



Clinical Pharmacy

A Newsletter of Drug and Prescribing Information

Prepared by
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ADVERSE DRUG REACTION REPORTS: MAY - AUG 2014

A total of 992 Adverse Drug Reactions (ADRs) were reported or detected by the Department of Clinical Pharmacy during May to August 2014. 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.

Amitriptyline	Tinnitus
Calcium Gluconate	Thrombophlebitis
Desvenlafaxine	Paroniria
Domperidone	Dyskinesia
Escitalopram	Cataplexy
Farmorubicin	Jerky movements
Heparin	Epistaxis
Isoniazid	Hiccups
Paracetamol	Leucopenia
Phenytoin	Phenytoin toxicity
Pregabalin	Xerostomia
Propranolol	Vasculitis
Streptokinase	Blurred vision
Torsemide	Hypoalbuminemia
Vincristine	Neuropathy

Heparin Induced Epistaxis: Heparin is highly-sulfated glycosaminoglycan, which widely used as an injectable anticoagulant. Heparin administration may lead to epistaxis, particularly in stressful patients and those with exacerbated hypertension. Reassurance, sedatives, heparin discontinuation, surgicell insertion and protamin administration are the main therapies. Regular tamponade is not recommended due to high possibility of mechanical mucosal microtraumas, which may lead to further bleeding.

Phenytoin Toxicity: An 18-year-old female diagnosed with seizure disorder and had been on Phenytoin 200 mg/day since five years, presented with gingival hypertrophy and bleeding gums, hirsutism, nodular lesions below the mandible, bilateral nystagmus, ataxia, impairment in tandem walking and bilateral lower limb proximal muscle weakness. All the side effects resolved after withdrawal of Phenytoin.

Vincristine Induced Neuropathy: Neuropathy is the dose-limiting side effect of Vincristine and it produces a predictable mixed motor and sensory neuropathy, as well as an autonomic neuropathy. Sensory symptoms are more severe than signs and start with numbness and tingling in a stocking distribution, glove distribution, or both. Because the pathophysiology of Vincristine neuropathy is not fully understood, preventive and therapeutic approaches are still experimental. Few case reports are reported full recovery of Vincristine-associated bilateral ptosis (cranial polyneuropathy) after treatment with pyridoxine and pyridostigmine.

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)

First Dengue Vaccine in Humans Shows Promise

A potential new dengue vaccine, the first to reach phase 3 clinical testing, has demonstrated that it protects 57% of subjects from the disease, according to research published in *The Lancet* in July 2014.

The new recombinant, live, attenuated, tetravalent dengue vaccine (CYD-TDV) developed by Sanofi Pasteur had previously been tested in a proof-of-concept efficacy trial, but did not meet its primary outcome; the vaccine was effective in 30.2% of the 4002 Thai children who participated in the trial. A new phase 3 trial took place across five countries in Asia-Pacific (three centres in Indonesia, two centres in Malaysia, two centres in the Philippines, three centres in Thailand, and two centres in Vietnam) where dengue is endemic. The calculated overall protective efficacy of vaccine was 56.5% and it was well tolerated.

The efficacy of the vaccine varies across the four different dengue serotypes. It gives low protection against DENV 2 (35%), for instance, but a fare better against DENV 1 (50%), and gives more than 75% protection against DENV 3 and 4.

Perhaps the most interesting finding of this trial was

that efficacy after at least one dose was almost as high as that after three doses. The question of whether sufficient efficacy can be achieved with a lower number of doses deserves further assessment.

However, there are some potential limitations of this study: 1) applicability of the findings of this study in Indian population is questionable due to unrepresentative sample from India, though India accounts for nearly one-third of all dengue cases reported globally; 2) Presence of conflict of interest due to the involvement of sponsor of the study in data analysis, data interpretation, and writing of the report; 3) Though the relative risk showing 56.5% efficacy to CYD-TDV, the absolute risk reductions was found to be very minimal, shows that the efficacy of CYD-TDV is only 2.1% more than placebo and at the same time number needed to treat was found to be high that is 48.

Reference:

Capeding MR, et al. Clinical efficacy and safety of a novel tetravalent dengue vaccine in healthy children in Asia: a phase 3, randomised, observer-masked, placebo-controlled trial. *Lancet* 2014;6736(14):61060-61066

Comparison of Renal Adverse Effects of Ibuprofen and Indomethacin in Preterm Infants

Ibuprofen and indomethacin are nonselective inhibitors of cyclooxygenase (COX), which are potent inhibitors of prostaglandin E2 synthesis and useful to close the patent ductus arteriosus (PDA).

