Misr International University
جامعة مصر الدولية

Drug Information Newsletter

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Champix® Black Box Warning Officially Removed

By: Sherif Tahoon

As a result of a large clinical trial review, The US Food and Drug Administration (FDA) is removing the Boxed Warning for serious mental health side effects from the Champix® drug label. (1)

FDA determined the risk of serious side effects on mood, behavior, or thinking with Champix® (varenicline) – a drug used in smoking cessation- is lower than previously suspected. The risk of these mental health side effects is still present, especially in those currently being treated for mental illnesses such as depression, or schizophrenia, or who have been previously treated for mental illnesses. Yet, most people who had these side effects did not have serious consequences such as hospitalization. The results of the trial conducted confirm that benefits of smoking cessation outweigh the risks. (1)

In fact, health care providers should counsel patients about the benefits of smoking cessation and how they can get help to quit, and discuss the benefits and risks of using medicines to help them quit smoking. Patients should stop taking Champix® and call their health care provider immediately if they notice any adverse reactions on mood, behavior, or thinking. (2)

This safety review was published by the FDA in December 2016.

References:
1. *"Chantix (varenicline) and Zyban (bupropion): Drug Safety Communication - Mental Health Side Effects Revised." FDA.GOV. 16 Dec. 2016. Web. 8 Jan.2017.*
2. *"Varenicline (Lexi-Drugs Multinational)." Lexicomp Online. Dec. 2016. Web. 8 Jan. 2017.*

Anesthesiologists Reveals New Facts About General Anesthesia while on ACE-Is or ARBs

By: Omar Hegab

The American Society of Anesthesiologists revealed that induction of general anesthesia with Angiotensin-converting Enzyme Inhibitors (ACE-Is) or Angiotensin II Receptor Blockers (ARBs) can cause hypotension and worsen outcome.(1)

The results from VISION — the Vascular Events in Non-cardiac Surgery Patients Cohort Evaluation — were discussed at Anesthesiology 2016.(1) The studies showed that, the induction of general anesthesia while using these drugs was significantly correlated with reduction in Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and Mean Arterial Pressure (MAP).(2) Rates of death, stroke and myocardial injury in patients undergoing non-cardiac surgery were alleviated when ACE-I or ARB were discontinued 24 hours before surgery.(1)

It is also reported that, there is a relation between ACE-I and increased need for volume replacement.(2) Interventions may be needed to sustain MAP >60 and SBP>85, as using IV Fluids, IV lactated ringer solution, or ephedrine.(2)

As the continuation of ACE-Is or ARBs has an undesirable hypotension after general anesthesia induction, it is recommended to hold these drugs 24 hours before surgery, so

"Stop ACE-I or ARB 24 Hours before Induction of Anesthesia in Non-Cardiac Surgery"

intra-operative hemodynamics can be safely managed.[1,2] The Canadian Cardiovascular Society now suggests withholding ACE-Is and ARBs in the Perioperative Management Guidelines.[1]

References:
1. *Stop ACE Inhibitors, ARBs before Noncardiac Surgery. Medscape. Nov 04, 2016.*
2. *Rajgopal, Rajesh, Sunil Rajan, Kavitha Sapru, and Jerry Paul. "Effect of Preoperative Discontinuation of Angiotensin-converting Enzyme Inhibitors or Angiotensin II Receptor Antagonists on Intra-operative Arterial Pressures after Induction of General Anesthesia." Anesthesia, Essays and Researches. Medknow Publications & Media Pvt Ltd, 1 Apr. 2014. Web. 13 Dec. 2016.*

FDA Adds a New Warning to Hepatitis C Drugs

By: Mahytab Abdel Aal

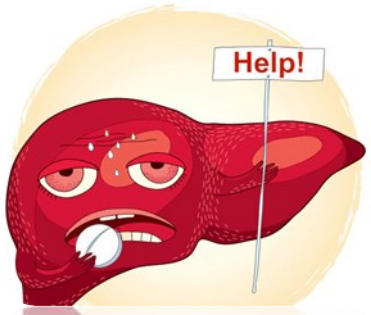
On October 2016, the US Food and Drug Administration (FDA) issued a black box warning of serious risks for patients who have current or previous infection with Hepatitis B virus (HBV) and treated with direct acting antiviral drugs for their hepatitis C virus (HCV). [1]

