



Better Pharmacist Knowledge

Jordan Drug Information and Toxicology Center 2023

March

2023

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Thiazide diuretics to augment diuresis in heart failure (February 2023)

In patients hospitalized with heart failure (HF), **the simultaneous use of a loop diuretic and a thiazide diuretic may augment diuresis, but the safety and efficacy of this approach is unknown.** In a trial that included over 300 in-patients with acutely decompensated HF who were receiving treatment with a loop diuretic, patients randomly assigned to receive additional therapy with hydrochlorothiazide (HCTZ) or placebo had similar changes in patient-reported dyspnea scores after 72 hours of therapy. Patients assigned to HCTZ had more weight loss but a greater decrease in kidney function and a higher risk of hypokalemia. We typically attempt combination diuretic therapy with a thiazide or other nonloop diuretic agent in patients with acutely decompensated HF who are refractory to high doses of loop diuretics (eg, furosemide equivalent of 200 mg/day). [1]

Resistant *P. aeruginosa* outbreak associated with artificial tears (February 2023)

In January 2023, a multistate outbreak caused by a rare strain of **extensively drug-resistant *Pseudomonas aeruginosa*** was reported by the United States Centers for Disease Control and Prevention (CDC). The outbreak was associated with use of **artificial tears**, especially the over-the-counter EzriCare brand. Clinical infections included keratitis, endophthalmitis, respiratory infections, urinary tract infections, and sepsis. The strain is resistant to almost all available antibiotics (a subset of strains were susceptible to cefiderocol). The CDC recommends immediate discontinuation of EzriCare artificial tears until further notice. [2]

Oral isotretinoin for acne and psychiatric outcomes (March 2023)

Patients are counseled about potential psychiatric adverse effects of oral **isotretinoin** because of uncertainty about the impact of isotretinoin on risk for depression and suicidal behavior.

A retrospective cohort study with over 150,000 patients found an increase in suicidal ideation among patients with a history of acne treated with isotretinoin when compared with patients treated with oral antibiotics, but found **no increase in risk for suicidal attempts or major depressive disorder.**

Risk for several other psychiatric conditions was lower in the patients treated with isotretinoin. This study provides additional support for the relative safety of isotretinoin therapy for multiple psychiatric conditions, but also supports continued investigation of the relationship between isotretinoin and psychiatric outcomes, particularly suicidal ideation. [3]



Revised CDC MIS-C case definition (February 2023)

The case definition for multisystem inflammatory syndrome in children (MIS-C) that was revised by the United States Council of State and Territorial Epidemiologists/Centers for Disease Control (CSTE/CDC) and implemented in 2023 aligns closely with the World Health Organization (WHO) MIS-C criteria. Both definitions require **fever, elevated inflammatory markers, at least two signs of multisystem involvement, evidence of SARS-CoV-2 infection or exposure, and exclusion of other potential causes.** One important change is that the CTSE/CDC MIS-C case definition designates Kawasaki disease (KD) as an alternative diagnosis that should trigger reporting to the CDC KD passive surveillance system. [4]



References:

1. Thiazide diuretics to augment diuresis in heart failure (February 2023), accessed online via uptodate, cited on 22 march 2023.
2. Resistant *P. aeruginosa* outbreak associated with artificial tears (February 2023), accessed online via uptodate, cited on 22 march 2023.
3. Oral isotretinoin for acne and psychiatric outcomes (March 2023), accessed online via uptodate, cited on 22 march 2023.
4. Revised CDC MIS-C case definition (February 2023), accessed online via uptodate, cited on 22 march 2023.

