Clinical Briefs in Primary Care

By Louis Kuritzky, MD

Evidence-based updates in primary care medicine

Online Supplement to *Clinical Cardiology Alert, Critical Care Alert, Infectious Disease Alert, Integrative Medicine Alert, Neurology Alert, OB/GYN Clinical Alert, Primary Care Reports*

Volume 23, Number 4 April 2018

Comparing GLP-1 Agonists

SOURCE: Ahmann AJ, et al. *Diabetes Care* 2018;41:258-266.

There are more similarities than differences among the seven currently available glucagon-like peptide-1 (GLP-1) receptor agonists. The most recently FDA-approved GLP-1 receptor agonist, once-weekly semaglutide (Ozempic), was compared in a head-to-head trial to once-weekly exenatide-ER (Bydureon).

In this open-label trial, adult subjects with type 2 diabetes (n = 813) taking one or more oral agents were randomized to receive either 1 mg/week of semaglutide or 2 mg/week of exenatide-ER. Subjects taking semaglutide underwent a titration from 0.25 mg/week for four weeks, then 0.5 mg/week for four weeks, and then 1.0 mg/week for the remainder of the trial; exenatide-ER subjects were started on 2.0 mg/week and maintained that dose throughout the trial. Baseline A1c was 8.3% in the exenatide group and 8.4% in the semaglutide group.

At the conclusion of the trial (56 weeks), the clinically meaningful differences in outcomes were the following: A1c was reduced by 1.5% with semaglutide vs. 0.9% with exenatide; weight declined 5.6 kg with semaglutide vs. 1.9 kg with exenatide; the fraction of subjects attaining an A1c < 7.0% was significantly greater with semaglutide (67% vs. 40%). While gastrointestinal adverse events were more common in the semaglutide treatment arm, injection site reactions were more frequent with exenatide. The efficacy advantages of semaglutide over exenatide-ER were both clinically meaningful and statistically significant. Generally, liraglutide has been regarded as the most potent GLP-1 receptor agonist. It will be interesting to see if semaglutide ultimately bests liraglutide, since both agents have demonstrated favorable cardiovascular outcomes in cardiovascular safety trials. ■

Rivaroxaban vs. Aspirin for Prevention of VTE

SOURCE: Anderson DR, et al. *N Engl J Med* 2018;378:699-707.

The combined benefits of improved efficacy and convenience of direct oral anticoagulants (i.e., apixaban, dabigatran, edoxaban, rivaroxaban) in the setting of atrial fibrillation makes them a preferred choice. For chronic anticoagulation subsequent to recurrent deep vein thrombosis or pulmonary embolism, direct oral anticoagulants are similarly attractive when compared to warfarin. Might direct oral coagulants offer some advantage for extended venous thromboembolism (VTE) thromboprophylaxis in patients undergoing knee or hip arthroplasty who are known to suffer an increased risk of VTE in the immediate postoperative period?

Anderson et al performed a double-blind, randomized, controlled trial of knee and hip arthroplasty patients. After a run-in period of rivaroxaban 10 mg daily through postoperative day five, subjects were randomized to either continue rivaroxaban or switch from rivaroxaban to aspirin (81 mg/d). This additional VTE thromboprophylaxis continued for nine days post-knee arthroplasty (hence, 14 days total thromboprophylaxis) and 30 days post-hip arthroplasty (hence, 35 days total thromboprophylaxis).

VTE events were rare in both groups (< 1%), and there was no statistically significant difference in VTE events between aspirin and rivaroxaban, nor was there any significant difference in rates of bleeding. For now, aspirin should remain the postoperative choice for extended prophylaxis after knee and hip arthroplasty. ■

Inhaled Corticosteroids and Fracture Risk

SOURCE: Gonzalez AV, et al. *Chest* 2018;153:321-328.

Clinicians have long been reassured by reports about the safety of inhaled corticosteroids (ICS) in asthma, which assert no long-term increased fracture risk, albeit a measurable decrement in bone mineral density (BMD) may be seen. On the other hand, most of the asthmatic population is comprised of younger patients who are not near the peak age of fracture risk. The potential consequences of ICS might be better demonstrated in persons with COPD, who are typically older than the asthma population. In addition, COPD itself is a risk factor for osteoporosis, as is cigarette smoking.

Using the large database of the Quebec healthcare system, fracture rates were assessed in a cohort of 240,110 subjects. Over a five-year follow-up period, more than 19,000 fractures occurred. The mean age of patients with a fracture and the comparison control group was 75 years.

Use of ICS for more than four years at a dose of ≥ 1,000 fluticasone equivalents/day was associated with a small but statistically significant 10% increase in relative risk (RR) for hip or upper extremity fracture (RR, 1.10; 95% confidence interval, 1.02-1.19). There did not appear to be any differential risk between men and women. Clinicians should strive to use the minimum ICS necessary to achieve symptomatic improvements in COPD patients. ■

Obstructive Sleep Apnea: Oral Appliances

SOURCE: Hamoda MM, et al. *Chest* 2018;153:544-553.