In extremely low-birth-weight infants, the percentage of PDA is 80%. The inhibition of prostaglandin E2 synthesis by nonselective inhibitor of COX is the usual therapeutic treatment option for closing the PDA.

To estimate the effects exerted by cyclooxygenase inhibitors on renal function, the following three parameters of renal function were considered in a review of published articles: 1) the urine output; 2) the serum creatinine concentration; and 3) the frequency of oliguria. The present results are consistent with the view that indomethacin reduces the urine output more extensively than ibuprofen; increases serum

creatinine concentrations; and causes an increase of frequency of oliguria more often than ibuprofen. Ibuprofen is associated with less severe renal adverse effects than indomethacin.

The subgroup analysis revealed that renal adverse effects due to indomethacin are more common in immature infants than in older infants, putting the premature infants at higher risk. Ibuprofen is less nephrotoxic than indomethacin and these two drugs have similar efficacy in closing PDA. Therefore ibuprofen should be used for the treatment of PDA.

Reference:

Pacifici GM. Differential renal adverse effects of ibuprofen and indomethacin in preterm infants: a review. *Clin Pharmacol* 2014;6:111-116

Vitamin D Deficiency and Risk of Schizophrenia

A comprehensive meta-analysis was revealed that individuals with Vitamin D deficiency are twice as likely to be diagnosed with schizophrenia as compared to those who have sufficient levels of the vitamin D. The researchers reviewed the findings of 19 observational studies that assessed the link between Vitamin D and schizophrenia. When combined, the studies looked at Vitamin D levels and the mental health of 2,804 adult participants. The studies used blood tests to determine each participant's Vitamin D levels. People with Vitamin D deficiency were 2.16 times more likely to have schizophrenia than those with sufficient Vitamin D in their blood.

Reference: Valipour G, Saneei P, Esmailzadeh A. Serum Vitamin D Levels in Relation to Schizophrenia: A Systematic Review and Meta-Analysis of Observational Studies. *J Clin Endocrinol Metab* 2014;jc20141887

N - Acetylcysteine: A Panacea for All Ills?

N – Acetylcysteine (NAC), a safe, low-cost compound has been in use since three decades primarily for relief from cough, wheeze and thick phlegm associated with cold and flu. Since its introduction it has found use for a number of other maladies including liver failure associated with acetaminophen toxicity, prevent influenza in aged individuals, chronic obstructive pulmonary (COPD) disease and helicobacter pylori infections. Renewed clinical interest in its broad-spectrum benefits is yielding fresh data on promising interventions for this compound.

NAC is a slightly modified version of the sulfur-containing amino acid cysteine. When taken internally, NAC replenishes intracellular levels of the natural antioxidant glutathione, helping to restore cells' ability to fight damage from reactive oxygen species. In acetaminophen toxicity, the body's glutathione reserves are overwhelmed which create widespread and irreversible liver damage. NAC restores protective levels of glutathione, thus preventing damage. It was a relatively obscure and poorly understood compound until the importance of glutathione metabolism and its deficiency in many disease states was understood.

Much of NAC's beneficial activity derives from its capacity to modulate expression of genes for a number of signaling molecules in the inflammatory response. NAC inhibits expression of pro-inflammatory cytokines following exposure to bacterial cell components and infection with influenza A virus. NAC also suppresses the nuclear factor-kappaB (NF-kB), which in turn prevents activation of multiple inflammatory mediators. NAC also regulates the gene for cyclooxygenase - 2 (COX-2), the enzyme that produces pain- and inflammation-inducing prostaglandins in many chronic conditions. Obesity-associated insulin resistance, which arises from production of inflammatory signaling

molecules in fat cells, can be sharply mitigated by NAC through regulation of their genes.

The most compelling evidence for NACs broad-spectrum benefits include:

- ♦ NAC reduces the frequency and duration of attacks of COPD and may slow the clinical course of idiopathic pulmonary fibrosis.
- ♦ NAC improves insulin sensitivity in people with some of the most difficult-to-treat metabolic disorders.
- ♦ Due to its action of regulating expression of many genes in the pathways that link oxidative stress to inflammation NAC may function as a cancer chemopreventive agent.
- ♦ NAC fights the stomach infection *Helicobacter pylori* on two fronts, inhibiting the organism's growth while reducing production of inflammatory cytokines that can lead to gastritis and cancer.
- ♦ NAC can protect against avian influenza and more common seasonal flu symptoms.

