SOP Newsletter

Drug Information News From the School of Pharmacy Faculty Members

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In this edition:

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TOPIC IN THE NEWS

Fouad Sakr, PharmD.

U.S. HEALTH OFFICIALS SAY EBOLA TREATMENT TRIAL TO START SOON IN LIBERIA

U.S. health officials said that they are planning to conduct larger phase 2/3 clinical trials starting in the next two weeks in Liberia to determine if an Ebola treatment being developed by GlaxoSmithKline and another by Newlink Genetics with Merck & Co is safe and effective.

Earlier, the World Health Organization said the epidemic in West Africa appears to be ebbing.

There have been 21,724 cases of Ebola reported in nine countries in the past year since the epidemic began in Guinea, including 8,641 deaths, according to the latest WHO figures.

The officials, speaking on a conference call, also said that they expect to soon start phase 1 and phase 2 clinical trials of the ZMapp Ebola virus treatment that is being developed by privately held Mapp Biopharmaceutical Inc. They said they believe they have produced enough ZMapp to supply the trials.

Source: Reuters Health Information

INTERESTING NEWS

Nermine Chouman, PharmD.

IS THIS VIRUS MAKING YOU STUPID?

Key point: Chlorovirus Acanthocystis turfacea chlorella virus 1 (ATCV-1) – is a new large DNA virus known to infect certain eukaryotic green algae in freshwater lakes and has not been previously shown to affect humans. However, latest study revealed that ATCV-1 virus appears to decrease cognitive functions in humans and mice which can shorten attention span and reduce spatial awareness.

Finer points: In fact, researchers from Johns Hopkins University in Baltimore and the University of Nebraska unexpectedly found ATCV-1 traces in human DNA samples when they were originally working on an unrelated study. The team obtained oropharyngeal samples by throat swabs from 40 of 92 adults without a psychiatric disorder or serious physical illness. Those who were infected with the virus performed 10 percent slower on certain cognitive tests that measured speed and accuracy of visual processing. The study found no link between reduced brain function and factors such as variances in sex, income, education level, race and smoking cigarette. To support their findings, in a separate experiment, the researchers also injected the virus in the digestive tracts of 9 - 11week-old lab mice. This inoculation resulted in a subsequent decrease in performance in several cognitive domains, including ones involving recognition memory and sensory-motor gating.

Tests showed the virus had broken through the barrier between blood and tissue, altering the activity of genes in the brains of the mice. In other words, these genes comprised pathways related to brain function, learning, memory formation, and the immune response to viral exposure. The impact similarity of the virus in humans and mice determines that ATCV-1 virus impairs the brain function to a certain level and it is apparently quite common in humans. The researchers suggest that not only swimmers or people who have come in direct contact may have got infected; instead, many people may have been infected with the virus but are unaware, however at this stage it is unclear how the virus is transmitted to humans and if it is contagious.

"ATCV-1 virus impairs the brain function to a certain level and it is apparently quite common in humans."

What you need to know: The discovery of the "stupid" virus which no one have suspected before, turned to have a very important biological effects on humans that point us in a direction of looking to see if we can improve people's cognition and their behavior.

Sources: Yolken RH, et al. Chlorovirus ATCV-1 is part of the human oropharyngeal virome and is associated with changes in cognitive functions in humans and mice. PNAS 2014; 111 (45): 16106-16111.

NEW DRUG OF THE MONTH

Samar Younes, PharmD.

FDA GIVES THUMBS UP TO OVARIAN CANCER DRUG LYNPARZA (OLAPARIB)

Key point: Ovarian cancer is the fifth leading cause of cancer death among women in the United States, mainly because it is often diagnosed late and has an extremely poor prognosis. For the 61% of ovarian cancer patients whose cancer has metastasized by the time of diagnosis, the five-year survival rate is only 27%. Up to 15% of women with ovarian cancer have a BRCA mutation, which is the most common cause of homologous repair deficiency. In BRCA-mutated tumor cells, homologous recombination is defective and DNA double-strand break repair is forced to occur via error-prone pathways, which can lead to genomic instability and cell death. On December 19th, 2014, the U.S. Food and Drug Administration (FDA) granted accelerated approval to LYNPARZA™ (olaparib) capsules (400mg twice daily) as the first monotherapy for patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm) advanced ovarian cancer, who have been treated with three or more prior lines of chemotherapy. Olaparib has been approved under the FDA's Accelerated Approval program, based on existing objective response rate and duration of response data.

Finer points: Olaparib is a poly ADP-ribose polymerase (PARP) inhibitor that exploits tumor

"FDA approval of LYNPARZA™ is a significant milestone for ovarian cancer"

DNA repair pathway deficiencies to preferentially kill cancer cells. It is the first PARP inhibitor to be approved for patients with germline BRCA-mutated advanced ovarian cancer. The efficacy of olaparib is based on analysis of 137 patients with measurable, germline BRCA mutated advanced ovarian cancer treated with three or more prior lines of chemotherapy. The trial results demonstrated an overall response rate of 34% (95% Confidence Interval: 26%, 42%). The median response duration was 7.9 months (95% Confidence Interval: 5.6, 9.6 months). Common side effects of Lynparza include nausea and vomiting, fatigue, diarrhea, indigestion, headache, appetite problems, common cold-like symptoms, cough, rash, and pain in joints, muscles, bones, back, and abdomen. Serious side effects can include the development of a bone marrow disorder, acute myeloid leukemia, and lung inflammation.

