy (HRT) until 3 months ago and is now on Paroxetine 10 mg OD for menopause. Treating neurologist has made diagnosis *"Drug induced Bruxism"* and asked the clinical pharmacist for possible role of paroxetine in treating post menopause syndrome and pharmacological, non pharmacological treatment options for bruxism.

Information Provided:

US FDA has approved the use of paroxetine, a SSRI (Selective Serotonin Reuptake Inhibitor) to treat moderate to severe hot flushes (vasomotor symptoms) associated with menopause. Serotonin plays an important role in thermoregulation and temperature increase associated with the hot flushes is linked with the overload of serotonin at receptor sites in hypothalamus. Balance between two 5-HT receptors, 5-HT_{1a} and 5-HT_{2a} are closely associated with regulation of temperature in mammals which can be modulated by the gonadal hormones and adrenal corticosteroids.

The safety and effectiveness of paroxetine were established in two randomized, double-blind, placebo-controlled studies in a total of 1,175 postmenopausal women with moderate to severe hot flushes (a minimum of seven to eight per day or 50-60 per week). The treatment period lasted 12 weeks in one study and 24 weeks in the other study. The results showed that paroxetine reduced hot flushes compared to placebo.

It is hypothesized that the mechanism for SSRI-induced bruxism may involve in excessive serotonergic action on the meso-cortical neurons arising from the ventral tegmental area. This action leads to a dopaminergic deficit, which causes a specific form of akathisia and akathisia-like movement of the jaw muscles, thereby leading to bruxism. Pharmacological treatment includes the use of buspirone is an agonist of the 5-HT_{1a} receptor that increases dopaminergic neuron firing in the ventral tegmental area and increases the synaptic release of dopamine in the prefrontal cortex. These effects ameliorate drug-induced bruxism. However, in this patient, use of buspirone should be considered as it interacts with paroxetine and increases the serotonin levels. Other drugs include, propronolol, gabapentine and botulin toxins.

Non pharmacological treatment includes use of appliance therapy i.e, use of flat-planed stabilization splint, also known as, an occlusal bite guard, bruxism appliance, bite plate, and night guard.

Report on AICTE Sponsored Staff Development Program

All India Council for Technical Education (AICTE) sponsored Staff Development Program (SDP) on "Teaching Learning methodologies for teachers teaching Pharmacy Practice subjects" scheduled for two weeks was inaugurated on 30th September, 2013 at 10.30 am in the JSS College of Pharmacy seminar hall. Dr. M.Manjunatha, Registrar, JSS University, was the Chief Guest of the function and Dr. P.A. Kushalappa, Director- Academics, JSS University, was the Guest of honor. The program was inaugurated with invocation and lighting of the lamp by the Guests. Dr. M.Ramesh, Professor, Department of Pharmacy Practice welcomed the participants, G.Parthasarathi, Professor & Head, Department of Pharmacy Practice briefed the gathering about objectives of the program, Dr. H.G.Shivakumar, Principal, JSS College of Pharmacy address the gathering and Dr. Adepu Ramesh, Professor, Department of Pharmacy Practice coordinated the program.

Inauguration of AICTE Sponsored SDP

Delegates with the Resource Persons

About 50 faculty involved in teaching of pharmacy practice subjects from various pharmacy colleges from South India had attended the program. Various topics covering clinical pharmacy services, pharmaceutical care, pharmacoepidemiology, pharmacoeconomics, clinical research and experiential education were covered by twelve internal resource persons and three external resource persons.

Awards

- **Mr. Krishna Undela,** Lecturer, Department of Pharmacy Practice, has won the **Best Oral Presentation Award** for his presentation entitled "Impact of Patient Medication Counselling on Medication Adherence in a Cardiology Outpatient Clinic" at the 8th Asian Conference on Pharmacoepidemiology held on 26-27 October, 2013 at Hong Kong University, Hong Kong.
- **Late Sri Murugappa Sirse Memorial Award 2013** was received for best poster presentation titled 'Assessment of medication errors in psychiatric practice in a tertiary care hospital' authored by **Hema Saithi,** Ibrahim, Manoranjini, Nanda Kishore, Madhan Ramesh and Juny Sebastian during Association of Pharmaceutical Teachers of India (APTI) conference held at Vikas Institute of Pharmaceutical Sciences, Rajahmundry during 25-27 October, 2013.