Other less compelling evidences for use of NAC include:

- ♦ Reduction of proteinuria in type 2 diabetes mellitus.
- ♦ Treat obsessive compulsive disorder.

References:

1. Rouhi H, et al. Effects of N-acetyl cysteine on serum lipoprotein (a) and proteinuria in type 2 diabetic patients. *J Nephropathology* 2013;2(1):61-66
2. Grant JE, et al. N-acetyl cysteine, a glutamate modulator, in treatment of trichotillomania: double-blind placebo-controlled study. *Arch Gen Psychiatry* 2009;66:756-763

Department Activities

Clinical Rotation of International Students

Ms. Hope Chang, Ms. Alexandria Edwards and Mr. Michael Oyewole, Pharm.D. students from School of Pharmacy, Howard University, USA undergone their international clinical rotation at Department of Clinical Pharmacy, JSS Hospital, Mysore as a part of their Advanced Pharmacy Practice Experience from 23rd June 2014 to 24th July 2014. During their rotation they were posted in different practice sites including JSS Hospital, Mysore, Asha Kirana Hospital, Mysore and Govt. Head Quarters Hospital, Ooty with a special emphasis on infectious diseases common in tropical countries. They were exposed to have an experience in drug distribution systems at JSS Hospital, Mysore and the operational procedure of different community pharmacies located in Mysore city. They involved in

various patient care activities of Pharmacy Practice department and got a chance to present cases observed in the ward. Also, they visited the external sites and have had an experience of provision of various clinical pharmacy services of the department at the external sites.



Howard University Students with Department Students

Training Program in Pharmacovigilance for ADR Monitoring Centres of South Zone

Department of Pharmacy Practice, JSS College of Pharmacy, Mysore organized a two days 'Training Program on Pharmacovigilance' in association with Pharmacovigilance Programme of India (PvPI) and Southern Regional Centre for Training and Technical Support, PvPI on 4th & 5th August 2014. A total of 48 participants from different adverse drug reaction monitoring centres (AMC) from South India attended to the training program.

dignitaries present during the occasion were Dr. B. Manjunatha, Registrar, JSS University, Mysore, Dr. H. Basavannagowdappa, Principal, JSS Medical College, Mysore, Mr. N. C. Dhawan, Advisor, Indian Pharmacopoea Commission, Dr. P. A. Kushalappa, Director, Academics, JSS University, Mysore, Dr. Kalaiselvan, Principal Scientific Officer, PvPI, Dr. H. G. Shivakumar, Principal, JSS College of Pharmacy, and Dr. G. Parthasarathi, Dean, Faculty of Pharmacy, JSS University, Mysore.



Inauguration of Training Program

The program was inaugurated on 4th August 2014 at 11.00 A.M in Rajendra Auditorium, JSS College of Pharmacy, Mysore. The inaugural function was presided by Dr. B. Suresh, Vice Chancellor, JSS University, Mysore & President, Pharmacy Council of India. Dr. S. Manivannan, Deputy Drugs Controller, CDSCO was the Chief Guest of the function. Dr. (Col). R. C. Chaturvedi, Director, JSS Hospital, Mysore and Dr. Arul Pitchai Narayanan, Director, ARMA Medical Foundation, Chennai were the Guests of honor. Other



Participants with Resource Persons

Dr. G. Parthasarathi, Coordinator, AMC welcomed the gathering. During the event, Dr. H. Basavannagowdappa released the course material of the training program, Dr. Arul Pitchai Narayanan released the PvPI Guidance document and Dr. B. Manjunatha released the Consumer reporting form. Dr. M. Ramesh, Professor & Head, Department of Pharmacy Practice proposed the vote of thanks.