A recent Health Canada safety review found that patients infected with HBV and being treated for HCV with direct-acting antivirals (DAA) may experience a reactivation of their hepatitis B.[2] Also, the European Medicines Agency (EMA) began a similar investigation in March, while Japan's Pharmaceuticals and Medical Devices Agency (PMDA) said it is also reviewing such drugs for links to a possible HBV reactivation.[1]

24 cases of HBV reactivation were reported to FDA and from the published literature in HCV/HBV co-infected patients treated with DAAs between 22 November 2013 and 18 July 2016.[1]

It was also reported that two patients died and one needed liver transplant. The agency mentioned that there are additional similar unreported cases.[1]

"Worries About Hepatitis B Reactivation, While on Hepatitis C Treatment "

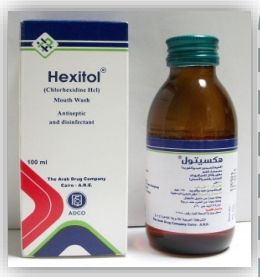


FDA Drug Safety Communication declared that HBV reactivation was not reported as an adverse event in the clinical trials submitted for the DAA approvals because patients with HBV co-infection were excluded from the trials.[3]

As a result, FDA required a Boxed Warning about the risk of HBV reactivation to be added to the labels of these DAA drugs directing health care professionals to do essential screening and monitoring for HBV in all patients receiving DAA treatment.[3] This warning is also to be added to the patient information leaflet or Medication Guides.[3]

FDA advises patients who receive DAA drugs to contact their health care providers immediately if they experience any side effect. Yet, patients should not stop their medication on their own to avoid another risk of drug resistance.[3]

References:
1. *Zachary Brennan. "FDA Adds Boxed Warning to Hepatitis C Drugs, Warns of Hepatitis B Reactivation Risk | RAPS." FDA Adds Boxed Warning to Hepatitis C Drugs, Warns of Hepatitis B Reactivation Risk | RAPS. N.p., n.d*
2. *" Canada: Direct-acting Antivirals, Used for Hepatitis C, May Reactivate Hepatitis B" The Government of Hong Kong. Drug Office, n.d. Web*
3. *FDA Drug Safety Communication: FDA Warns about the Risk of Hepatitis B Reactivating in Some Patients Treated with Direct-acting Antivirals for Hepatitis C." FDA Drug Safety Communication: FDA Warns about the Risk of Hepatitis B. N.p., n.d.*



Chlorhexidine: Threat of Colistin-Resistant Strains

By: Sherif Tahoon

A group of researchers at Public Health England's laboratories at Porton Down released a disturbing study linking the exposure of Klebsiella pneumonia to chlorhexidine , to an increased resistance to colistin.(1)

The scientists tested the ability of K. pneumoniae to survive exposure to increased concentrations of chlorhexidine. They found that some strains died on exposure to chlorhexidine, while others gained ability to survive much higher concentrations of the antiseptic.(2) The surviving isolates first adapted to chlorhexidine and then developed cross-resistance to colistin.(2)

When the investigators tried to discover the mechanism behind the resistance, they found that the critical role was played by an efflux pump (smvA/R). They also noted that this same efflux pump is found in a number of different species.(2)

Infection control is a vital part of maintaining a safe healthcare facility.(3) Chlorhexidine is a common disinfectant used in hospitals and home settings. It is also used to clean injuries, used as a mouth gargle and also used in surgery preparations.(2, 3) Also, Colistin is considered a last resort antibiotic for multidrug-resistant infections.(2)

This discovery has clinical implications for both infection prevention procedures and treatment of multidrug resistance. The new discovery raises concern that disinfectant use correspond to a novel path for bacteria to develop resistance.(2)

References:
1. *Bioquell UK Ltd. "Chlorhexidine driven Colistin Resistance." Bioquell. 2016. Web. 29 Dec. 2016.*
2. *Pullen, Lara C. "Chlorhexidine Linked to Colistin Resistance." Medscape. 2 Nov. 2016. Web. 29 Dec. 2016.*
3. *Wolf, Julie. "Chlorhexidine Use May Select for Colistin Resistance." American Society for Microbiology. 1 Nov. 2016. Web. 29 Dec. 2016.*

