Prepared by
Department of Clinical Pharmacy
JSS College of Pharmacy at
JSS Hospital, Mahatma Gandhi Road,
Mysuru – 570004

Clinical Pharmacy

A Newsletter of Drug and Prescribing Information

Editors:
Dr. G. Parthasarathi, Dr. M. Ramesh, Ms. Karin Nyfort-Hansen, Ms. Juny Sebastian and Mr. Krishna Undela

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ADVERSE DRUG REACTION REPORTS: MAY - AUG 2016

A total of 799 Adverse Drug Reactions (ADRs) were reported or detected by the Department of Clinical Pharmacy during May to August 2016. The following are some of the suspected ADRs that were either reported to or detected by the Department of Clinical Pharmacy. 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 ADR.

Betamethasone	.....	Tinea Corporis
Cefoperazone	.....	Teary Eyes
Dalteparin	.....	Hematoma
Doxorubicin	.....	Congestive Cardiac Failure
Gemcitabine + Cisplatin	.....	Myelosuppression
Glimepiride	.....	Lichenoid Drug Erruption
Isoniazid + Rifampicin + Pyrazinamide +Ethambutol	.....	Xerosis
Oxaliplatin	.....	Burning Epiglottis
Paroxetine	.....	Asthenia
Prednisolone	.....	Ecchymosis
Prulifloxacin	.....	Fixed Drug Eruption
Risperidone	.....	Hyperprolactinemia
Tenofovir	.....	Fanconi Syndrome
Topiramate	.....	Diplopia
Vincristine	.....	Discoloration of Vein

Tenofovir induced Fanconi Syndrome : Three mechanisms are suggested for the cause of reaction, those area Drug Interactions in the Proximal Tubule through the multidrug resistance transporter MRP4, Polymorphisms in Genes Encoding Drug Transporters in the Proximal Tubule and Mitochondrial Toxicity. Increased age, low body weight, pre-existing decrease in kidney function, and concomitant use of nephrotoxic drugs are the risk factors for the development of this reaction. Underlying polymorphisms in genes encoding proximal tubule transporters also may have a role in producing the reaction. This adverse effect can be discovered early by urinalysis and switched to an alternate antiretroviral therapy.

Prednisolone induced Ecchymosis : Chronic use of steroids causes inhibition of the mitotic activity of fibroblasts resulting in reduction of collagen and glycosaminoglycan synthesis and inhibits the collagenase. Elastin fibres in the layers of the dermis becomes thin and fragmented as a result atopic changes such as striate and Ecchymosis developed. Reducing the dose of Prednisolone, Hydrogen peroxide 15% and Carbamide gel may represent a novel treatment for Ecchymoses.

Risperidone induced Hyperprolactinemia : The mechanism by which conventional neuroleptics cause increased prolactin is a dopamine blockade in the tubero-infundibular tract of the hypothalamus, which in turn reverses the dopaminergic inhibition of prolactin in the anterior pituitary. The length of time it takes for prolactin to increase after initiation of conventional neuroleptics varies from a few hours to nine days. Neuroleptic-induced hyperprolactinemia is more common in women than men, and prolactin increase by conventional neuroleptics is also higher in women. Reducing the dose or withdrawal of the antipsychotic and substitution with one with a lower potential to elevate prolactin is the management for the reaction.

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 2335555 Extn. 5577 or SMS to 07411137840 (Format: ADR / IP or OP Number/ Name of the patient/ Ward)

Non-steroidal Anti-inflammatory Drugs Can Cause Heart Failure?

A nested case control study was done to investigate the cardiovascular safety of non-steroidal anti-inflammatory drugs (NSAIDs) and estimate the risk of hospital admission for heart failure with use of individual NSAIDs. Participants were enrolled from five population based healthcare databases from four European countries (the Netherlands, Italy, Germany, and the United Kingdom).

The study results suggest that the use of any NSAID (use in preceding 14 days) was found to be associated with a 19% increase of risk of hospital admission for heart failure (adjusted odds ratio 1.19; 95% confidence interval 1.17 to 1.22), compared with past use of any NSAIDs (use >183 days in the past). Risk of admission for heart failure increased for seven traditional NSAIDs (diclofenac, ibuprofen, indomethacin, ketorolac, naproxen, nimesulide, and piroxicam) and two COX 2 inhibitors (etoricoxib and rofecoxib). Odds ratios ranged from 1.16 (95% confidence interval 1.07 to 1.27) for naproxen to 1.83 (1.66 to 2.02) for ketorolac. Risk of heart failure doubled for diclofenac, etoricoxib, indomethacin, piroxicam, and rofecoxib used at very high doses (≥2 defined daily dose equivalents), although some confidence intervals were wide. Even medium doses (0.9-1.2 defined daily dose equivalents) of indomethacin and etoricoxib were associated with increase risk. There was no evidence that celecoxib increased the risk of admission for heart failure at commonly used doses.

