

The Prudent Prescriber

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March 2018

Two New Approaches to *Clostridium difficile*

The incidence of *Clostridium difficile* infection (CDI) has more than doubled in the past 10 years in the United States. Greater than 20% of patients with CDI experience an initial treatment failure and 40% to 65% of these have a second recurrence.

An Easy Pill to Swallow?

Fecal microbiota transplantation (FMT) has been shown to be effective in treating recurrent *Clostridium difficile* infection. Kao *et al* (JAMA.2017; 318(20): 1985-1993) from Alberta, Canada randomized 116 patients, 60% women, average age 58 years, who had experienced at least three documented episodes of CDI to FMT by oral capsule or by colonoscopy. Seven healthy volunteer donors provided stool for all participants. The primary outcome was the proportion of patients without recurrent CDI at 12 weeks after fecal microbiota transplantation. They also looked at adverse effects, changes in quality-of-life and patient satisfaction.

Pharm Reps \neq Rational Prescribing

(PR)



(RP)

Antibiotics do NOT

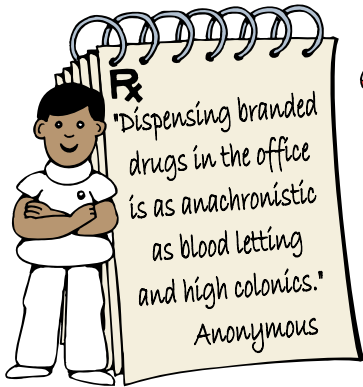


help acute bronchitis

β -blockers in post-MI save lives



Pill splitters save BIG



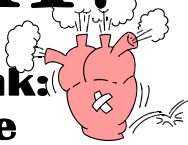
"Dispensing branded drugs in the office is as anachronistic as blood letting and high colonics."
Anonymous



CHE?

Think:

Ace
Aldactone
B-blocker
Dig
Diuretic

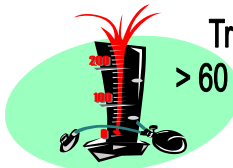


Avoid these expensive "me-too" drugs:

Intermezzo
Vimovo
Livalo
Gralise
Viibryd
Edarbi
Daliresp



Treat patients > 60 years to 150/90



NOW AVAILABLE
ON THE
GENERIC MARQUEE

Viagra \rightarrow sildenafil
Effient \rightarrow prasugel
Strattera \rightarrow atomoxetine
Asacol HD \rightarrow mesalamine DR
Pristiq \rightarrow desvenlafaxine

Results: The prevention of recurrent CDI after a single treatment was achieved in 96.2% in both the capsule group (51/53) and the colonoscopy group (50/52). Rates of minor adverse events were 5.4% for the capsule group versus 12.5% for the colonoscopy group. There were no significant between-group differences in quality-of-life.

My take: Oral capsules of FMT offer real world economic and aesthetic advantages. There are still issues to work out in terms of the size of the oral dose, whether or not to use acid blocking agents (PPIs increase risk of *C. diff*) and how to taper vancomycin that is often onboard in these patients. Stay tuned.

Whither Probiotics and *C. diff* ?

The data supporting using probiotics to prevent CDI in hospitalized patients on antibiotics have swung from favorable to disappointingly dismal (PLACIDE Trial, 2013).

In a new study, Shen *et al* (*Gastroenterology*, 2017; 152: 1889-1900) again reverse that trend and may explain why previous trials, like PLACIDE were negative. This systematic review and meta-analysis focused on randomized controlled trials looking at probiotics for the prevention of CDI in hospitalized patients taking antibiotics. The authors included 19 trials with 6,061 patients (3,077 on probiotics and 2,984 controls), including the PLACIDE trial. There was no evidence of publication bias.

Results:

* The risk of CDI in the control group ranged from 0% to 40%, and the risk in the probiotic group ranged from 0% to 11%. The median incidence of CDI in the control groups of the 19 studies was 4%, this translates to a NNT of 43 patients treated with probiotics, rather than no treatment, to prevent one case of CDI. As a comparison, with the commonly advocated practice of heparin for prophylaxis of venous thromboembolism in hospitalized patients, the NNT = 250.