FDA Clears New Drug for Pregnancy Related Nausea and Vomiting

By: Mariam Yasser

On November 2016, the Food and Drug Administration (FDA) approved Bonjesta® for the management of nausea and vomiting during pregnancy when the use of the traditional management such as lifestyle and dietary modifications are not enough.(1)

Bonjesta® is available as extended release tablet that consists of both enteric coated core and an intermediate release coating; each contains 10 mg of Doxylamine Succinate which is an antihistamine and 10 mg pyridoxine which is a vitamin B6 analogue.(2)

The recommended dose is one tablet at the bedtime on empty stomach with a glass of water. If symptoms are not adequately controlled, the patient may start taking 2 tablets daily, one tablet is taken in the morning and the other one is taken at bedtime.(2)

Bonjesta® may cause somnolence and drowsiness. Activities that require mental alertness should be temporarily stopped.(3)

Well controlled studies have shown no risk of fetus malformation during the first trimester and there is no proof of increased risk in late trimesters. (1) Therefore, Bonjesta® is holding a FDA pregnancy category A. (2)

References:
1. *"FDA Approves Bonjesta for Pregnancy-Related Nausea and Vomiting." MPR. N.p., 11 Nov. 2016. Web. 16 Dec. 2016. <http://www.empr.com/news/fda-approves-bonjesta-for-pregnancy-related-nausea-and-vomiting/article/572369/>.*
2. *Doxylamine/pyridoxine (Rx)." Medscape. N.p., Nov. 2016. Web. 16 Dec. 2016. <http://reference.medscape.com/drug/diclegis-bonjesta-doxylamine-pyridoxine-999838>.*
3. *Bonjesta Extended-Release Tablets (Doxylamine Succinate and Pyridoxine Hydrochloride): Side Effects, Interactions, Warning, Dosage & Uses." RxList. N.p., Nov. 2016. Web. 16 Dec. 2016. <http://www.rxlist.com/bonjesta-drug.htm>.*

USPSTF Finalizes Statin Recommendations for CVD Prevention

By: Fatma Abdel Gaffar

"Most Expressed Disagreements with Many of Its Key Details while Others Expressed Their Strong Support."

The US Preventive Services Task Force (USPSTF) released on November 13, 2016 the final statin recommendation for primary prevention of cardiovascular disease (CVD) in adults, published by the Journal of the American Medical Association (JAMA).[1]

Yet, these final recommendations were subjected to a debate where most expressed disagreements with many of its key details and others expressed strong support for the concept of primary prevention with statins; but with different underlying philosophies about how to be implemented.[2]

The main published recommendations are:[1]

- "Low- to moderate-dose statins in adults aged 40 to 75 years who do not have a history of CVD but who do have one or more CVD risk factors (dyslipidemia, diabetes, hypertension, or smoking) and who have a 10% or greater risk of having a CVD event (myocardial infarction or stroke) over the next 10 years (B recommendation)."
- "On the basis of a discussion with patients, clinicians should selectively offer low- to moderate-dose statins to adults aged 40 to 75 years who do not have a history of CVD but who have one or more CVD risk factors and a 7.5% to 10% risk for a CVD event in the next 10 years (C recommendation)."

- "Evidence is insufficient for the benefits and harms of starting statins in adults aged 76 years and older (I statement)."

Some experts see that USPSTF was not aggressive enough regarding primary prevention as it is focusing on the CVD risk factors and not on the cholesterol level. While other experts see that USPSTF did not mention statins harmful side effect especially on muscles.[2]

On the other hand, supporters see that focusing on CVD event and excluding high LDL level or hypercholesterolemia is because they are not actually involved in primary prevention.[2]

References:

1. *Hackethal V. Medscape log in. medscape. http://www.medscape.com/viewarticle/871837. Accessed December 15, 2016.*
2. *Husten L. Debate ensues as USPSTF Finalizes Statin primary prevention guideline. cardiobrief. http://cardiobrief.org/2016/11/13/debate-ensures-as-uspstf-finalizes-statin-primary-prevention-guideline/. Accessed December 15, 2016.*

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