Mr. Krishna Undela receiving the award

Ms. Hema Sahithi with award

Overseas Visitors

Ms. Grace Wong, Senior Clinical Pharmacist, Austin Repatriation Hospital, Melbourne, Australia visited Department of Pharmacy Practice, JSS College of Pharmacy, Mysore during 11th and 12th of November, 2013. During her visit, she delivered a guest lectures on 'Pharmacy Practice in Australia' and 'Medications and Hemodialysis' to PharmD and Postgraduate Pharmacy Practice students. In her first talk, she highlighted a current scenario of Pharmacy Practice in Australia where students had an opportunity to understand current health care policy in Australia, role of pharmacist in health care and different types of government health benefit schemes available to Australian citizens.

In her second talk, she described the role of clinical pharmacist for hemodialysis patients where she emphasized how pharmacist should review medication regimens before and after hemodialysis, where pharmacists can suggest dosing recommendations and educate the patients. Also, she briefed about concept of home medication review and role of pharmacist in home medication review. Grace Wong moderated two case presentations on renal disease and gave her valuable feedback to students. Also, she interacted with the staff of Department of Pharmacy Practice and appreciated the efforts of the department in providing the patient care services.

Ms. Grace Wong with department staff

Ms. Christine Birnie, Associate Professor & Chair, Pharmaceutical sciences, Wegman School of Pharmacy, New York visited our department on 5th December 2013 and delivered a talk on Practice of Pharmacy in USA. This interactive session was attended by final year Pharm. D students wherein she clarified all the queries of students regarding the scope and practice of pharmacy in USA.

Ms. Christine Birnie delivering the talk

Adverse Event Following Immunization Report

Active monitoring of Adverse Events Following Immunization (AEFI) program was started at JSS Hospital, Mysore in the year 2013. From Jan - Dec 2013, 193 AEFIs have been reported to the department of Clinical Pharmacy including 189 (98%) vaccine reactions, two program errors and two injection reactions. Fever was the frequently reported AEFI.

Health Screening Camps

Health Screening Camps were organized by the Department of Pharmacy Practice on 25th September, 2013 on the occasion of World 'Pharmacist's Day' and 20th November, 2013 on the occasion of 'National Pharmacy Week' celebration at 6 different places in Mysore town including Balbhavan, Cheluvamba Park, Chamundi Hill Footsteps, Chamundi Vihar Stadium, Kukkeralli Lake and Lalitha Mahal Palace Helipad. During this camp, staff and student volunteers were involved in health screening and about 1000 people benefited from the camp.

Lung Cancer Awareness Rally

The department staff and students participated in the rally organized by Bharath Hospital & Institute of Oncology, Mysore on 30th November, 2013 for creating awareness on Lung Cancer and its preventions. About 700 participants from different hospitals and nursing colleges participated in the rally. Department of Clinical Pharmacy distributed the leaflets on lung cancer among general public and it covers global statistics of lung cancer, its causes, preventions and important warning signs of lung cancer.

Students at Rally

The Drug & Poison Information Service

Our Department can help you with any questions you might have on the use of medicines or the management of poisoned patients. We can also assist you with any medication related problems you face in your daily practice. The services are made available on all working days and it is provided free of cost. We request you to avail the drug and poison information services.

Toll free - 1800-425-0207 Extn. 8404 E-mail: dic.jsscp@jssuni.edu.in; pic.jsscp@jssuni.edu.in;
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Your suggestions are welcome. Please send your comments/suggestions to the editors at: dic.jsscp@jssuni.edu.in

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