

Drug Information News

TSU-COPHS

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Drug Information Center

Texas Southern University's Drug Information Center is now located in the Texas Medical Center at the John P. McGovern Campus on Holcombe Blvd. The center provides comprehensive drug information services to clients including: hospitals, HMOs, nursing homes, home infusion companies, community pharmacies, and governmental entities. Our Mission is to provide unbiased, comprehensive, evidence based drug information to health care professionals and affiliated institutions within a student-centered learning facility, which will enhance the overall delivery of patient care and optimize therapeutic outcomes in a safe and cost effective manner.



Services Offered by the Drug Information Center

- Formulary Management
- Drug Literature Evaluations
- Joint Commission Accreditation Assistance
- Drug Usage Evaluations
- Monitoring Programs
- Pharmacy Practice Materials
- Disease Treatment Recommendations
- Antibiotic Management Programs
- Committee Support (P&T, IRB, QA)
- Education Seminars

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Studies Show Proton Pump Inhibitors Decrease the Effectiveness of Clopidogrel

By: Imoisi Ehiometalor, Doctor of Pharmacy Candidate

It is the way life goes, a problem arises and finding a solution is the next step. But what if the solution has a problem of its own? This is the dilemma that has researchers baffled with the clopidogrel (Plavix®) and proton pump inhibitor (PPI) interaction. "Aspirin-clopidogrel antiplatelet therapy is widely prescribed worldwide with PPI's frequently associated to prevent gastrointestinal bleeding".¹ The problem with this nearly perfect resolution is that several studies show the effect of clopidogrel is significantly reduced by PPIs in general. The OCLA (Omeprazole Clopidogrel Aspirin) study which was a randomized double blinded study, involved patients who underwent coronary artery stent implantation. The patients received aspirin (75mg/day) as well as clopidogrel (300mg loading dose, followed by 75mg/day) and were randomized to receive either omeprazole (20mg/day) or placebo for 7 days. The study included 140 patients divided evenly into two groups. The primary outcome in the study was to compare the primary reactivity index value (PRI); the higher the PRI value, the higher the chances of thrombosis with clopidogrel. A Student t-test was used to assess the results during a 7-day treatment period. The secondary end points were the PRI variation during the 7-day treatment period in the 2 groups and a chi-square comparison of the proportion of patients with PRI below 50% in the 2 groups.² The results of the study revealed that clopidogrel decreases the PRI value by dephosphorylation of intraplatelet vasodilator-stimulated phosphoprotein (VASP). This verifies that omeprazole drastically reduced clopidogrel's inhibitory effect on platelet P2Y12 as assessed by VASP phosphorylation test.¹ The omeprazole group had an average PRI value of 39.8% compared to the placebo group which had 51.4%, meaning the patients receiving omeprazole showed a decrease in clopidogrel's activity, hence an increase in thrombosis. Although the researchers do not recommend the use of a systemic PPI with clopidogrel, the clinical implications of these results needs to be further investigated before any drastic decision is made.

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Gardasil[®] is FDA approved to prevent two more cancers

