RxNews

Information and updates from Sky Lakes Pharmacy

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Newsletter's Mission

RxNews is a newsletter written by pharmacy residents, staff, and students. The goal of this newsletter is to provide new and up to date clinical information to all Sky Lakes Medical Center employees. If there is anything you would like to see included in future issues, please feel free to share your suggestions. We will do our best to include your ideas! Email us at:

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Thank you for reading! - Sky Lakes Pharmacy Staff

How Much Potassium Does It Really Take to Correct Hypokalemia?

A summary of: *The effect of potassium supplementation and concomitant medications on potassium homeostasis for hospitalized patients*

By: Arlo Willhoft, PharmD Candidate

Introduction: There is a common rule of thumb that clinicians often use when correcting serum potassium: each 10 mEq of potassium supplementation is expected to increase serum potassium by 0.1 mEq/L. The original source of this guidance is unclear. A 1942 study examining renal clearance of K and insulin after a single large dose of potassium salt in 7 patients is often cited. Modern data for K supplementation in non-critically ill hospitalized patients is scarce. The objective of this study was to identify the impact of oral and/or IV K+ supplementation on serum K+ levels in hospitalized patients.

Methods: This was a retrospective descriptive study conducted using data from an academic hospital in Pittsburgh, PA. A random sample of patients who received oral and/or IV K+ supplementation between April 2021 and April 2022 was chosen from the billing code list. Patients were included in this study if they (1) received at least one dose of oral and/or IV KCl in the general medicine ward of the hospital and (2) had K+ values determined before and after supplementation. Patients were excluded if they were pregnant or incarcerated; under 18 years of age; receiving amphotericin B; receiving K+ as part of fluid replacement or total parenteral nutrition; undergoing hemodialysis; or administered K+ solely in ICU or inpatient rehabilitation setting. Patients who had only hemolyzed K+ values, active orders for KCl supplementation that were never administered, or an unknown first day of K+ administration were also excluded. The primary outcome was the daily median change in serum K+ normalized per 10 mEq of supplementation administered. Secondary outcomes included the impact of concomitant medication use on changes in serum K+ levels and the incidence of episodes of hyperkalemia.

Results: Of 1,307 eligible patients, a total of 800 patients were included in the study. Approximately 53% were women, 78% were white, and the median age was 68 years. Across the 800 patients in the study, 1,291 daily episodes of K+ supplementation were assessed. A total of 445 patients (55.6%) had 1 day of supplementation included in the analysis, 219 (27.4%) had 2 days included, and 136 (17.0%) had 3 days included. On average, patients received a median of 40 mEq (IQR, 40-60 mEq) of supplementation per day. Overall, the median daily change in serum K+ was 0.05 mEq/L per 10 mEq of supplementation delivered (IQR, 0.00-0.12 mEq/L). Table 2 shows how medication use modifies the median daily change in serum K+ level. Only loop diuretics significantly altered the impact of K+ supplementation compared to no concomitant medication.

Table 2. Impact of Concomitant Medication Use on Potassium Levels Following Supplementation

	Taking selected medication		Taking only selected medication	
Concomitant medication	**No.**	**Change in K^+ per 10 mEq[c]**	**No.**	**Change in K^+ per 10 mEq[c]**
None	494	0.07 (0.00-0.13)	NA	NA
Insulin[a]	304	0.05 (0.00-0.13)	110	0.08 (0.01-0.13)
Loop diuretic[a]	268	0.03 (–0.02 to 0.09)	89	0.03 (–0.04 to 0.08)[d]
Magnesium supplement[b]	225	0.05 (0.00-0.10)	83	0.07 (0.02-0.10)
Potassium phosphate[b]	206	0.05 (0.00-0.11)	81	0.06 (0.01-0.10)
ACEi/ARB[b]	191	0.06 (0.00-0.11)	59	0.08 (0.00-0.10)
Thiazide diuretic[a]	34	0.04 (0.00-0.08)	7	0.04 (–0.05 to 0.09)
Aldosterone antagonist[b]	45	0.05 (0.00-0.09)	1	0.08 (0.08-0.08)
Sacubitril/valsartan[b]	17	0.05 (0.03-0.10)	1	0.25 (0.25-0.25)
SGLT2 inhibitor[a]	2	0.04 (0.01-0.07)	0	NA

Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; NA, not applicable; SGLT2, sodium-glucose cotransportor-2.
[a]A decrease in potassium is anticipated based on the effects of the drug class.
[b]An increase in potassium is anticipated based on the effects of the drug class.
[c]Changes in potassium levels are represented as the median (interquartile range) in mEq/L.
[d]Statistically different (by Kruskal-Wallis and Dunn's test) compared to no concomitant medications.