Continuous positive airway pressure (CPAP) has been the traditional recommended intervention for obstructive sleep apnea for more than three decades. Unfortunately, limitations on the ultimate application of CPAP to treat obstructive sleep apnea include expense and (for many) poor tolerability. Among the alternative interventions are oral appliances, typically divided into two categories: tools that stabilize the tongue in a forward position, and tools that stabilize the mandible in a forward position. The recently FDA-approved device that employs an electrical curren to activate oropharyngeal musculature with improved tongue muscular tone is not included in this review.

Using technical metrics for success, such as degree of improvement of the apnea-hypopnea index, CPAP has been shown to outperform oral appliances. On the other hand, patient-centered outcomes (sleepiness, quality of life, and driving performance) have been found to be equally well-improved by oral appliances as CPAP. Perhaps the most important bottom line is that many patients find compliance with CPAP difficult, and the limited data on oral devices suggest significantly greater compliance with them than with CPAP.

Aside from efficacy and tolerability, cost may be the ultimate deal maker (or breaker). Mandibular advancement devices that may be created at home by the patient cost as little as $30. While dental experts may offer more complex, sophisticated oral appliances, success attained with simple do-it-yourself home kits is quite appealing for many. Fortunately, the diversity of treatment options currently available should stimulate optimism that the consequences of obstructive sleep apnea can be improved successfully in most patients. ■

Influenza Increases Rate of Myocardial Infarction

SOURCE: Kwong JC, et al. *N Engl J Med* 2018;378:345-353.

It is obvious that influenza is an important cause of morbidity and mortality. Exploration of the causes of death related to influenza is a bit more complicated. Reporting on influenza epidemics usually includes the single broad category "influenza and pneumonia," since that category tracks directly with incident cases of influenza each year.

But even with that clarification, the proportion of patients who succumb to influenza pneumonia vs. those who incur bacterial pneumonia (typically Staph) subsequent to pneumonia vs. all other incident pneumonias that occur concomitantly with flu season is not readily discernible. The association between cardiovascular event rates and influenza has been recognized since the 1930s, but few direct studies of rates of myocardial infarction in patients with acute influenza have been performed. To that end, Kwong et al reported that in a study of subjects with laboratory-confirmed influenza (n = 19,045), myocardial infarction rates were six-fold higher in the "risk interval" (i.e., seven days after influenza identification) than in the "control interval" (i.e., one year immediately before and after the risk interval). Although other viral infections, such as respiratory syncytial virus, also were associated with increased risk for myocardial infarction, of the viruses studied, influenza incurred the greatest relative risk increase. ■

Promising News About Zika Vaccine

SOURCE: Modjarrad K, et al. *Lancet* 2018;391:563-571.

Zika virus infection during pregnancy can cause microcephaly and other serious neurologic defects. Protection from infection with Zika virus has been demonstrated in animal studies using a formalin-inactivated Zika virus vaccine derived from a 2015 Puerto Rican virus strain, similar to the 2015 Brazilian Zika virus strain. In preclinical trials in mice and nonhuman primates, two doses of vaccine (day 1 and day 29) produced high antibody levels within two weeks after the second dose.

Modjarrad et al reported on the first study in humans, using an aluminum hydroxide adjuvant Zika virus vaccine. Zika seronegative adults (n = 67) were randomized to Zika vaccine or placebo. Intramuscular vaccine was administered on day 1 and day 29. Efficacy was determined by the percent seroconversion (i.e., attainment of a microneutralization titre of ≥ 1:10).

By day 57, seroconversion had occurred in 92% of vaccine recipients. Tolerability of the vaccine was good, with only mild-moderate adverse events reported. These results compare well with trials of Japanese encephalitis virus and yellow fever virus that have used the same seroconversion status as a surrogate for protection from infection. Clinicians look forward to confirmation of vaccine efficacy in a large population. ■

Editor's Note: Clinical Briefs in Primary Care is being discontinued. This is the final issue.

CLINICAL BRIEFS IN PRIMARY CARE™
is published monthly by AHC Media, a Relias Learning company.

Editor: Jonathan Springston
Executive Editor: Leslie Coplin
Physician Editor: Stephen Brunton, MD

STATEMENT OF FINANCIAL DISCLOSURE
To reveal any potential bias in this publication, and in accordance with Accreditation Council for Continuing Medical Education guidelines, Dr. Brunton reports he is a retained consultant for Abbott Diabetes, Becton Dickinson, Boehringer Ingelheim, Janssen, Lilly, Merck, Novo Nordisk, and Sanofi; he serves on the speakers bureau of AstraZeneca, Boehringer Ingelheim, Janssen, Lilly, and Novo Nordisk. Dr. Kuritzky (author) is a consultant for and on the speakers bureau of Amgen, Boehringer Ingelheim, and Shire. Ms. Coplin, Mr. Springston, and Editorial Group Manager Terrey L. Hatcher report no financial relationships relevant to this field of study.

SUBSCRIBER INFORMATION
Customer Service: (800) 688-2421
Email Address: jspringston@relias.com
Website: AHCMedia.com

Address Correspondence to: AHC Media, a Relias Learning company, 111 Corning Road, Suite 250, Cary, NC 27518

RELIAS
Formerly AHC Media