The GI tract in PD: From Beginning to End

Lauren Seeberger, MD
Associate Professor, Neurology
University of Colorado, Denver
The Problems

Problem

Solution
Introduction

• More details have emerged about the extent of the GI dysfunction in PD
  • Weight loss
  • Dental decay
  • Drooling
  • Swallowing difficulty
  • Impaired gastric emptying
  • Decreased BM frequency
  • Difficulty passing stool
Oral Health

- Oral health problems have been reported, but not uniformly
  - Includes loss of teeth, periodontal disease, chewing difficulty
- 70-80% PD patients note excess saliva (compare to 6% of controls)
- Saliva production
- Propensity to drooling

“The saliva fails of being directed to the back part of the fauces (mouth), and hence is continually draining from the mouth” JP
Dyphagia “so much are the actions of the muscles of the tongue, pharynx, &c. impeded by impaired action and perpetual agitation, that the food is with difficulty retained in the mouth until masticated; and then as difficultly swallowed” JP
Weight loss

• Commonly reported
  • One report up to 50%
  • with ¼ of patients had greater than 28 lb loss
  • Mean weight loss in another study showed 7.2 lb loss
  • More likely in women

• Should be modest and should stabilize

• Cause is unknown

• Some may gain weight after DBS surgery
  and may see weight gain if compulsive eating on DA therapy
Gastroparesis

Slow stomach emptying

- Impaired or delayed gastric emptying in PWPD
- 1/5 of PWPD complain of nausea and almost ½ bloating even before on medication therapy

- Etiology unknown, may be central or peripheral
- Dysmotility may predispose to small intestine bacterial overgrowth
Consipation

- Bowels “that have all along been torpid, now, in most cases, demand stimulating medicines of very considerable power” JP
- Decreased frequency of BMs
- Fewer than 3 BMs per week
- May be seen in up to 80-90% PWPD
- Slowness of transit present early in course

- Constipation may precede motor PD
- Average colon transit time is twice that of controls
Defecation

• Takes coordinated effort of muscles
• Dysfunction results from lack of coordination of these muscles
• No treatments uniformly studied in PD

“The expulsion of the faeces from the rectum sometimes requiring mechanical aid” JP
The Consequences
Levodopa Availability

1. **Swallowing oral therapy**
   Impaired swallowing (dysphagia) in advanced disease

2. **Stomach**
   Variable absorption of levodopa due to irregular gastric emptying

3. **Jejunum**
   Competition with dietary amino acids for active transport across the intestinal wall

4. **Peripheral tissues**
   Reduced levodopa bioavailability due to enzymatic breakdown by AADC and COMT

5. **Blood–brain barrier**
   Competition for transport across the blood–brain barrier with large neutral amino acids limits the amount of levodopa reaching the striatum

6. **Striatum**
   Conversion of levodopa to dopamine

---

**Figure 2: Delay in gastric emptying**
Photograph taken during gastroscopy. Arrow points to a carbidopa tablet remaining intact in a patient’s stomach about 1.5 h after intake.
SIBO

Small intestine bacterial overgrowth can be seen as a consequence of slowed stomach emptying and slowed gut transit time.

Associated with intestinal symptoms and motor symptoms.

May contribute to local inflammation and “leakage of the bacteria and toxins across the intestinal wall.”

Newly dx PWPD had increased intestinal permeability c/w healthy controls.
The Management

Identifying symptoms to treat is crucial first step!
Dental Problems and Drooling

• Good dental hygiene and twice yearly visits to dentist for cleaning
• Consider implants versus dentures as easier to manage
• Drooling
  • Medications studied in PD
    • Glycopyrrolate 1-2 mg twice to three times a day
    • Clonidine 0.15 mg once per day
    • Modafinil 100 mg once per day
  • Topical medication studied in PD
    • Atropine, sublingual 1%, one drop twice a day
    • Ipratropium, 21-42 micrograms, 1 to 2 sprays up to four times a day
  • Injectable medications studied in PD
    • Botulinum toxin
Swallowing Problems

Expiratory Muscle Training

Video-assisted Swallowing Therapy
Gastroparesis = slow stomach emptying

• Best clinical test 4 hr radiographic assessments after a labeled meal

• Treatments
  • Small frequent meals may help, avoid high fat, lactose
  • Dopamine Antagonists
    • Metoclopramide-crosses into brain, not recommended for those with PD
    • Domperidone-Withdrawn from US market due to cardiac concerns
  • Serotonin Agonists (5-HT4 agonists)
    • Two approved then withdrawn due to cardiac toxicity
    • New clinical trial of prucalopride, chronic constipation, not yet in PD
  • Erythromycin-the antibiotic, prokinetic, issues with long term use
  • Gastric pacemaker has been used in other conditions
Infections

• H. pylori-can cause bacterial infection of the stomach or upper small intestine that causes gastritis
  • Diagnosed by urea breath test, blood test, stool test or direct gastroscopy.
  • Treatment of the infection has been shown to help motor fluctuation
  • Inconsistent conclusions re: antibiotic regimens best and length of treatment

• Small intestinal bacterial overgrowth
  • Diagnosed by culture, lactulose or glucose breath test
  • Eradication of SIBO improved motor fluctuations in trial
  • High rate of relapse at 6 months
  • No consensus on best treatment, dose or duration
Treatment of Constipation

• Conservative Measures
  • Increased fluids 1.5 l
  • Fiber 15-20 grams
  • Diet
  • Probiotic supplements
  • Digestive yogurts
  • Exercise

• Pharmacologic Therapies
  • Osmotic agents-polyethylene glycol 17 gm/day has been shown effective
  • Recently, lubiprostone, enhances colon secretions tested in PD
  • Treat like chronic constipation
  • For defecation problems-relaxation therapies, botox in anal sphincter
Treatments to Bypass GI dysfunction in PD
Thank you!