Discussion: This paper found that in a sample of non-ICU general medicine patients, a median daily rise of 0.05 mEq/L was seen for every 10 mEq of K+ delivered; among patients taking no concomitant medications thought to impact K+, the median daily rise was 0.07 mEq/L per 10 mEq of K+ delivered. Limitations of this paper are its retrospective nature and somewhat homogeneous study population (single center, 78% white). The results of this study suggest that the rule of thumb "10 mEq of K+ supplementation for 0.1 mEq/L of serum K+" often utilized by institutions with K+ order sets, may be an overestimate of the effect of K+ supplementation, especially among patients taking medications that impact K+ levels.

Citation: Montepara CA, Bortmas MR, Cochenour CJ, et al. The effect of potassium supplementation and concomitant medications on potassium homeostasis for hospitalized patients. Am J Health Syst Pharm. 2024;81(6):183-189. doi:10.1093/ajhp/zxad310

Does Your Choice of P2Y12 Inhibitor Post PCI Matter?

A summary of: *Ticagrelor or Clopidogrel Monotherapy vs Dual Antiplatelet Therapy After Percutaneous Coronary Intervention: A Systematic Review and Patient-Level Meta-Analysis*

By: Arlo Willhoft, PharmD Candidate

Introduction: Dual antiplatelet therapy (DAPT) consisting of aspirin and a P2Y12 inhibitor is commonly used after percutaneous coronary intervention (PCI) to reduce the risk of ischemic events. This reduction in ischemic events comes at the cost of an increased bleed risk. A previous patient level meta analysis (done by the same authors) demonstrated that P2Y12 inhibitor monotherapy, after 1 to 3 month DAPT, was associated with a similar risk of death, myocardial infarction (MI), or stroke and a lower risk of major bleeding compared with standard DAPT. However, this study was unable to determine if the choice of P2Y12 inhibitor mattered due to the small number of patients treated with clopidogrel monotherapy. In this follow-up/update to their original patient-level meta-analysis the authors sought to ascertain whether the efficacy of monotherapy depends on the type of P2Y12 inhibitor used.

Methods: This was a systematic review and individual patient data meta-analysis of data from six large clinical trials comparing P2Y12 inhibitor monotherapy with DAPT in patients without indication for oral anticoagulation undergoing PCI. MEDLINE, Embase, TCTMD, and the European Society of Cardiology website were searched, and six unique citations dating from June 16, 2020 to September 10, 2023, were identified. Five of these trials had been included in the author's previous meta analysis. The dataset from the new trial was checked for completeness, pooled with the datasets from the other five trials and analyzed. The primary endpoint was the composite of all-cause death, MI, or stroke. The key secondary endpoints were major bleeding, and net adverse clinical events (NACE), defined as the composite of the primary end point and major bleeding. A 1-step meta-analysis was used to model patient-level data from available trials using a mixed-effects Cox regression model with baseline hazards stratified by trial and a random slope to account for variation between trials in treatment efficacy.

Results: A total of 25,960 patients were available for the intention-to-treat analysis, including 12,960 patients assigned to P2Y12 inhibitor monotherapy and 13,000 patients assigned to DAPT. 24,394 patients were retained in the per-protocol analysis. Trials of ticagrelor monotherapy were conducted in Asia, Europe, and North America while trials of clopidogrel monotherapy were all conducted in Asia. Baseline characteristics of the ticagrelor or clopidogrel monotherapy groups were well-balanced compared with the DAPT groups. The mean (SD) age was 64 (11) years with ticagrelor and 67 (11) years with clopidogrel, and female patients comprised 23% of participants in both groups. The median (range) treatment duration was 334 (300-334) days. Ticagrelor was noninferior to DAPT for the primary endpoint (HR, 0.89; 95% CI, 0.74-1.06; P for noninferiority = .004), but clopidogrel was not

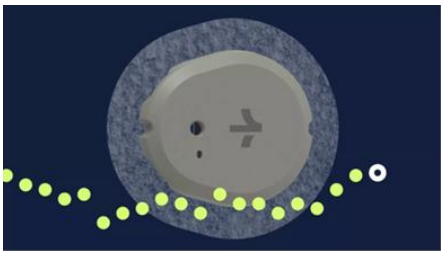
noninferior (HR, 1.37; 95% CI, 1.01-1.87; P for noninferiority > .99), with this finding driven by noncardiovascular death. The risk of major bleeding was lower with both ticagrelor (HR, 0.47; 95% CI, 0.36-0.62; P < .001) and clopidogrel monotherapy (HR, 0.49; 95% CI, 0.30-0.81; P = .006; P for interaction = 0.88). NACE were lower with ticagrelor (HR, 0.74; 95% CI, 0.64-0.86, P < .001) but not with clopidogrel monotherapy (HR, 1.00; 95% CI, 0.78-1.28; P = .99; P for interaction = .04).