By: Allyson Davis, Doctor of Pharmacy Candidate

On September 12 2008, the FDA approved two new indications for the human papillomavirus vaccine Gardasil[®] including vulvar and vaginal cancers in females ages 9 to 26. Gardasil[®] was originally approved in 2006 to prevent four HPV types that potentially can cause cervical cancer, genital warts, or precancerous lesions. This new FDA approval was a result of a 2 year follow-up-analysis of 15,000 participants that participated in the original Gardasil[®] studies. In the beginning of the original studies, half of the participants received the vaccine, and the other half served as the control group and did not receive the Gardasil[®] vaccine. In the control group, 10 participants developed precancerous vulvar lesions and 9 participants developed precancerous vaginal lesions; none of the vaccinated participants developed any lesions. According to the FDA, the results of the final analysis showed "strong evidence" that Gardasil[®] prevents precancerous vaginal and vulvar lesions which can be caused by HPV types 16 and 18. These two particular types of HPV cause 70% of cervical cancer and an undetermined percentage of vulvar and vaginal cancer. Vulvar and vaginal cancer is actually very rare, but the FDA explains that the potential to prevent them is a very important additional benefit of the Gardasil[®] vaccine. HPV is ranked the most common sexually transmitted infection in the United States and 6.2 million Americans become infected with genital HPV every year according to the Centers for Disease Control and Prevention. There are 100 different strains of HPV that exist and more than 30 of them can be transmitted sexually. Most strains of the virus are actually harmless, but a small number of them can cause cervical cancer. In most cases a woman's immune system can eliminate HPV on its own and prevent serious health complications. However, there are a few HPV types that can cause abnormal cell changes in the vagina, cervix, vulva, and many other areas which can lead to cancer. Gardasil[®] was created to prevent specifically those few types. After Gardasil was approved by the FDA in 2006, the majority of the adverse events have been mild-to-moderate in nature. The most common adverse events that occur are fainting, pain at the injection site, headache, nausea, and fever. Fainting is most common in adolescents after administration of the vaccine. A patient falling as a result of fainting is what causes serious injuries, such as head traumas; therefore, all patients should remain seated for 15 minutes after vaccination to prevent such events from occurring. Merck and Co, inc. is participating in a safety surveillance study of 44,000 women and girls in a managed care organization, which was part of the original approval by the FDA. This study will examine short and long-term effects of Gardasil[®] only for the approved indications. In addition to the FDA approving two new indications for Gardasil[®], Merck and Co, inc. revised the label for Gardasil[®] to now say that there is a lack of sufficient data available to determine if women over the age of 26 are protected by the vaccine, and that women who receive the vaccine are protected from only HPV types (6, 11, 16, and 18) which is contained in the vaccine.

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Atypical Antipsychotics and the Risk of Stroke

By: Noble Koruthu, Doctor of Pharmacy Candidate

Antipsychotics are the mainstay for treating a number of serious psychiatric disorders, including schizophrenia, mania, delusional disorder, and psychosis. These antipsychotics can be categorized into two classes: typical and atypical. The typical or first generation antipsychotics are used to treat the positive symptoms such as delusion, hallucinations and thought disorder whereas the atypical or second generation antipsychotics are used to treat positive and negative symptoms that include anhedonia, flat affect and cognitive disorders. In clinical settings, the atypical drugs are preferred over the typical drugs because they are capable of treating negative symptoms and are less likely to cause extrapyramidal symptoms and tardive dyskinesia. Yet the use of both these classes can be seen in various medical institutions. Recently, there has been a growing concern linking the use of antipsychotic drugs to the risk of having a stroke. In the British Medical Journal, a study was published evaluating the incidence of developing stroke in 6790 patients taking both typical and atypical antipsychotics. The results showed that all antipsychotics are associated with an increased risk of stroke, and the probability might be higher in patients receiving atypical antipsychotics compared to those receiving typical antipsychotics. The study also showed that patients diagnosed with dementia had higher chance of having a stroke if they were on an antipsychotic medication. Atypical antipsychotics that are currently available in the market include clozapine, quetiapine, ziprasidone, olanzapine, aripiprazole, risperidone and paliperidone. In 2005, the U.S. Food and Drug Administration requested all the manufacturers of atypical antipsychotics to add a black box warning to their products informing the users about the increased risk for stroke. In spite of all the concern, the potential mechanisms associating antipsychotics with stroke, or why the risk appears higher with atypical compared to the typical antipsychotics have not yet been deciphered. In summary, there is an increased risk of stroke associated with the use of antipsychotics. As consequence, prescribing or recommending antipsychotics for patients should be case based and patients on antipsychotics with dementia should be monitored more frequently.

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FDA Scrutinizes Long Acting β -2 Adrenergic Agonists

