Digestive System (Gut) Involvement in Scleroderma

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17TH Annual Scleroderma National Conference
Medical Report:

Digestive system (Gut) involvement in scleroderma

Updated January 2012

Dinesh Khanna

Medical Report:

Eating well with scleroderma

Updated January 2012

Linda Kaminski and Dinesh Khanna
Digestive System Involvement

- Esophagus - Food Pipe
- Stomach
- Small intestine
- Large intestine (Colon) and rectum
- Liver
Gut Involvement

- Esophagus
- Stomach
- Small intestine
- Large intestine and rectum
- Liver
Gut Involvement

- 75%-90% of patients with scleroderma have gut involvement.
- Most of the people have symptoms.
- Interferes with day-to-day activities and impairs quality of life.
## Frequency of GI symptoms (209 SSc patients)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heartburn</td>
<td>71</td>
</tr>
<tr>
<td>Trouble swallowing</td>
<td>52</td>
</tr>
<tr>
<td>Bloating</td>
<td>80</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>51</td>
</tr>
<tr>
<td>Constipation</td>
<td>51</td>
</tr>
<tr>
<td>Fecal Incontinence</td>
<td>35</td>
</tr>
</tbody>
</table>

Scleroderma Foundation survey 2010
Function of the Gut

◆ To push the food down, extract and absorb nutrients!!
◆ Does it by well orchestrated motion of the gut MUSCLE.
◆ Also known as PERISTALSIS.
Gut Involvement

♦ The primary event that causes trouble in the gut is progressive weakening of muscle motion in the gut.

♦ Virtually every gut symptom is the result of weakening of the gut muscle.

♦ The weakening that starts in the esophagus and stomach, works its way down the small and large intestine.
Oropharyngeal Involvement

- Facial involvement interfere with mastication
- 20% Sjogren’s syndrome (dry eyes/ dry mouth)

TREATMENT

- Small bolus
- Liberal fluid intake
- Regular dentist appointment
- Trial of pilocarpine and cevimeline therapy
Oral moistures

◆ Commercial
  – Oasis
  – ACT Dry Mouth
◆ Home remedy
  – ¼ tsp salt
  – ¼ baking soda
  – 1 quart water
Oral moistures and protection

- Xylitol containing products
- Naturally occurring carbohydrates
- Tastes like sugar
- 1/3 calories
Minimize enamel erosion

◆ Dental appointments and fluoride varnish to prevent enamel erosion
◆ Treat GERD
Reflux Disease

- Liquid content of the stomach regurgitates (backs up, or refluxes) into the esophagus (also known as GERD).

- Caused by
  - weakening of the gut muscle.
  - weakening of the esophagus-stomach junction sphincter.
Upper gut in scleroderma

- Decreased Salivary Production
- Esophageal Dysmotility
- Hypotensive LES
- Gastric Dysmotility
Upper gut in scleroderma

- Decreased Salivary Production
- Esophageal Dysmotility
- Hypotensive LES
- Gastric Dysmotility
Acid reflux is caused by weak gastro-esophageal (GE) sphincter and gut muscle.
Symptoms of Reflux Disease

- Heartburn
- Difficulty swallowing
- Chest pain
- Mouth ulcers/ burning
- Change in voice
- Chronic cough
- Asthma
Barium study to look for gut muscle weakness

Barium sulfate is drunk before the X-rays are taken.

It helps to look for motility of the gut and ulcers in the esophagus and stomach.

It is relatively convenient but can miss ulcers etc.
Acid reflux leads to ulcers and stricture (narrowing)
Erosive esophagitis
HIGH RESOLUTION MANOMETRY WITH IMPEDANCE
Why do we need to treat Reflux

◆ To relieve symptoms and improve quality of life.
◆ Acid produced in the stomach may flow back while sleeping and get to the lungs causing lung inflammation.
◆ Continuous high acid production for a long time can cause inflammation and scarring of the esophagus, which may lead to a pre-cancerous lesion.
Anti-reflux measures

♦ Head of the bed elevated (i.e., wedge pillow, blocks under head of bed, electric bed). NOT extra pillows.
♦ Biggest meal at noon, small meals otherwise.
♦ Do not eat late (after 6 pm); do not drink fluids late (after 8 pm).
♦ Frequent small meals (5-6 per day).
♦ No tight garments around waist.
Anti-reflux measures