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Toxicity with combined acetaminophen/opioid products (March 2023)

Patients taking combined **acetaminophen/opioid** formulations are at risk for **unintentional acetaminophen overdose and hepatotoxicity**. As a consequence, in 2011 the US Food and Drug Administration announced a mandate (effective in 2014) limiting acetaminophen to 325 mg in combined opioid formulations. An interrupted time-series analysis of a large hospitalization database and multicenter liver failure study group (nearly 40,000 and 465 cases of combined acetaminophen/opioid toxicity, respectively) found that since 2011 there has been a significant decrease in hospitalizations and percentage of acute liver failure cases caused by combined acetaminophen/opioid products. In patients taking medications containing acetaminophen and in those who present with unexplained liver injury, it is important to review the total daily acetaminophen dose to prevent hepatotoxicity and to investigate a cause for hepatotoxicity, respectively. [5]

Prophylactic antibiotics before vaginal birth (February 2023)

Antibiotic prophylaxis to reduce the risk of postpartum maternal infection is standard practice before cesarean birth but not for laboring patients planning to give birth vaginally. However, in a randomized trial among nearly 30,000 patients ≥ 28 weeks of gestation in early labor planning a vaginal birth in seven low- and middle-income countries (LMIC), **a single 2-gram oral dose of azithromycin reduced the composite risk of maternal sepsis or death compared with placebo (1.6 versus 2.4 percent)**. Neonatal sepsis and death rates were unchanged. A similar trial in different LMIC reported a reduction in maternal sepsis that was not statistically significant (0.1 versus 0.2 percent). Based on these findings, *we would consider use of azithromycin prophylaxis in LMIC with clinical settings that mirror the first trial's setting, but not in other countries or clinical settings*. [6]

Extending low molecular weight heparin until closer to delivery (March 2023)

Some obstetricians replace low molecular weight (LMW) heparin with **unfractionated heparin** at 36 to 37 weeks of gestation to improve the patient's chances of receiving neuraxial anesthesia for labor and delivery, if desired. However, an analysis of data from the Highlow trial of LMW heparin prophylaxis in pregnancy found

that most patients were eligible for neuraxial anesthesia at the unplanned onset of labor, including 82 percent of patients on low-dose and 61 percent of patients on intermediate-dose LMW heparin. Numbers of eligible patients were higher for planned labor (93 and 81 percent). **These results support extended use of LMW heparin prophylaxis to 38 to 39 weeks or even until onset of labor in many individuals**. [7]

Hydrochlorothiazide and prevention of recurrent kidney stones (March 2023)

Thiazide therapy can lower urinary calcium excretion and has been shown in prior randomized trials to reduce the risk of kidney stone recurrence in patients with calcium stones. A recent trial in over 400 patients with recurrent calcium kidney stones found that once daily hydrochlorothiazide (HCTZ; 12.5, 25, or 50 mg), compared with placebo, did not reduce the risk of a composite of symptomatic or radiologic stone recurrence over a median of three years. However, there was a reduction in the rates of radiologic stone recurrence in patients receiving higher doses of HCTZ. For patients with recurrent calcium oxalate stones and higher than desired urine calcium, *we continue to suggest treatment with a thiazide diuretic to lower urinary calcium excretion*. [8]

ADHD medications and risk of cardiovascular events (February 2023)

The risk of cardiovascular (CV) events in patients receiving attention deficit hyperactivity disorder (ADHD) medications has been the focus of several large cohort studies. A recent meta-analysis of 19 observational studies including 3.9 million patients did not detect an association between ADHD medication use and the overall risk of adverse CV events. In an analysis of nine studies that reported rates of sudden cardiac death (SCD), cardiac arrest, or tachyarrhythmia, *the risk was slightly higher among individuals using ADHD medications, but the finding was not statistically significant*. The absolute rates of SCD in these studies were very low. Based on these data, we suggest that children and adolescents who are starting ADHD medications be assessed with a complete history and physical examination. If this assessment does not suggest cardiac disease, no additional evaluation is necessary. [9]

References:

5. Toxicity with combined acetaminophen/opioid products (March 2023), accessed online via uptodate, cited on 22 march 2023.
6. Prophylactic antibiotics before vaginal birth (February 2023), accessed online via uptodate, cited on 22 march 2023.
7. Extending low molecular weight heparin until closer to delivery (March 2023), accessed online via uptodate, cited on 22 march 2023.
8. Hydrochlorothiazide and prevention of recurrent kidney stones (March 2023), accessed online via uptodate, cited on 22 march 2023.
9. ADHD medications and risk of cardiovascular events (February 2023), accessed online via uptodate, cited on 22 march 2023.

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