Discussion: This meta analysis found that ticagrelor monotherapy after 1 to 3 months of DAPT was noninferior to standard DAPT for the composite of all-cause death, MI, or stroke and superior for major bleeding and NACE. In contrast, clopidogrel monotherapy after 1 to 3 months of DAPT was associated with similarly reduced major bleeding but was not noninferior to standard DAPT for all-cause death, MI, or stroke and did not decrease NACE. Some important limitations to consider are that five of the six trials were open label, and that the inferiority of clopidogrel is primarily driven by the results of one trial that exclusively included East Asian patients that saw an excess of noncardiovascular death in the clopidogrel group.

Citation: Valgimigli M, Gragnano F, Branca M, et al. Ticagrelor or Clopidogrel Monotherapy vs Dual Antiplatelet Therapy After Percutaneous Coronary Intervention: A Systematic Review and Patient-Level Meta-Analysis. *JAMA Cardiol*. Published online March 20, 2024. doi:10.1001/jamacardio.2024.0133

First FDA Approved Over-the-Counter Continuous Glucose Monitor: Dexcom Stelo

By: Storm Lotomau, PharmD Candidate



Continuous glucose monitors (CGMs) have proven its utility both for healthcare providers and for individuals with diabetes because they provide real-time insights into blood glucose levels; which enable proactive management and reduces the risk of complications. However, obtaining CGMs can be challenging for patients due to access-limiting factors such as high costs, insurance coverage limitations, and varying eligibility criteria.

On March 5, 2024, the FDA approved the first over-the-counter continuous glucose monitor (CGM).[1] This significant occasion marks a step forward in empowering individuals with diabetes to monitor their blood glucose levels with accuracy and convenience.

The Dexcom Stelo monitor is a small wearable sensor that is placed on the back of the upper arm. It pairs with a smartphone application which allows users to access their blood glucose levels 24/7 for up to 15 days per sensor. About 80% of sensors last for the entire duration. The FDA recommends users to not make medical decisions based on the device's readings without consulting their healthcare provider first.

The Dexcom Stelo monitor is indicated for people 18 years or older who are not on insulin and who do not have problems with hypoglycemia. The device is not designed to alert its user for drops in blood glucose levels. Data showed that the device performed similarly to other CGMs while adverse events reported in the study included local infection, skin irritation and pain or discomfort.

Stelo is projected to be available for purchase online without a prescription in the US starting summer of 2024. To date, CGM's have been costly for patients (up to $300 monthly without insurance), however, Stelo is intended to come at a more competitive price for people who have to pay out of pocket. More information on cost and availability will be available closer to the product launch this summer.

Citation: [1] Commissioner, Office of the. "FDA Clears First Over-the-Counter Continuous Glucose Monitor." U.S. Food and Drug Administration, FDA, 5 Mar. 2024, www.fda.gov/news-events/ press-announcements/fda-clears-first-over-counter-continuous-glucose-monitor

FDA Approves Semaglutide for Cardiovascular Risk Reduction

The US Food and Drug Administration (FDA) has approved Semaglutide (Wegovy) for reducing cardiovascular risk in adults who are overweight or obese and have established cardiovascular disease. The newly approved indication that has been added to the product label, includes use of the once-weekly glucagon-like peptide 1 (GLP-1) agonist for reducing risks for major adverse cardiovascular events (MACEs) including cardiovascular death, nonfatal heart attack, or nonfatal stroke. Wegovy is now indicated for use in combination with a reduced calorie diet and increased physical activity. The director of the Division of Diabetes, Lipid Disorders, and Obesity in the FDA's Center for Drug Evaluation and Research, John Sharretts, MD states "Wegovy is now the first weight loss medication to also be approved to help prevent life-threatening cardiovascular events in adults with cardiovascular disease and either obesity or overweight..."

The approval was based on results from the 3-year SELECT trial, which randomly assigned 17,604 patients with cardiovascular disease and body mass index ≥ 27 to weekly Semaglutide or placebo; although none of the patients had diabetes, two-thirds of the participants did meet prediabetes criteria. The incidence of MACEs was reduced by 20%: the risk reduction of 15% for cardiovascular death and 19% for death from any cause. Participants also lost a mean of 9.4% of body weight over the first 2 years with Semaglutide vs 0.88% with placebo. Discontinuation of treatment due to adverse effects of the medication occurred in 16.6% in the Semaglutide group, mostly gastrointestinal effects, and in 8.2% in the placebo group.

Citation: Tucker, M. E. (2024, March 13). FDA approves semaglutide for cardiovascular risk reduction. *Medscape*. https://www.medscape.com/viewarticle/fda-approves-semaglutide-cardiovascular-risk-reduction-2024a10004ix?ecd=mkm_ret_240326_mscpmrk_card_cv_etid6396034&uac=435111HV&impID=6396034