The study concluded that the risk of hospital admission for heart failure associated with current use of NSAIDs appears to vary between individual NSAIDs, and this effect is dose dependent.

Reference

Arfè A, Scotti L, Varas-Lorenzo C, Nicotra F, Zambon A, Kollhorst B, et al. Non-steroidal anti-inflammatory drugs and risk of heart failure in four European countries: nested case-control study. BMJ 2016;354:i4857

Palbociclib - A Novel Antineoplastic Drug

Palbociclib is a recently approved orally available Cytokinin Dependant Kinase (CDK) inhibitor with potential antineoplastic activity selectively inhibits CDK4 and 6 thereby inhibiting retinoblastoma protein phosphorylation early in the G1 phase leading to cell cycle arrest. This suppresses Deoxyribose Nucleic Acid (DNA) replication and decreases tumour cell proliferation. CDK4 and 6 are serine/threonine kinases that are up-regulated in many tumour cell types and play a key role in the regulation of cell cycle progression.

It is the first of its own class and is indicated for use in post menopausal women with Estroge Receptor (ER) positive and Her2/Neu negative metastatic breast patients with the aromatase inhibitor e.g. letrozole. As per the US Food and Drugs Administration (FDA) approval it has to be given as 125mg once daily dose for 21 days along with letrozole 2.5mg once daily dose followed by a week off the treatment and then the cycle repeated. This regimen can be continued till the disease progresses.

FDA Approval

Palbociclib received its FDA approval on February 3, 2015 for use in combination with letrozole (an aromatase inhibitor) for ER+ve, Her2/neu ve post menopausal metastatic breast cancer as a first line endocrine based therapy. The approval was based on a randomized, multicentre, open label trial in post menopausal women with ER+ve and Her2-ve locally advanced or metastatic breast cancer who had not received any previous systemic treatment for advanced disease. There were 165 patients enrolled in the trial. They were randomly allocated into two groups viz palbociclib + letrozole and letrozole alone. The result showed that progression free survival rate increased from 10.2 months to 20.2 months (P=0. 0004) and overall response rate shown by combination was 55.4% as compared to 39.4% in letrozole alone.

Mechanism of Action

There is a restriction point R after G1 phase. In some of the tumour cells there is a deregulation at this point and there is no check on the cells from G1 to S phase which results in excessive synthesis and cell proliferation. This restriction is controlled by retinoblastoma tumour suppressor gene (RB) which is a negative regulator of the cell. The deregulation occurs either due to direct mutation or loss of RB1 or amplification and / or over expression of D type cyclin that increases the CDK 4 and -6 activity. Tumors in which RB1 function is intact rely on the activity of Cyclin D CDK4 / 6 complexes to inactivate RB1 and progress through the G1 restriction point into S phase. This RB works by preventing the premature cell division by inhibiting G1/S transition. Inactivated form of RB releases the inhibitory control on the cell cycle and allows the cell to proceed for division. The activation prevents the cell from proceeding to S phase. The function of RB gets deregulated in some tumours thus G1/S transition takes place uncontrolled. Palbociclib targets this step and prevents cell division.

Hormone receptor positive breast cancers are one such type of tumor where RB1 function is intact but de-regulation of CDK4 / 6 cyclin D is seen. Thus a new approach in the treatment modality includes targeting CDK 4 and -6 thus putting a stop on cell proliferation.

Drug Interactions

Avoid concurrent use of strong CYP3A inhibitors. If patients must be administered a strong CYP3A inhibitor, the Palbociclib dose to be reduced to 75mg/day.

Adverse Drug Reactions

The major adverse effects include neutropenia (grade 3 57%, grade 4 5%), infections (55%, grade 3 / 4 5%), pulmonary embolism (5%), decreased haemoglobin (83%), decreased leukocytes (95%), decreased lymphocytes (81%) and decreased platelets (61%).

Reference: Palbociclib (IBRANCE Capsules) http://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm487080.htm

Is There a Link Between Statin Use and Risk of Parkinson's Disease?