A full review of data from either of two ongoing studies under the SOLO (Study of OLaparib in Ovarian cancer) Phase III clinical program will be required for the accelerated approval of olaparib in BRCA-mutated advanced ovarian cancer to be converted to a full approval: SOLO2 is evaluating olaparib compared to placebo as a maintenance therapy and SOLO3 is evaluating olaparib compared to standard chemotherapy for relapsed disease.

What you need to know: The FDA approval of LYNPARZA™ is a significant milestone for ovarian cancer patients as currently there are only limited treatment options available to women with ovarian cancer who carry the BRCA mutation.

Source: 1. Ledermann J et al. Olaparib maintenance therapy in patients with platinum-sensitive relapsed serous ovarian cancer: a preplanned retrospective analysis of outcomes by BRCA status in a randomised phase 2 trial. Lancet Oncology. 2014. http://dx.doi.org/10.1016/S1470-2045(14)70228-1. 2.Kaufman B, Shapira-Frommer R, Schmultzler RK et al. Olaparib Monotherapy in Patients With Advanced Cancer and a Germline BRCA1/2 Mutation. Journal of Clinical Oncology 2014. http://jco.ascopubs.org/content/early/2014/10/30/JCO.2014.56.2728

ENDOCRINOLOGIC DISORDERS

Etwal Bou Raad, PharmD.

ALBIGLUTIDE: A NEW GLP-1 RECEPTOR AGONIST FOR THE TREATMENT OF TYPE 2 DIABETES

Key point: The Food and Drug Administration (FDA) has approved albiglutide (Tanzeum, GlaxoSmithKline), a once-weekly injectable glucagonlike peptide 1 (GLP-1) receptor agonist to treat type 2 diabetes.

Finer points: Albiglutide lowers glycosylated hemoglobin (A1C) and reduces weight by stimulating glucose-dependent insulin secretion, suppressing glucagon secretion, delaying gastric emptying, and promoting satiety. Albiglutide has a long half-life as a result of resistance to degradation by dipeptidyl peptidase-4 and fusion to albumin, thus allowing once-weekly dosing. Albiglutide has been studied as monotherapy and add-on therapy to metformin, sulfonylureas, thiazolidinediones, insulin glargine, and varying combinations of these agents. Clinical studies have shown albiglutide to be superior to placebo, sitagliptin, and glimepiride and noninferior to insulin glargine and insulin lispro at reducing A1C in T2D patients, with A1C changes from baseline ranging from -0.55% to -0.9%. Non inferiority was not achieved when compared to liraglutide and pioglitazone. Weight changes ranged from +0.28 to -1.21 kg. The most common side effects are upper-respiratory-tract infections, diarrhea, nausea, and injection-site reactions. Albiglutide is the fourth GLP-1 RA approved in the United States. Advantages include once-weekly dosing and fewer gastrointestinal side effects compared with liraglutide, but it is less effective at reducing A1C and weight compared to liraglutide. It has not been compared head to head with other GLP-1 RAs.

"Albiglutide… a once-weekly injectable glucagonlike peptide 1 (GLP-1) receptor agonist"

What you need to know: Albiglutide is a new treatment option for the millions of people living with type 2 diabetes. It can be used alone or added to existing treatment regimens to control blood sugar levels in the overall management of diabetes.

Source: Ann Pharmacother. 2014 Nov;48(11):1494-501.

CARDIOVASCULAR DISEASES

Michelle Cherfan, PharmD.

GUIDELINES FOR THE PRIMARY PREVENTION OF STROKE

Key point: Over the years, there have been numerous advances in preventing stroke, including medications to control blood pressure and lipids, anticoagulants for at-risk patients with AF, revascularization, smoking cessation program, and changes in diet and physical activity level. In December, 2014 the American Heart Association (AHA) and American Stroke Association (ASA) have released updated guidelines on the primary prevention of stroke.

Finer points: The guidelines still considers the use of a risk assessment tool such as the AHA/ACC CV Risk Calculator (http://my.americanheart.org/cvriskcalculator) reasonable. It can help identify individuals who could benefit from therapeutic interventions.

What you need to know: Although liraglutide has received approval for the long-term treatment of obesity, the serious adverse events have required its monitoring through post-marketing trials, which will show if it will eventually remain in the market or be removed as other obesity treatments.

Source: 1.Tucker M. FDA Panel Endorses Liraglutide as Obesity Treatment September 12, 2014.(Available at: http://www.medscape.com/viewarticle/831609.) 2. Endocrinologic and Metabolic Drugs Advisory Committee Meeting Hyattsville, MD September 11,2014 (http://www.fda.gov/downloads/advisorycommittees/committeesmeetingmaterials/drugs/endocrinologicandmetabolicdrugsadvisorycommittee/ucm416154.pdf). 3. Colman E, Golden J, Roberts M. The FDA's assessment of two drugs for chronic weight management. N Engl J Med. 2012;367:1577-1579.