By: Adlia M. Ebeid, Pharm D, Drug Information Resident

On December 10 2008, the Pulmonary-Allergy Drugs Advisory Committee (PADAC), Drug Safety and Risk Management Advisory Committee (DSaRM), and the Pediatric Advisory Committee (PAC) to the FDA met to conduct a benefit risk assessment of long acting beta-2 adrenergic agonists (LABA) for the treatment of asthma in adults and children. After two days of continuous discussion and presentations addressing several considerable components of the risks and benefits associated with LABA from various perspectives including those of Astra Zeneca, Novartis, and GlaxoSmithKline, the committee voted to remove asthma as an indication of formoterol (Foradil[®]) and salmeterol (Serevent[®]).^{1,2} These inhalers known as single agent LABAs are indicated to be used in combination with inhaled corticosteroids (ICS) as maintenance therapy for long term control of chronic asthma in patients who do not adequately respond to other asthma treatments.^{3,4} Despite the FDA's black box warning issued in 2005, and updated product labeling and medication guides, it was reported that 48% of the asthma patients taking LABA's never take the medication with an ICS which could result in possible respiratory related life threatening experiences.¹ This shocking misuse of LABA's could be a result of improper patient, understanding, inappropriate physician prescribing or a combination of both. With the availability of combination agents like Advair[®] and Symbicort[®] patients can receive both safe and effective treatment that is easy to comply with where prescribing errors are minimized and without the increased risk of asthma related death. Others argue that the benefit of single-agent LABAs allows physicians to customize treatment regimens and facilitates dosing modifications necessary to optimize therapy. It has not been officially decided what the result of this advisement will be and what it will mean for patients, prescribers, and pharmaceutical companies. Removing formoterol (Foradil[®]) and salmeterol (Serevent[®]) is less likely to occur seeing that the national guidelines still recommend them for the management of chronic obstructive pulmonary disease (COPD), however serious considerations will be made to evaluate the recommendation of removing asthma as an indication. With a disease that affects over 22 million people and more than 6 million children in the United States alone, it is imperative that disease management guidelines are clear, accurate and appropriate across various patient populations.^{5,6}

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Rosuvastatin May Reduce Elevated C-reactive protein Levels – An Indicator for Cardiovascular Events

By: Angela George, Doctor of Pharmacy Candidate

Heart attacks and strokes are known as a silent killer because patients who experience these health conditions usually present with no symptoms. Typically, these events occur in patients when they have uncontrolled cholesterol levels. Two components of cholesterol, low density lipoproteins (LDL) and high density lipoproteins (HDL), contribute to the overall composition of cholesterol. Unusually high levels of LDL ("bad" cholesterol) and low levels of HDL ("good" cholesterol) are strongly associated with cardiovascular diseases due to formation of plaque buildup in the arteries, a condition known as atherosclerosis. Another significant indicator of heart disease is the C-reactive protein. The C-reactive protein is a marker of inflammation in the arteries. When C-reactive proteins are elevated, it can create a serious problem because the walls of the arteries can become unstable and burst leading to a sudden blood clot and heart attack. The Nurses' Health Study (NHS) and the Health Professionals Follow-up Study (HPFS) are prospective cohort investigations that examined plasma levels of C-reactive protein as markers of risk for coronary heart disease among women and men. After adjustment for matching factors, there was a significant increased risk of coronary heart disease in both sexes, and the relative risk among all participants was 1.79 for those with C-reactive protein levels of at least 3.0 mg per liter, as compared with those with normal levels of less than 1.0 mg per liter. The results of the study indicated that elevated levels of inflammatory markers, particularly C-reactive protein, signified an increased risk of coronary heart disease. Although plasma lipid levels were more strongly associated with an increased risk than were inflammatory markers, the level of C-reactive protein remained a significant contributor to the prediction of coronary heart disease.² Recently, a study involving nearly 18,000 people with normal cholesterol (LDL levels of <130 mg/dl) and elevated levels of C-reactive protein (> or = 2.0 mg/L) were given 20 mg of rosuvastatin daily. Previous studies have revealed that rosuvastatin was the most effective statin at lowering cholesterol and slowing the progression of heart disease. The trial was stopped after a median of 1.9 years due to the promising endpoints. In both the rosuvastatin and placebo groups, the median LDL cholesterol level was 108 mg/dl and the high sensitivity C-reactive protein level was 4.2 and 4.3 mg/L. At the 12 month visit, patients enrolled in the rosuvastatin group had LDL levels of 55 mg/dl and C-reactive protein levels of 2.2 mg/L. Overall, there was 50% lower median LDL cholesterol and a 37% lower median C-reactive protein level in the rosuvastatin group. The overall combined endpoint of myocardial infarction, stroke, or death from cardiovascular causes in patients receiving rosuvastatin verses placebo were 0.45 and 0.85, respectively.^[1] Compared to those who received placebo, patients receiving the drug rosuvastatin had a 48% reduction in stroke, a 46% reduction in the need for interventions to reopen blocked blood vessels and a 20% drop in all-cause mortality," said Paul M. Ridker, M.D., lead author of the study and director of the Center for Cardiovascular Disease Prevention at Brigham and Women's Hospital in Boston. This study may dramatically change the practice of medicine by encouraging millions of people with normal

