DRUG DIALOGUES – Medication news and new medications

Risk of intracranial bleeding with antidepressants and NSAIDs

Concomitant use of antidepressants and nonsteroidal anti-inflammatory drugs (NSAIDs) is associated with a significantly increased risk of intracranial haemorrhage (ICH) in the first 30 days after the drugs are taken together, a large cohort study published in The BMJ (2015;351:h3517) has found. Using a national Korean health insurance database to create a propensity score matched cohort, the researchers calculated a hazard ratio (HR) for ICH of 1.6 (95% confidence interval [CI] 1.32—1.85) for combined use of antidepressants and NSAIDs versus use of antidepressants alone. Subgroup analysis indicated that the risk was higher in men than in women, with HRs of 2 (95% CI 1.93—3.42) and 1.2 (95% CI 0.89—1.57), respectively, but did not vary depending on the other characteristics examined, which included age, ICH subtype, comorbidity and other medication. Also, the risk of ICH did not differ among different classes of antidepressants, namely, tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRIs) and serotoninnor-epinephrine reuptake inhibitors.

The researchers say they undertook their study because, while antidepressants and NSAIDs are each known to increase the risk of gastrointestinal bleeding, little was known about the combined effect of these drugs on the risk of ICH. The addition of NSAIDs to antidepressant treatment increased the risk of intracranial haemorrhage within 30 days of starting the combination especially in men. Both antidepressants and NSAIDs are widely prescribed; furthermore, NSAIDs are often used without prescription. Although NSAIDs bought over the counter are often taken for a short period only, the study reported elevated bleeding risk within 30 days of a new prescription. Patients with risk factors for increased bleeding tendency who are taking an antidepressant should use a NSAID with caution.

New treatment for chronic hepatitis C

The US Food and Drug Administration has approved daclatasvir for use with sofosbuvir to treat hepatitis C virus (HCV) genotype 3 infections. Daclatasvir is the first drug that has demonstrated safety and efficacy to treat genotype 3 HCV infections without the need for co-administration of interferon or ribavirin. The safety and efficacy of daclatasvir in combination with sofosbuvir were evaluated in a clinical trial of 152 treatment-naïve and treatment experienced participants with chronic HCV genotype 3 infection. Participants received daclatasvir 60 mg with sofosbuvir 400 mg once daily for 12 weeks and were monitored for 24 weeks post treatment. The studies were designed to measure whether a participants hepatitis C virus was no longer detected in the blood 12 weeks after finishing treatment (sustained virologic response), suggesting a participant’s infection had been cured. Results showed that 98% of the treatment-naive participants with no cirrhosis of the liver and 69% with cirrhosis achieved sustained virologic response. The most common side-effects of daclatasvir with sofosbuvir were fatigue and headache. Serious symptomatic bradycardia and cases requiring pacemaker intervention have been reported when amiodarone is co-administered with sofosbuvir in combination with another HCV directacting antiviral.

PCSK9 inhibitors for hypercholesterolaemia

Evolocumab, the first biologic drug for the treatment of hypercholesterolaemia, is set to launch in Europe following a positive opinion from the European Medicines Agency (EMA). It is the first monoclonal antibody for treating high cholesterol and the first inhibitor of proprotein convertase subtilisin/kexin type 9 (PCSK9) to be recommended for approval. Evolucumab provides a new option for people who are unable to control their cholesterol levels with current treatments such as statins and other lipid-lowering drugs. It is also an alternative therapy for people who are statin-intolerant. Late last month, the US FDA approved another PCSK9 inhibitor, alirocumab injection for the same indication as evolocumab. Alirocumab is approved for use in addition to diet and maximally tolerated statin therapy and still require additional lowering of LDL cholesterol. Alirocumab is marketed as Parulent® by Sanofi.

Source: CMC Pharmacy Bulletin, a publication of the Pharmacy Service (DISH), CMC, Vellore
Newer contraceptive pills associated with higher risk of clots

Combined contraceptive pills containing one of the newer progestogens are associated with a higher risk of venous thromboembolism (VTE) than pills containing older progestogens, a study published in the BMJ on 26 May 2015 has found. The increased risk associated with combined oral contraceptives is well known, but previous studies have used different methods to examine this link, meaning the relative risks associated with different hormone combinations have been unclear. To address this, researchers from the University of Nottingham used prescription data from two large UK general practice databases to measure the associations between use of the different types of combined oral contraceptives and risk of VTE in women aged 15—49 years, adjusting for other known risk factors. A total of 1,340 practices were covered by the two databases from which 10,562 eligible VTE cases were identified and matched with 42,034 controls. The results showed that current users of any combined oral contraceptive had a threefold increased risk of VTE compared with non-users of similar age and health status (adjusted odds ratio 2.97, 95% CI 2.78—3.17). When different pill combinations were looked at, women using combined pills containing older progestogens (Levonorgestrel, norethisterone and norgestimate) had around a four times increased risk of VTE compared with women not using any form of pill, while women using pills containing newer progestogens (drosperenone, desogestrel, gestodene and cyproterone) had around a four times increased risk of VTE. In absolute terms, the number of extra VTE cases per year per 10,000 women was lowest for Levonorgestrel and norgestimate (6 extra cases), and highest for desogestrel and cyproterone (14 extra cases).

New treatment for schizophrenia and depression

Brexpiprazole tablets have been approved by the US FDA last month to treat adults with schizophrenia and as an add-on treatment to an anti-depressant medication to treat adults with major depressive disorder (MDD). The effectiveness of brexpiprazole in treating schizophrenia was evaluated in 1310 participants in two 6week clinical trials. Brexpiprazole was shown to reduce the occurrence of symptoms of schizophrenia compared to placebo. Its effectiveness as an add-on treatment for MDD was evaluated in two 6week trials that compared brexpiprazole plus an anti-depressant to placebo plus an anti-depressant in 1046 participants for whom anti-depressant alone did not adequately treat their symptoms. The participants taking brexpiprazole reported fewer symptoms of depression than those taking the placebo. Brexpiprazole and other drugs used to treat schizophrenia have a warning alerting health care professionals about an increased risk of death associated with the off-label use of these drugs to treat behavioral problems in older people with dementia related psychosis. No drug in this class is approved to treat patients with dementia related psychosis. The most common side effects reported by participants taking brexpiprazole in clinical trials included weight gain and inner sense of restlessness, such as feeling the need to move. Brexpiprazole is manufactured by Tokyo-based Otsuka Pharmaceutical Company Ltd. and is marketed as Rexulti®.

Sacubitril/valsartan combo for heart failure treatment

Early last month the US FDA approved sacubitril and valsartan combination tablets for the treatment of heart failure. Sacubitril acts by inhibiting the enzyme neprylsin. The combo was studied in a clinical trial of more than 8000 adults and was shown to reduce the rate of cardiovascular death and hospitalizations related to heart failure compared to enalapril. Most patients were also receiving currently approved heart failure treatments including beta-blockers, diuretics, and mineralocorticoid antagonists. The combo was reviewed under the FDA’s priority review program, which provides for expedited review of drugs that are intended to treat a serious disease or condition and may provide a significant improvement over available therapy. The most side effects in clinical trial participants treated with this combo were hypotension, hyperkalaemia and renal impairment. Sacubitril/valsartan combo is contra-indicated in pregnancy. If pregnancy is detected while on treatment, the drug should be discontinued as soon as possible. The drug is manufactured by Novartis, New Jersey and is marketed as as Entresto®.

Source: CMC Pharmacy Bulletin, a publication of the Pharmacy Service (DISH), CMC, Vellore