RECOMMENDATIONS FOR PRIMARY PREVENTION OF ISCHEMIC STROKE INCLUDE THE FOLLOWING:

Section	Recommendation
Diet	• Patients should follow the Mediterranean diet supplemented with nuts and reduce sodium intake.
Exercise	• Healthy adults should perform at least moderate- to vigorous-intensity aerobic physical activity at least 40 min a day 3 to 4 d/wk.
Hypertension	• Hypertensive patients should attempt to control their blood pressure (BP) through Self-measured BP monitoring. • There is no antihypertensive of choice. Treatment should be individualized on the basis of other patient characteristics and medication tolerance.
Dyslipidemia	• Therapeutic lifestyle changes and treatment with statin medication is recommended in patients estimated to have a high 10-y risk for cardiovascular (CV) events. • Treatment with nonstatin lipid-lowering therapies may be considered in patients who cannot tolerate statins, but their efficacy in preventing stroke is not established.
Diabetes	• Target BP for patients with type 1 and type 2 diabetes is <140/90mmHg. • The usefulness of aspirin for patients with low 10-y risk of CV disease is unclear.
Obesity	• Weight reduction is recommended for overweight and obese individuals.
Migraine	• Alternatives to oral contraceptives, especially those containing estrogen, might be considered in women with active migraine headaches with aura.
Atrial fibrillation	• For patients with valvular atrial fibrillation (AF) and CHA2 DS2 - VASc score of ≥2, warfarin is recommended at a target INR of 2.0 to 3.0. • For patients with nonvalvular AF and a CHA2 DS2 -VASc score of ≥2, oral anticoagulants including any of warfarin (INR, 2.0 to 3.0), dabigatran, apixaban, or rivaroxaban is recommended. • For patients with nonvalvular atrial fibrillation and CHA2 DS2 -VASc score of 0, it is reasonable to omit antithrombotic therapy. • For patients with nonvalvular atrial fibrillation, a CHA2 DS2 -VASc score of 1, no antithrombotic therapy, anticoagulant therapy, or aspirin therapy may be considered.
Antiplatelet agents and aspirin	• The use of aspirin for CV (including stroke) prophylaxis is reasonable for high 10-y risk people (>10%) for the benefits to outweigh the risks associated with treatment. • Aspirin might be considered in patients with chronic kidney disease (ie, estimated glomerular filtration rate >30ml/min). • Cilostazol may be reasonable in people with peripheral arterial disease. • Antiplatelet regimens other than aspirin and cilostazol are not recommended.

ONCOLOGIC DISEASES

Razan Mhanna, PharmD.

"FASTING" CHALLENGES IMMUNOSUPPRESSION CAUSED BY CHEMOTHERAPY

Key points: A new study conducted at the University of Southern California suggests that prolonged fasting not only helps prevent immune system damage, but also produces hematopoietic stem cells which generate blood cells in the immune system.

Finer Points: Traditional chemotherapy is toxic to both cancer and normal cells. One of its side effects is the suppression of the immune system by damaging adult stem cells, which impairs tissue repair and regeneration.

Fasting is the act of consciously depriving oneself of food and/or drink for 24 hours or more. Periods of 2-4 days at a time over a 6-month period was found to destroy aged and damaged cells. Interestingly, this principle can theoretically be applied to cancer patients undergoing chemotherapy.

The mechanism is that when you starve, the system tries to save energy, and one of the things it can do to save energy is to recycle a lot of the immune cells that are not needed or may be damaged. Scientists noticed that the white blood cell count goes down with prolonged fasting. To examine this mechanism, scientists used mice that were deficient in IGF-1 (Insulin-like growth factor) that controls cells multiplication. When these IGF-1 deficient mice were treated with cyclophosphamide, they showed similar results to the prolonged fasting mice: reduced activity of PKA (protein kinase A) that controls stem cell regeneration and reduced levels of hematopoietic stem cell damage.

What you need to know: Fasting reduces the number and size of cells and then re-feeding at 72 hours causes a rebound. That could be potentially useful because it is not a long time of food deprivation for a cancer patient. However, many researchers remain skeptical of the research.

Sources: 1. Cheng CW et al. Prolonged Fasting Reduces IGF-1/PKA to Promote Hematopoietic-Stem-Cell-Based Regeneration and Reverse Immunosuppression. Cell Stem Cell 2014; 14(6): 810-823. 2. Fasting Can Regenerate the Entire Immune System: Here's How. Retrievedfrom:http://themindunleashed.org/2015/01/fasting-can-regenerate-entire-immune-system-heres.html at January 17, 2015.

SMOKING CESSATION

Jihan Safwan, PharmD.

IS THERE REALLY A DRUG BETTER THAN NICOTINE FOR SMOKING CESSATION?

Key point: Clinicians are always looking for effective smoking cessation modalities to counter one of the most potent enemies to the health of humans.

Finer points: Nicotine replacement therapy, which can be undertaken in a variety of methods, is the most widely used method to date. However, short- and long-term smoking cessation is not very widely achieved through the use of nicotine itself.