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cholesterol to now get tested for the C-reactive protein. Physicians may elect to prescribe rosuvastatin to at risk patients with normal cholesterol, and elevated levels of C-reactive protein, in order to reduce their risk of developing cardiovascular events. More studies are currently being conducted to substantiate the benefits of statins in the reduction of C-reactive protein and the reduction of cardiovascular events³. It is possible in the near future to see C-reactive protein levels become a guideline for initiating prophylactic therapy. Hopefully, this study will become a major cornerstone in heart attack and stroke prevention and excite other researchers to design similar studies to validate these results.

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Endemic Fungal Infections in Patients on Tumor Necrosis Factor Antagonist

By: Janae D. Williams, Doctor of Pharmacy Candidate

The diagnosis of endemic fungal infections in patients on tumor necrosis factor (TNF) – alpha antagonist have eluded medical practitioners resulting in the U.S. Food and Drug Administration’s call for a heightened boxed warning. Currently, four monoclonal antibody (MAB) TNF antagonists other TNF antagonists exist, derived by means different from those of MABs. Normally TNF is employed as one of the biological cytokines secreted from macrophages. They promote acute phase proteins such as complement, clotting factors, and C-reactive protein in an inflammatory and immune reaction. Patients with the diseases in Table 1 have elevated TNF levels causing chronic inflammation. By blocking elements of the immune response, patients receiving the TNF antagonist are successfully relieved of their disease but are at risk of mycosis especially those residents or travelers of areas where endemic fungi are prevalent. There are several mycosis causing fungi: histoplasmosis, blastomycosis, sporotrichosis, penicilliosis, coccidioidomycosis, and paracoccidioidomycosis endemic to the Ohio and Mississippi River Valleys and the southwestern region of the United States. According to The Center for Drug Evaluation and Research health alert, the FDA has reviewed 240 reports of histoplasmosis in patients receiving mainly Remicade® and other TNF antagonist agents. Furthermore, medical professionals have failed to identify fungal infections delaying medical treatment resulting in the death of some current and past patients of TNF antagonist. In a case report an individual treated with TNF living in Beaumont, Texas was exposed to *Coccidioides immitis* (native to soils penetrated by rodents) from inhaled fomite railcar dust at a construction site near his home. The railcar held crushed rock from Arizona. Dust from the site covered his home and car for several months. The patient presented with three weeks of progressive dyspnea, fatigue and productive cough. Chest x-rays illustrated nodular and linear densities while chest CT showed bilateral infiltrates. Aspirate of a bronchial lymph tissue exposed granuloma and intercellular spherules

implicating coccidioidomycosis. The patient was in fact discharged prior to the commencement of antifungal treatment and soon returned several weeks later with fever and respiratory failure with a positive histoplasmosis diagnosis. The patient had to eventually be mechanically ventilated while started on amphotericin and itraconazole. Seven weeks later, he was released on itraconazole. Antifungal therapy should commence if a fungal infection is suspected especially in patients that have received a TNF-alpha antagonist even without positive cultures. Healthcare professionals should be cognizant of indicators signifying a fungal infection including fever, malaise, weight loss, sweats, cough, dyspnea, pulmonary infiltrates on x-ray, or serious systemic illness leading to shock. Prior to the initiation of TNF-alpha antagonist therapy, an initial chest x-ray should be obtained without regard to patient’s non-endemic residency.

Table 1. Disease States Requiring Treatment with TNF-alpha antagonists.

Indication	Adalimumab (Humira®)	Certolizumab Pegol Cimzia®	Etanercept (Enbrel®)	Infliximab (Remicade®)
Ankylosing Spondylitis	√		√	√
Crohn’s Disease	√	√		√
Juvenile Idiopathic	√		√	
Plaque Psoriasis	√		√	√
Psoriatic Arthritis	√		√	√
Rheumatoid Arthritis	√		√	√
Ulcerative Colitis				√

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