A recent study carriedout on 20,000 Parkinsn's disease (PD) patients to evaluate the association between use of statins and high or low risk of PD shwed that use of statin is associated with incresed risk of PD. This finding is contrast to previous research suggesting the statins have a protective effect for PD. While high cholesterol has been shown to have a protective effect on the risk for PD, the role of statin use now has been the subject of debate.

In the recent cross-sectional analysis, the use of cholesterol-lowering drugs, including statins or nonstatins, was associated with a significantly higher prevalence of Parkinson's disease (odds ratio [OR], 1.61 - 1.67; $P < .0001$) after adjustment for age, sex, and other comorbidities, such as hyperlipidemia, diabetes, hypertension, and coronary artery disease. The associations of cholesterol-lowering medications with PD were strongest among patients with hyperlipidemia, and there were no significant differences between lipophilic or hydrophilic statins, as well as the other nonstatin cholesterol-lowering drugs, in their effect on PD risk.

Scientists suggest the possibility of statins blocking not only the cholesterol synthesis but also synthesis of coenzyme Q10 that is essential for cell function as the mechanim increased risk of PD. In the cross-sectional analysis, both statins and nonstatin cholesterol-lowering drugs were associated with PD, but in the lagged case-control analysis of treatment duration, only statins remained significantly associated with PD risk.

Reference: Nancy A. Melville. Statin Use Linked to Increased Parkinson's Risk. American Neurological Association (ANA) 2016 Annual Meeting.

DEPARTMENT ACTIVITIES

Advanced Level Workshop on Pharmacovigilance

Department of Pharmacy Practice organized an 'Advance Level Workshop on Pharmacovigilance' in association with National Coordination Center - Pharmacovigilance Programme of India (PvPI) & Regional Training Center, JSS Medical College & Hospital on 5th & 6th August 2016 at JSS College of Pharmacy, Mysuru.

Dr. M Ramesh, Dr. Shanthy Gunasekaran, Dr. G. Parthasarathi and Dr. B. Manjunatha during the inauguration

The aim of this workshop was to provide training in order to advance the knowledge and develop skills amongst technical associates and coordinators of Adverse Reaction Monitoring Centres located in the States of Karnataka, Kerala, Puducherry & Tamil Nadu under PvPI, Ministry of Health & Family Welfare, Govt. of India. Dr. G. Parthasarathi, Coordinator, PvPI briefed about objectives of the workshop to the participants. Dr. B. Manjunatha, Registrar, JSS University highlighted about growth of JSS University in the area of pharmacovigilance. And, Dr. Shanthy Gunasekaran, Deputy Drugs Controller, CDSCO, Bengaluru updated the participants on 'Current Scenario of PvPI and its Implications'. During this two-days workshop, several topics were covered including extended scope of pharmacovigilance, adverse event following immunisation (AEFI), pharmacovigilance in special population, communications in Pharmacovigilance, causality assessment and signal detection. Pharmacovigilance experts from JSS College of Pharmacy, Mysuru; Uppsala Monitoring Centre, Sweden; and Pharmaceutical Industry, Bangalore were the resource persons.

Participants interacting with the faculties of the program

Plenty of opportunities was provided to the participants to interact with JSS University Staff, Faculty Experts and fellow workshop participants. A total of 27 participants from 18 adverse drug reaction monitoring centers attended this workshop. All the participants unanimously told that this workshop helped them to gain advance level of knowledge and understanding especially in the clinical practice setting, and it would help them to further strengthen the Pharmacovigilance activities in their respective hospitals.

Poison Information Centre Activities

The Poison Information Centre (PIC) located at Department of Clinical Pharmacy, JSS Hospital, Mysuru conducted a Poison Information Awareness Program in Nagarle Village and Nanjangud taluka in Mysuru District on 19th August 2016. The aim of the program was to create awareness among the villagers about safe handling of pesticides and also about the first aid measures in case of accidental/ intentional poisoning. During the awareness program, villagers were

Glimpses from the awareness program

educated about the safe handling, utilization, storage, transport and disposal of pesticides. They were also educated about the first aid measures they must follow in case of the snake bites. In addition, Community Pharmacists working in the Community Pharmacies were made aware of the facility and services available at PIC located at JSS Hospital, Mysuru. Also they were educated about the safe use of medications in the elderly as well as pediatric populations, and advised them to percolate the information to the consumers in order to prevent accidental poisonings due to medications in elderly and pediatric population.