An agonist of the nicotine acetylcholine receptor, such as varenicline, seems to be more effective than nicotine replacement therapy without unacceptably serious adverse events.

Cytisine (not to be confused with the nucleic acid base cytosine) is a plant alkaloid that is a partial agonist of the nicotinic receptor. It has been used mainly as a smoking cessation modality in Eastern Europe, from which a few clinical trials show efficacy in smoking cessation.

The present trial was conducted in New Zealand. Investigators recruited 1310 long-term smokers who were motivated to quit smoking. They were randomly assigned to receive oral cytisine for 25 days or nicotine replacement (via patches, gum, or lozenges) for 8 weeks. The trial design was "open-label" and "noninferiority." The primary outcome was continuous smoking abstinence at 1 month.

What you need to know: Cytisine was found to be superior to nicotine-replacement therapy in helping smokers quit smoking, but it was associated with a higher frequency of self-reported adverse events. Efficacy of cytisine has been demonstrated in this clinical smoking cessation trial; however it is not yet approved as a smoking cessation medication by regulatory authorities outside eastern and central Europe.

Source: N Engl J Med. 2014;371:2353-2362

ENDOCRINOLOGIC DISORDERS

Nisreen Mourad, PharmD.

DOES THE FUTURE HOLD PHOTOSWITCHABLE SULFONYLUREA?

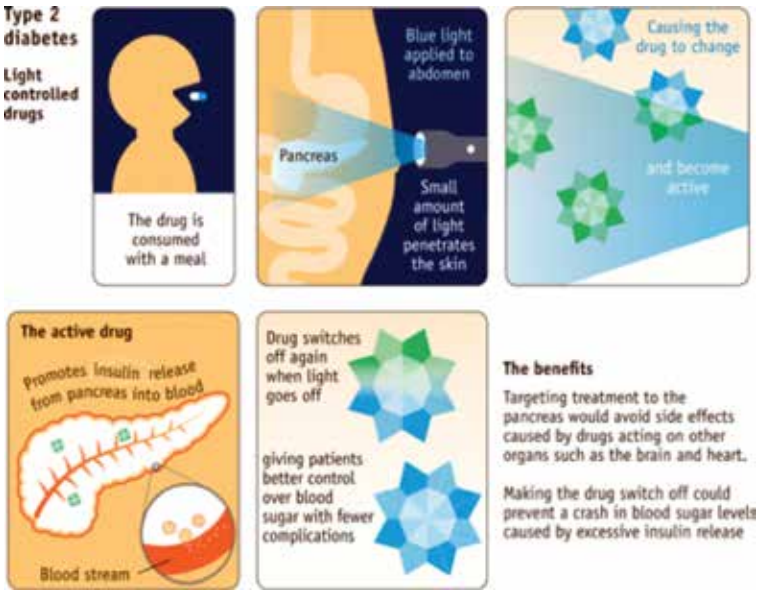
Key point: Type 2 diabetes mellitus (T2DM) is a global endocrine disorder that currently affects 1 in every 12 of the adult population which is around 350 million people worldwide. This disease is commonly associated with many complications, and the search for safer and more effective drugs is always a major goal in the medial field. A class of drugs called sulfonylureas are a mainstay of diabetes therapy, where they target the ATP-sensitive potassium (K+) (KATP) channels to promote secretion of insulin from the pancreatic beta cell mass to restore glucose homeostasis. Although they are very effective however they carry the risk to induce side effects such as hypoglycemia and cardiovascular disease, both potentially fatal complications. To help reduce these side effects, researchers at Imperial College London and Ludwig Maximilian University of Munich have developed a photoswitchable sulfonylurea.

Finer points: Their study "Optical control of insulin release using a photoswitchable sulfonylurea" was published in the journal Nature Communications. The researchers described their prototype drug "JB253", a light-sensitive fourth-generation sulfonylurea based on glimepiride that bears an azobenzene photoswitch.

They demonstrated that JB253 was capable of reversibly and repeatedly blocking KATP channel activity, and thus stimulating insulin release from pancreatic cells only when exposed to blue light in laboratory experiments. The concept is that the light-sensitive drug could be administered in the form of a pill where it would remain inactive under normal conditions, but a patient could in theory activate it when necessary after a meal using blue LEDs stuck to the skin. Only a small amount of light would be needed to penetrate the skin and change the drug's shape to turn it on. This change is reversible, thus once the light stimulation is turned off, the drug is switched off too by reverting to its inactive form.

What you need to know: Hopefully, this type of therapy will improve the treatment of T2DM, by allowing better control over blood sugar levels and reducing the incidence of side effects since light can be controlled to target the receptor of interest with very high specificity. Until it is approved, JB253, with its distinguishing properties will remain a valuable research tool that could induce a shift in the management of Type 2 diabetes mellitus patients.

Source: 1. Johannes Broichhagen et al. 'Optical control of insulin release using a photoswitchable sulfonylurea.' Nature Communications, 14 October 2014. DOI: 10.1038/ncomms6116. 2. http://diabetesnewsjournal.com/2014/10/15/light-activated-drug-could-reduce-type-2-diabetes-medication-side-effects/. 3. http://www3.imperial.ac.uk/newsandeventspggrp/imperialcollege/newssummary/news_13-10-2014-12-0-41



METABOLIC DISORDERS

Fouad Sakr, PharmD.