* The incidence of adverse events in the 15 of 19 studies that collected these data was similar in the probiotic (14.2%) and the control groups (15.9%). The most common adverse events were cramping, nausea, fever, soft stools, flatulence, and taste disturbance. There were no cases of probiotic bacteremia or fungemia.

* The timing of probiotic administration was a significant predictor of probiotic efficacy in preventing CDI. **The probiotic efficacy was cut in half if probiotics were begun more than two days after antibiotics were started.** The PLACIDE trial was an outlier, allowing probiotics to be initiated as late as seven days after antibiotics.

My take:

- Most guidelines for management of CDI still give probiotics a "I" rating (insufficient data to make a decision). Shen's study is an important step forward.
- Other issues remaining are selection of the best probiotic and the appropriate dose. Are certain probiotics species more effective with certain antibiotics?
- If I am hospitalized and need antibiotics, I want probiotics (whatever is on the shelf) started with the antibiotics.

A Good Prescription to Remember

Opioid induced constipation is a crappy problem. Sridharan in the Journal of Pain and Symptom Management (volume 55, number 2, February 2018) in a network meta-analysis of randomized controlled trials compared treatments for opioid induced constipation.

Bottom line: None of these drugs work well and all are pricey. Methylnaltrexone (Relistor), given subcutaneously, works the best, but at a price of \$3,270 per month.

A better approach to this problem: **prophylaxis**. Both Dr. Michael Appel, Pharm. D., the oncology department at Community Hospital, and geriatrician Dr. Amy Mohler recommend:

1 docusate (Colace) 100mg
+
one senna tablet 8.6 mg
for every 30 mg oral morphine equivalent
the patient is taking per day.

It is inexpensive and it works well to prevent opioid induced constipation.

For Fun: Let's talk about the weather and drug prices

Acute Low Back Pain? Don't Blame the Weather!

I have a picture in my mind from 70 years ago. My grandfather, an Iowa pig farmer, standing in his dimly lit kitchen, holding his back and predicting that a storm was coming soon. Twenty five hundred years ago, Hippocrates noted that many illnesses are related to changes in the season.

Beilken *et al* in an inventive study (Pain Medicine 2017; 18: 1139-1144) took 981 participants with a new episode of acute low back pain and investigated the association of various weather parameters on the risk of developing an episode of low back pain. In this case – crossover study from Australia, the investigators asked adult outpatients complaining of the acute onset of low back pain to recall the date of onset of their symptoms. They then attempted to match the weather patterns (precipitation, humidity, wind speed, wind gusts, wind direction and barometric pressure) with the onset of the patients' back pain.

Results: Weather patterns were not associated with the onset of acute low back pain

My take: Perhaps my grandfather, like many of us, was fallible to confirmation bias and susceptible to so-called patternicity, where we see patterns in meaningless noise. (Rev Gen Psychol 1998; 2(2) 1775-220.)

The First Million Dollar Drug?

It was only a matter of time. My Pharm. D. colleague, Zach, was eager to lay it out:

LUXTURNA \$1,020,000.00

Gene therapy for patients with retinal dystrophy!
What is it worth to get your vision back?

- ICER says that some gene therapies (all are pricey) are appropriately priced for the value delivered.
- Zach says that the retail price is only about \$870,000.

Post Script

In the February 2018 Prudent Prescriber, I rued the incestuous relationship wherein Big Pharma pays the FDA for the approval process of their new drugs. I proposed an “independent federal agency.” Reader Dr. Gary Mohr from Westcliffe responded, “We don’t need to establish an independent federal agency; one might argue such a beast does not exist.” Dr. Mohr comments further, “The FDA itself is neither safe nor effective.” Well said, Gary!

You may access previous issues at <https://www.rmhp.org/i-am-a-provider/provider-resources/publications-for-providers>.

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