Another awareness program was conducted at Farooqia College of Pharmacy and Sarada Vilas College of Pharmacy, Mysuru on 25th and 26th August 2016, respectively. The aim of the program was to create awareness among the Students about the first aid measures they must follow in case of the accidental poisoning as well as poisoning due to snake bites. Also, students were educated about the safe use of medications in the elderly and pediatric populations to prevent accidental poisonings and they were advised to percolate the information to the community in order to create awareness regarding the safe use of medications in elderly and pediatric population.

The leaflet includes the education material on safe use of medications in elderly and pediatric patients, first aid measures to be followed during accidental poisonings and snake bites were distributed. A healthy response was seen from the students as well as college management.

Awareness program at Sarada Vilas College of Pharmacy

Awareness program at Farooqia College of Pharmacy

Visit of Students from Howard University, USA

As a part of MoU between JSS University, Mysuru and Howard University, Washington, USA, two students Ms. Annabelle Tupas Dorion and Ms. Beatrice Belangeli Efamba from Howard University visited Department of Clinical Pharmacy, JSS Hospital, Mysuru as a part of the student excahnge program.

The purpose of the experiential program was to expose the students to an international clinical rotation focused on public health and infectious diseases that are common in developing countries. The international students underwent experiential training for 5 weeks from 28th August to 26th September 2016. During the training period, students were posted one week each in Medicine and Pediatric Departments. During their clinical posting, they could understand the therapeutic management of most of the common diseases seen in India and appreciate the differences that exist in the management of such diseases in United States. Also, students were exposed to various departments like Pulmonology and DOTS centre, Immunization centre, Cardiology, Emergency, Psychiatry, Dermatology and Gastroenterology.

Howard University Students with Department Staff

Howard University Students with Staff & Students of Department of Clinial Pharmacy

Also, students were posted to Asha Kirana Hospital and Bharath Hospital & Institute of Oncology for a period of one week to learn about various opportunistic infections associated with HIV and Cancer management respectively. Towards the end of their clinical rotation, students were posted for a week at Govt. Head Quarters Hospital, Ooty which is a practice site of JSS College of Pharmacy, Ooty to provide them an opportunity to understand the healthcare delivery system at Government settings.

Guest Lectures

The Department of Pharmacy Practice organised a guest lecture on the topics 'Medication Errors - A Silent Threat to Patient Safety' and at JSS College of Pharmacy, Mysuru on 6th of August 2016. Mr. Rajesh Thalapparambath, Senior Pharmacist, Pharmaceutical Care and Drug Utilization Services, John Hopkins Aramco Health Care, Dhahran, Saudi Arabia delivered the lectures. The first topic of the guest lectures was on 'Medication Errors [a] Silent Threat to Patient Safety'. During his talk, Mr. Rajesh highlighted about various types of medication errors, system elements in medication errors and severity ratings of medication errors. Also, he briefed on medication errors in Indian health care settings. During his second talk on the topic 'Technological Innovations in Pharmaceutical Care', he highlighted about advancement of technology in health care field with a special emphasis on computerized physician order entry (CPOE) and Pharmacists role in CPOE. Also, he briefed about unit dose drug distribution system, automation in pharmacy, sterile compounding and ambulatory care, and barcoding system. Fifth year Pharm.D students and staff of Pharmacy Practice Department attended and benefited from this guest lectures.

Mr. Rajesh delivering the lecture

Faculty Attended International Conference

Mr. Himanshu Patel and Mrs. Savitha R.S., Assistant Professors, Department of Pharmacy Practice, JSS College of Pharmacy, Mysuru attended 32nd International Conference on Pharmacoepidemiology & Therapeutic Risk Management scheduled from 24th - 28th August 2016 at Dublin, Ireland. Both received scholarship of USD 1825 by International Society for Pharmacoepidemiology, USA to attend this event with complimentary registration to conference and pre-conference workshops. Mr. Himanshu Patel presented three research papers entitled 'Pharmacovigilance of Anti-Cancer Agents in a Developing Country', 'Role of Clinical Pharmacist in Monitoring Radiation Related Adverse Events in Patients with Chemo-radiation Therapy' and 'Role of Medication Therapy Management in Managing Co-morbidities in Cancer Patients' during the conference. Mrs. Savitha R.S. presented a paper on 'Assessment of Pharmacist Interventions of Drug Related Problems among Patients with Impaired Renal Function'.

Mr. Himanshu Patel and Mrs. Savitha R.S. at 32nd ICPE, Dublin

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; 0821-2335577; Extn. 5577; E-mail: dic.jsscp@jssuni.edu.in; pic.jsscp@jssuni.edu.in;
Website: picjsscp.jssuni.edu.in

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