EVEN A LITTLE MORE DAILY ACTIVITY MAY REDUCE MORTALITY LEVELS

Key point: Encouraging sedentary adults to move just a little more everyday could produce more widespread population health benefits than urging everyone to meet the current guideline of 150 minutes or more of moderate activity each week, say the authors of two new analyses. Although the 150-minute goal is still ideal, it may be a barrier to the most sedentary and to some older people. In fact, it may take far less than 150 minutes to achieve a significant reduction in mortality risk in sedentary people.

Finer points: The sedentary population has been the least responsive to calls for increased physical activity during the last 2 decades. Across the US population, the percentage of people engaging in no physical activity has remained stable, at 25%, between 1996 and 2014. In contrast, people who were active became more active, with the number of people who participate in sufficient physical activity rising from 22% in 1996 to 51.6% in 2014.

A mounting body of research shows that too much sitting is associated with increased all-cause mortality, as well as higher mortality from cardiovascular disease and cancer. Sitting is also associated with a higher incidence of heart disease, cancer, and type 2 diabetes.

Data from 7000 adults, aged 20 to 79 years, in the US National Health and Nutrition Examination Survey were analyzed. Those data show low levels of moderate and vigorous physical activity in all age groups, with only the youngest adults, ages 20 to 29 years, reaching the recommended 30 minutes of exercise daily. At the same time, the study found that all adults sat longer than 7 hours a day, the amount identified in earlier research as being associated with increased mortality. The youngest people (aged 20 to 29 years) sat 7.7 hours daily, and the oldest group (70 to 79 years) sat 9.6 hours daily. A study in the United Kingdom found similar results.

Collectively, these findings from the US and UK indicate that, even when exercise intensity is adjusted for age related decline in physical capacity, only some 10-15% of free living, older adults are meeting the minimum standard for "sufficient activity" (>150 min/week of moderate intensity activity).

Several studies have shown the benefits of any increase in exercise, the authors of both analyses report. In seven large longitudinal, observational studies, researchers showed that the greatest differences in mortality risk were between the most sedentary and the slightly more active, suggesting that sedentary people can greatly reduce their risk of all cause mortality with relatively minor increments in physical activity. All but one of the seven studies showed that people judged "somewhat active" were at a lower mortality risk compared with inactive people, with risk reductions for the "somewhat active" group ranging from 14% to 37% across the studies.

In a study conducted in Norway among 56,072 people, those who engaged in a single weekly exercise session had lower cardiovascular mortality than inactive people, leading to a relative risk in men of 0.71 (95% confidence interval, 0.59 - 0.86) compared with inactive men. In women, the single session dropped the relative risk even more dramatically, to 0.56 (95% confidence interval, 0.44 - 0.71).

What you need to know: Small incremental increases in physical activity should be promoted in a slowly progressive manner to maximize health benefits and minimize potential adverse effects. It is advised that exercise recommendations focus on introducing light activity throughout the day, increasing light activities by 30 minutes daily, and reducing prolonged sitting by suggesting standing or strolling 1 or 2 minutes every hour. People could be advised to get up from their chair during commercials, pace during telephone conversations, and take 5-minute walks three times a day.

It is not proposed that the 150 minute a week standard be abandoned. Rather, the purpose is to remind colleagues that a broad perspective to counseling is already embedded in the guidelines and that a whole day approach for older sedentary patients may help them move towards the recommended activity levels.

Source: Barreto P. Global health agenda on non-communicable diseases: Has WHO set a smart goal for physical activity? BMJ 2015;350:h23

WOMEN'S HEALTH

Fouad Sakr, PharmD.

USE OF HORMONAL CONTRACEPTIVES LINKED TO BRAIN CANCER

Key point: An association between hormonal contraceptives and an increased risk for glioma in younger women has been found in a Danish nationwide case–control study. That risk increases with the duration of use according to a study published in the British Journal of Clinical Pharmacology. A nearly two-fold increased risk of glioma was observed among long-term users of hormonal contraceptives.

Finer points: However, it is important to keep this apparent increase in risk in context. While a statistically significant association between hormonal contraceptive use and glioma risk was found, a risk/benefit evaluation would still favor the use of hormonal contraceptives in eligible users. As well, although the findings of this study must be interpreted with care, it is an important contribution and it is hoped that the findings will spark further research on the relationship between female hormonal agents and glioma risk.

Search for Glioma in Health Registries

Oral contraceptives are known to influence the risk for certain cancers, but few studies have examined any link to central nervous system tumors. The researchers used Danish administrative and health registries to identify all women in Denmark 15 to 49 years of age with a first-time diagnosis of glioma from 2000 to 2009. The registries provided information on hormonal contraceptive prescriptions filled from 1995 to 2009.

