PALLIATIVE CARE CASE OF THE MONTH

"Treating Non-Infectious Diarrhea"
by
Robert Arnold, MD

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Case 1: Mr. Jones is a 58-year-old man with short gut syndrome. Palliative Care was consulted for goals of care, however quickly it became clear uncontrolled diarrhea was a larger priority. He said having to change the bag every few hours completely interfered with his living a normal life. He said, "I'd rather die than have all of this diarrhea."

Case 2: A 62-year-old woman with non-small cell lung cancer is receiving immunotherapy. She has done quite well but is distressed by her diarrhea. She tried Lomotil and Imodium but neither worked. When seeing her palliative care doctor, she said, "It isn't worth treating my cancer if I can't live a normal life."

Discussion: Diarrhea is a common and significant problem among seriously ill patients. Subjectively it is defined as the frequent passage of loose stool with urgency. Objectively defined, diarrhea is the passage of more than three unformed stools in 24 hours.[1,2] It can be debilitating, and at times life threatening because it contributes to dehydration, electrolyte imbalance, malnutrition, and pressure ulcer formation. Patients – like the ones in the above cases – say it decreases their quality of life, as they are unable to do anything unless they are close to a bathroom. [3]

As clinicians, we know that diarrhea has a very large differential depending on whether it is acute (less than 14 days) or chronic (more than a month), infectious or noninfectious, secretory or non-secretory. It can be caused by the primary illness (Crohn's disease) or the treatment (chemotherapy or radiation therapy), infection (such as Mycobacterium avium complex in advanced HIV) or a number of less common etiologies.[4,5] This case of the month will focus on the management of diarrhea, focusing on decreasing and solidifying the number of stools. Reviews of the importance of rehydration [6,7] and treatments of specific causes of diarrhea are available.[4,5]

First, one should evaluate the patient's diet. Many people, particularly when one gets older, become lactose intolerant with gut injury and thus, changing to a lactose-free diet can be helpful. Diarrhea by be exacerbated by dietary supplements, high fiber foods, indigestible sugars, caffeine, and foods high in fat. Moving patients to a BRAT (bananas, rice, applesauce, toast) diet may help. Easily digestible foods such as pasta, or scrambled eggs should be encouraged.[8]

Non-pharmacologic bulking agents such as psyllium, barberry root bark tea, and pectin are often recommended to solidify the diarrhea (although there is little data supporting this). Pectin and bile sequestering agents may interfere with the absorption of drugs, and thus one needs to check for drug-drug interactions and separate them from other pharmacologic agents.

Three drugs are used because of their ability to slow down the gut, allowing for more time for absorption of intestinal fluids a decrease of diarrhea. The most well-know is loperamide, a synthetic opiate which has minimal absorption. The dosing is 4 mg after one's first bowel movement and then 2 mg after every unformed stool, up to 16 mg (in palliative care patients there is some data for use up to 54 mg).[9, 10] Loperamide should be continued for 12 hours after diarrhea is stopped. Adverse effects include mostly constipation, abdominal cramps, nausea and rarely CNS effects like fatigue or dizziness. Cases of torsades de pointes and death have been reported with higher than recommended doses.[9]. This also is the cheapest medicine at a cost of roughly three cents a tablet.

Diphenoxylate is a synthetic opiate chemically related to meperidine and inhibits excessive GI motility. Commercial preparations (Lomotil®) contain a subtherapeutic amount of atropine to discourage abuse. Recommended dose is 5 mg four times daily until diarrhea is controlled. Once control is achieved, the dose is lowered the minimal amount needed to control the diarrhea. The maximal dose is 20mg/day; if there is not benefit after 10 days of use at maximal dose it is unlikely to work. Excessive doses of diphenoxylate atropine can result in symptoms of excessive cholinergic and central opiate effects including drowsiness, flushing, dry mouth and dilated pupils.[11] Lomotil is 0.70/tablet or 1.40/ml.

There are no randomized trials comparing loperamide to diphenoxylate. However, efficacy data from double blind crossover studies in a variety of settings suggest that loperamide is more effective and provides more rapid control of diarrhea. It also has a more favorable side effect profile and thus should be the preferred agent. [12]

Tincture of opium also is used for the treatment of diarrhea. The dosing is 10-15 drops or 0.6 ml every 3-4 hours. One needs to be careful to use this deodorized tincture of opium (10mg/ml or morphine) rather than the camphorated tincture (paregoric) as the former is much stronger than the latter. The side effect profile ranges from dizziness and drowsiness, constipation, urinary retention and bradycardia (all from the minimal systemic opiate absorption). Again, there is no data comparing this with the other drugs although anecdotally I have good results from tincture of opium when loperimide does not work. However, it is more expensive at roughly $6.27/ml.

Activated charcoal has been recommended as an agent because of its ability to attract and expel toxins from the gastrointestinal tract. The data is largely anecdotal with only four low quality studies showing its use.[13] Proponents tout its lack of side effects and suggest it as a second- or third-line drug.

Discussion Continued

Finally, octreotide can be used for severe diarrhea. It results in the suppression of gastrointestinal/pancreatic hormones, such as VIP, serotonin, gastrin, secretin, and pancreatic polypeptide. It also it prolongs intestinal transit time, promotes intestinal absorption, and decreases secretion of fluids and electrolytes. The usual starting dose is 100-150 mcg of subcutaneously or IV three times daily. Because there is dose response relationship, the dose can be titrated up to 500 mcg subcutaneously three times a day or a continuous infusion of 20-50 mcg per hour. A long acting, very expensive formulation has been developed for once per month intramuscular dosing. (Its use should be reserved for cases that respond to IV or SC dosing) The major side effects are bradycardia, fatigue, headache, dizziness, itching, and pain (all above 10%). Anemia, hyperglycemia and hypothyroidism can occur. It also is much more expensive than the other options. (AWP for the 100 mcg/ml injection is roughly 7 dollars which would be 600 dollars a month at the lowest dose).[14]

Conclusion:

1. The patient had hyperglycemia with octreotide and thus it was stopped. A combination of loperamide and tincture of opium thickened his stool although he still had diarrhea.
2. Neither Lomotil nor loperamide helped. Tincture of opium twice a day however, completely resolved her diarrhea.

References:

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