Guest Lecture by Dr. V.V. Pillay

The Department of Pharmacy Practice organised a guest lecture on the topic 'Substance Dependence and Abuse – New Drugs on the Block' on 16th August 2014. Dr. V. V. Pillay, Head, Poison Control Centre, Amrita Institute of Medical Sciences, Kochi, Kerala delivered the lecture. Dr. V. V. Pillay, renowned expert in the field of Forensic Medicine and Toxicology, during his lecture emphasised on the dire issues of substance abuse, their identification, characteristics and harms. He highlighted on most common substance of abuse like Alcohol, Tobacco and bigger devils like Cocaine, Heroin, Amphetamine and Club drugs like MDMA (3,4-methylenedioxy-N-methylamphetamine), Fentanyl, Ketamine and Gamma Hydroxy Butyrate. Also, he stressed upon the need to awaken and realise the very imminent nature of this problem in India. Overall, the session enlightened the participants on current scenario of drug abuse and the fact that the price

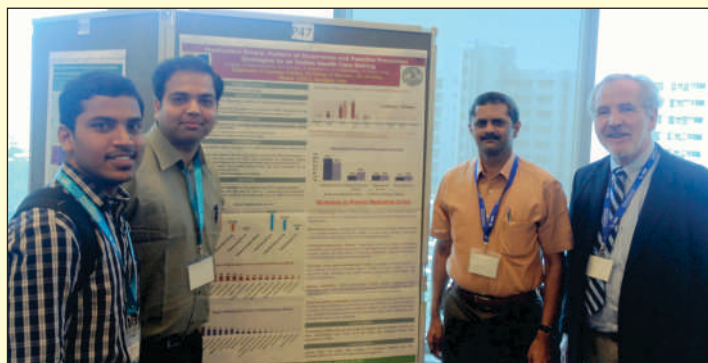
of freedom from drug abuse is eternal vigilance. The Staff, Research Scholars and students of Pharm.D & M. Pharm attended the guest lecture. The participants interacted with Dr. V. V. Pillay at the end of the session. Dr. M. Ramesh, Professor & Head, Department of Pharmacy Practice welcomed the Dr. V. V. Pillay.



Dr. V.V. Pillay Delivering the Lecture

ISPE Student Chapter at JSS University

International Society for Pharmacoepidemiology (ISPE) Student Chapter is now started at Faculty of Pharmacy, JSS University. JSS University is the first University in India and second in Asia to take this initiative in order to bring awareness among student community (future health care professionals) about the science of Pharmacoepidemiology and the importance of quality and safe use of medicines. This initiative (ISPE Student Chapter) will provide early and continuing access to the students, the ISPE benefits and scholarships for emerging scholars and future Pharmacoepidemiologists from JSS University. To guide and support the activities of ISPE Student Chapter, council is formed with the following members.



Right to left: ISPE Student Chapter Faculty Advisor (Mr. Frank W. May), President (Dr. G. Parthasarathi), Member (Mr. Himanshu Patel) and Secretary (Mr. Krishna Undela)

Faculty Attended International Advanced Vaccinology Course

Ms. Juny Sebastian, Lecturer, Department of Pharmacy Practice, JSS College of Pharmacy Mysore had attended 14th International Advanced Vaccinology Course in Asia Pacific Region held at International Vaccine Institute (IVI), Seoul, South Korea from 12th to 16th May 2014. Ms. Juny received a fellowship of 4000 USD from IVI for attending the course.

Department of Clinical Pharmacy in collaboration with the Department of Pediatrics monitors the vaccine safety at JSS Hospital. Ms. Juny Sebastian participated in the said course to develop an expertise in the area of vaccine safety surveillance.



Ms. Juny Sebastian Receiving Participation Certificate

MoU between JSS Colleges of Pharmacy and Uppsala Monitoring Centre

JSS University has signed a MoU with WHO International Drug Monitoring Programme located at Uppsala, Sweden to establish a strategic framework for collaboration to conduct training programmes for capacity building in Pharmacovigilance for the Asia region.

Through the collaboration, periodic training courses will be offered including education on the scientific principles of Pharmacovigilance and training on practices in Pharmacovigilance based on global experiences adapted to local needs of the national Pharmacovigilance systems in the region and will emphasize the importance of compliance with global standards.



Dr G. Parthasarathi, Dean, Faculty of Pharmacy, JSS University with Chief Operating Officer of Uppsala Monitoring Centre, Uppsala, Sweden

JSS University Receives ACPE Certification for Pharm.D. Program

The Accreditation Council for Pharmacy Education – International Services Program (ACPE-ISP), USA, has granted certification to Pharm.D. Program of JSS University offered at Colleges of Pharmacy, Mysore and Ooty.

The ACPE Board review and certification was based on due consideration of the evaluation team report (ETR), the self study report and the recommendation of ACPE's international commission.

The purpose of seeking certification is to set benchmark for the quality of Pharm.D. program (teaching, training

and experiential education) that the university provides in the region with that of global standards and expectations.

JSS University Colleges of Pharmacy are the first in India and second institute outside USA to obtain ACPE certification.



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.

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