The researchers defined "nonuse" as one or no hormonal contraceptive prescriptions, and "ever use" as at least two prescriptions. In the ever-use category, "current/recent use" was defined as at least one prescription in the 2 to 5 years before the initial diagnosis of glioma, and "past use" was defined as no recorded prescription in the 2 to 5 years before initial diagnosis.

The 317 patients in the case group and the 2126 in the control group were similar in age, parity, and years of schooling. Overall, 58.7% of case subjects and 50.1% of control subjects were ever users (P = .004). Among ever users, the odds ratio (OR) for glioma was 1.5 (95% confidence interval [CI], 1.2 - 2.0). The risk for glioma was higher for current/recent use (OR, 1.7; 95% CI, 1.3 - 2.4) than for past use (OR, 1.2; 95% CI, 0.8 - 2.0). The risk was elevated for oral contraceptives consisting of a combination of estrogen and progestogen (OR, 1.4; 95% CI, 1.0 - 1.8), but was highest for progestogen-only contraceptives (OR, 2.8; 95% CI, 1.6 - 5.1). The use of both types of contraceptives was also associated with increased risk (OR, 1.5; 95% CI, 0.8 - 3.0). The risk for glioma increased as the use of oral contraceptives of any type increased. With use for less than 1 year, the OR was 1.4 (95% CI, 0.8 - 2.3); for 5 years or more of use, the OR was 1.9 (95% CI, 1.2 - 2.9).

Progesterone Exposure Associated With Highest Risk

The researchers highlight the fact that progestogen exposure was associated with the highest increased risk for glioma in their study. Progesterone increases proliferation of high-grade astrocytoma cell lines, as well as growth factor levels, which is in line with increased progesterone receptor protein mRNA with glioma grade.

The study has limitations, they acknowledge. For one, the results could be biased if contraceptive users were more likely to undergo brain imaging because of socioeconomic factors. However, because the Danish National Health Service provides equal access to healthcare for all Danish citizens, socioeconomic status is not likely to be a factor. Another limiting factor is the lack of information on anthropometric measures, such as body mass index; some studies have found an association between obesity and glioma risk.

Research on Risks and Benefits a Challenge

For many years, numerous studies have weighed the various health risks and benefits of hormonal contraception, but questions remain. This area of research poses unique challenges that make these questions difficult to answer. For example, detailed data collection with lengthy follow-up is necessary because the hormonal contraceptives have changed over time. Doses of estrogen have changed, progestins have been added, patterns of use have changed with the elimination of placebo pills, and hormonal IUDs have been introduced.

Determining how to model hormonal contraceptive use is challenging. Ever use may be of the most interest, but age at first use, duration, and even time since last use are important factors.

What you need to know: The new findings provide evidence that hormonal contraception may increase the risk of glioma, that the risk increases with hormonal contraception duration, and is most elevated with progesterone-only methods and among younger women.

The findings are interesting for a number of reasons, but need to be replicated. Overall, there are countless benefits of hormonal contraception, but continued research on potential health risks, especially in light of these findings, is essential.

Source: 1. Andersen L, Friis S, Hallas J, Ravn P, Kristensen BW, Gaist D. Hormonal contraceptive use and risk of glioma among younger women a nationwide case-control study. Br J Clin Pharmacol. 2014. DOI: 10.1111/bcp.12535. 2. Brynhildsen J. Combined Hormonal Contraceptives: Prescribing Patterns, Compliance, and Benefits versus Risks. Ther Adv in Drug Safe. 2014;5(5):201-213

MEN & WOMEN's HEALTH **Bahia Chahine, PharmD.**

NEW PREGNANCY AND LACTATION LABELING: RETIREMENT OF RISK CATEGORIES

Key point: The FDA issued the final pregnancy and lactation labeling rule that will replace the current letter labeling categories—A, B, C, D, and X—on prescription drugs and biological products with three detailed subsections that describe risks within the real-world context of caring for pregnant women who may need medication.

Finer points: The rapid development and increased availability of novel pharmacologic therapies and pharmaceutical products has amplified the potential for drug exposure during pregnancy. Many drugs are beneficial for disease state management during pregnancy and provide significant fetal and maternal health benefits. However, insufficient safety data combined with the imprecision of the current risk category system renders risk versus benefit assessment difficult.

In response to decades of criticism, the FDA issued a new pregnancy and lactation labeling rule believing that a narrative structure rather than a category system is best able to capture and convey the potential risks of drug exposure based on animal or human data, or both.

Under this new rule, sponsors of drugs will now be required to label their products with three sections:

- Pregnancy
- Lactation
- Females and Males of Reproductive Potential

The new section—females and males of reproductive potential—will provide information "on pregnancy testing, contraception and infertility," FDA explained in its guidance. The inclusion of men in the pregnancy section follows FDA's realization that some drugs can cause fetal risk through men at the time of contraception, or might cause infertility.

Each subsection must include three main categories:

- **Risk summary:** It replaces the current pregnancy letter category. For drugs that are absorbed systemically, the "Risk Summary" must include statements based on the risk of adverse developmental outcomes such as structural abnormalities, embryo/fetal/infant mortality, functional impairments or growth problems potentially caused by a drug.
- **Clinical considerations:** It includes the relevant information that help health care providers make prescribing decisions and counsel women about the use of the drug during pregnancy such as dose adjustments during pregnancy and the postpartum period, maternal adverse reactions, and fetal/neonatal adverse reactions
- **Data:** The data supporting the risk summary are summarized under this heading.

What you need to know: The FDA will soon terminate the use of pregnancy letter categories. A new detailed pregnancy and lactation labeling has been released to facilitate prescribing decisions. FDA expects changes to labeling for existing drug products to take "several years" to complete. Companies will have between three and five years to finalize their labeling, according to the rule. New applications will need to conform to the rule as of 30 June 2015. Labeling for over-the-counter (OTC) medicines will not change.

Source: U.S. Food and Drug Administration. (2014, December 3). Pregnancy and Lactation Labeling Final Rule. http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/Labeling/ucm093307.htm

MEDICATION SAFETY

Mariam Dabbous, PharmD.

EMA SUSPENDS DOZENS OF DRUGS BASED ON FLAWED STUDIES

Key point: A committee of the European Medicines Agency (EMA) has recommended suspending the sale of roughly four dozen generics for conditions such as diabetes, depression, and hypertension because their approvals were based on flawed clinical studies conducted in India. The US Food and Drug Administration (FDA) has not yet taken action on the issue.

Familiar names on the list include candesartan, donepezil, escitalopram, esomeprazole, and metformin. The list extends more than 120 pages because the drugs are marketed individually in multiple European Union (EU) nations in various dosages, and therefore appear over and over. Abbott Laboratories, Actavis, Dr Reddy's Laboratories, Mylan Pharmaceuticals, Sandoz, and Takeda Pharmaceuticals are some of the many manufacturers involved.

The EMA recommendation to suspend the drugs would apply across the entire EU. Drug regulators in France, Germany, Belgium, and Luxembourg have already acted to stop the sales of 25 drugs.

Finer points: The clinical studies in question were conducted by GVK Biosciences, a contract research organization in Hyderabad, India. The recommendation of the EMA's Committee for Medicinal Products for Human Use to suspend the drugs was based on a French inspection of GVK Biosciences that revealed data manipulations of electrocardiograms during the conduct of some studies of generic medicines, apparently over the course of at least 5 years. The systematic and prolonged nature of these manipulations and the number of staff involved cast doubt on the integrity of the trial methodology and the reliability of the data generated, said the EMA.

However, there is no evidence of harm or lack of effectiveness linked to the conduct of studies by GVK Biosciences. In a statement posted on its website, GVK Biosciences called the EMA recommendation unprecedented and highly disproportional. It said that the EU agency had extrapolated findings about the suspect electrocardiograms in nine studies to all studies conducted at its Hyderabad facility. The company quoted French inspectors who said that the electrocardiograms are not essential given the demonstration of bioequivalence, and that their observations should not be extrapolated to the bioanalytic, pharmacokinetic, and statistical aspects of its research.

FDA Has Taken No Action After Its Own GVK Inspection

FDA said that some 40 drug applications received from 2007 to March 2012 contained GVK clinical data, and that some of these applications were approved. The FDA declined to identify the drugs in question or indicate those that had been approved.

According to the FDA statement, the agency inspected GVK Biosciences in September 2014 on the heels of the French inspection in May 2014 and failed to find any evidence that affects the safety or efficacy of drug products subject to pending applications or products approved in the US. The agency promised to take swift and appropriate action to protect consumers if it identifies issues concerning GVK Biosciences that relate to products approved by the FDA.

Exceptions Can Be Made

The EMA investigation of drugs studied at GVK Biosciences encompassed more than 1000 individual generics in various forms and strengths as individually approved in 29 EU nations. Of this group, 300 generics had enough supporting clinical data from other sources to warrant staying in the market, according to the EMA. That left roughly 700 generics that should be suspended, the EMA said. However, individual countries can make an exception for drugs that are critically important because there are no alternatives to meet patients' needs.

What you need to know: The EMA recommendation goes to the European Commission, the EU's executive agency, for a legally binding decision that will apply to all EU nations, including those that already have suspended the generics in question.

Source: European Medicines Agency Website. http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/referrals/GVK_Biosciences/human_referral_000382.jsp&mid=WC0b01ac05805c516f. Accessed January 26, 2015.

PUBLIC HEALTH

Dalal Hammoudi, PhD

USE OF MEDICATIONS AMONG HIGH SCHOOL ADOLESCENTS IN LEBANON: PREVALENCE, COMMON TRENDS AND ASSOCIATED RISK FACTORS

Key point: Medication use among adolescents has grown dramatically in both industrialized and developing countries. The indiscriminate use of medications by this population, especially without medical guidance, marks a status of transition to self-care, yet it poses serious effects and potential health risks. Many demographic, socioeconomic and cultural factors affect this practice; among these are gender, age, smoking, socioeconomic status, parents' education level, family influence, and access to medications.

Finer points: A cross-sectional study was conducted by Lebanese International University School of Pharmacy, Bekaa Campus, to assess self-medication among Lebanese high school students in 4 private schools in Bekaa Valley. An optional, self-administered questionnaire addressed medication use in the previous two months, and was filled by students in the presence of a pharmacist. Two hundreds and eighty-nine high school adolescents participated in the survey, with a mean age of 15.8 years; 79% of the participants used medication without physician referral. Parents constituted the primary source of information about drugs (63%), whereas pharmacists, other family members, friends and the internet, constituted less frequently referred sources. Medications used without physician supervision were pain killers (81%), cough and cold medications (24%), vitamins (16%), dermatological products (14%), antibiotics (10%), and others. The unavailability of hospitals was the only significant (p=0.016) factor associated with the use of medications without prescription. Gender, history of living abroad, parents' education and employment were non-significant factors. Fifty-two percent of the participants rated pharmacists as the most knowledgeable source regarding drugs; 56% were aware of the correct Lebanese law regarding dispensing of drugs, while 21% rated their personal information about drugs as good.

While this was the first study exploring medication use among high school adolescents in a rural area of Lebanon, two previous studies, published by researchers from the American University of Beirut, have addressed the non-medical use of prescription drugs among youth. In the first study, university students resorted to self-medication to treat pain, anxiety, and sleeping disorders, whereby parents and pharmacists were the first two sources of medications. In the second one, data indicated that students from private and public high schools in Beirut were also practicing self-medication with the same groups of drugs, in addition to stimulants and antidepressants, and water pipe smoking was a significant risk factor for this practice.

"The non-guided use of medications by adolescents enfolds unawareness of adverse effects"

What you need to know: Lebanon is a country with very limited restriction on drug use, and self-medication is prevalent due to poor regulation of drug dispensing and unchecked access to medications. The non-guided use of medications by adolescents enfolds unawareness of adverse effects and serious risks when combined together or with alcohol. Findings from the above studies warrant close monitoring of adolescent consumption of medications. Interventions to upsurge awareness should involve adolescents themselves, parents, physicians, pharmacists, government, and other stakeholders, in order to support positive medication use among youth.

Source: 1. Hammoudi D, Farah Z, and Rahal M. Use of Medications Among High School Adolescents in Lebanon: Prevalence, Common Trends and Associated Risk Factors. Oral communication at 17th conference of pharmacy schools in Arab World. Ain Shams University. Oct 16-17, 2014. Cairo, Eygpt. 2. Ghandour LA, El Sayed DS, Martins SS. Prevalence and patterns of commonly abused psychoactive prescription drugs in a sample of university students from Lebanon: an opportunity for cross-cultural comparisons. Drug Alcohol Depend. 2012 Feb 1;121(1-2):110–7. 3. Zahlan L, Ghandour L, Yassin N, Afifi R, Martins SS. Double trouble: Exploring the association between waterpipe tobacco smoking and the nonmedical use of psychoactive prescription drugs among adolescents. Drug Alcohol Depend. 2014 Dec 1;145:217–23.

ANNOUNCEMENTS

EVENTS

- The extracurricular activities committee organized the 9th annual pharmacy dinner for the pharmacy graduates. It took place at Le Commodore Hotel on October 31st, 2014.
- In its continuous pursuit to learn more and be always up to date, the School of Pharmacy at the Lebanese International University invited Dr. Rakan Naserddine, who is a medical doctor and an infectious diseases specialist, to deliver a presentation entitled: "Updates on Ebola Infection" on Wednesday, November 26th, 2014 at LIU Beirut campus.
- The Continuing Education Committee organized and attended a CE lecture as part of the Continuing Education Program (CEP) in collaboration with the Lebanese Order of Pharmacists. The lecture was attended by many pharmacists from all over Lebanon and 2 CE credits were granted to the attendees.
  - ◊ "Diabetes: Review and Treatment Updates", presented by Dr. Fadi Hdaib
    - * Date: December 9th, 2014
    - * Place: Movenpick Hotel, in cooperation with Pfizer
- Faculty members at the School of Pharmacy of the Lebanese International University attended the 2014 ASHP Midyear Meeting and Exhibition in Anaheim, California during the month of December 2014 from the 7th till the 11th in Anaheim Convention Center. The faculty members who attended the conference included doctors Michelle Cherfan, Faraj Saade, Marwan Akel, and Jihan Safwan.
- During the festive season of Christmas and New Year holidays, the extracurricular activities committee distributed chocolate boxes to the medical directors and hospital pharmacists as a token of gratitude for their continuous support.

Useful Links

Pharmacy-related
- LIU e-library: www.liu-elibrary.com
- Order of Pharmacists of Lebanon: www.opl.org.lb
- Ministry of Health: www.moph.gov.lb
- Scientific Association of Colleges of Pharmacy in the Arab World: www.asscph-aw.net
- U.S Food and Drug Administration: www.fda.gov
- Center for Disease Control and Prevention: www.cdc.gov

LIU Social Media
- Facebook: www.facebook.com/liu.edu.lb
- Youtube: www.youtube.com/lebintuni
- Twitter: @lebintuni
- Instagram: @lebintuni
- BBM: 25b43b71

The Scope
- Facebook: www.facebook.com/thescopeliu
- Youtube: www.youtube.com/thescopeliu
- Twitter: @thescopeliu