♦ Take anti-secretory and pro-motility agents.
♦ Stop smoking (if currently smoking).
♦ Avoid or minimize reflux producing foods (fat, chocolate, coffee).
♦ Certain medications such as Nifedipine (taken for Raynaud’s) can weaken GE sphincter causing reflux symptoms.
## Anti-secretory Agents (dose ins 2-4 times used in general population)

<table>
<thead>
<tr>
<th>Agent</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prilosec</td>
<td>20-40mg 1-2x per day</td>
</tr>
<tr>
<td>Prevacid</td>
<td>15-30mg 1-2x per day</td>
</tr>
<tr>
<td>Aciphex</td>
<td>20 mg 1-2 x per day</td>
</tr>
<tr>
<td>Protonix</td>
<td>40 mg 1-2 x per day</td>
</tr>
<tr>
<td>Nexium</td>
<td>20-40 mg 1-2 x per day</td>
</tr>
<tr>
<td>Dexilant</td>
<td>60 mg 1 x per day</td>
</tr>
</tbody>
</table>
Side effects of PPI based on recent studies

- Diarrhea—may rarely cause *Clostridium difficile* infection
- Risk of osteoporosis
- Dementia
- Chronic kidney disease
Making sense of the literature

♦ Retrospective review of large databases
  – Insurance claims database
  – Large single insurance
♦ No information about scleroderma
♦ Although the effect may support role in large population, it is unknown what effect will it have at an individual level
Other choice

- Risk vs. benefit of PPI intake
  - Esophageal stricture, pain, difficult swallowing, potential risk of esophageal cancer
- Consider H2 blocker such as Pepcid and Tagamet twice a day or in the PM
- Consider “on demand” PPI but may not be effective in significant GERD
## Pro-motility agents

<table>
<thead>
<tr>
<th>Agent</th>
<th>Frequency</th>
<th>Part of Gut</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reglan</td>
<td>10 mg TID-QID</td>
<td>Whole</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>100-123 mg TID</td>
<td>Stomach</td>
</tr>
<tr>
<td>Domeperidone*</td>
<td>10-20 mg QID</td>
<td>Stomach and Small Bowel</td>
</tr>
<tr>
<td>Propulsid†</td>
<td>10-20 mg TID</td>
<td>Whole</td>
</tr>
</tbody>
</table>

*Domeperidone not approved in USA--can obtain in Canada or Mexico
†US CALL 1-800-JANSSEN (Restricted use)
How to use it?

- PPI/h2 blockers and prokinetics 30 to 60 minutes before each meal
- Start PPI agent once a day
- *Increase to twice a day
- *Add Domperidone 1 hour before the meals
- *Add Pepcid or Tagamet at bedtime

* If the heartburn or other symptoms continue for 2 weeks
Barrett’s esophagus

- Barrett’s esophagus (a pre-cancerous lesion) is a complication of long-standing GERD.
- Present in 7%-13% consecutive people with scleroderma receiving chronic therapy with PPI.
- Similar incidence seen in non-SSc GERD.
- Barrett’s esophagus is associated with adenocarcinoma in SSc.
- If Barrett’s esophagus is diagnosed, very close follow-up with a gastroenterologist and regular endoscopies.
Surgery

- Surgery for GERD is relatively contraindicated.
- Surgery result in severe dysphagia secondary to the surgically induced narrowing of the GE junction, coupled with distal esophageal hypomotility.
- Generally restricted to patients with severe, poorly controlled, and complicated reflux.
- Fundoplication and laparoscopic modified Roux-en Y gastric bypass (RYGB) both are effective.
- IF SURGERY NEEDED, GO TO AN EXPERIENCED SURGEON.
The main problem encountered is slow emptying of the stomach into the small intestine. Leads to symptoms of:

- Bloating
- Nausea and vomiting
- Abdominal pain
- Excessive flatulence
- Result in weight loss
Diagnosis

◆ A gastric emptying study is performed to diagnose abnormal emptying of food from the stomach.

◆ The food and radioactive material remain in the stomach longer than normal (usually hours) before emptying into the small intestine.
NORMAL EMPTYING STUDY
Less than 50% Remaining (or Greater than 50% Emptying) at 90 minutes
Gastric Emptying Study
# Pro-motility agents

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Watermelon Stomach

♦ Telangiectasia (dilated blood vessels) in the stomach.
♦ Can cause anemia due to slow (or rapid) blood loss.
♦ Can be without stomach symptoms or may be only feeling VERY tired and fatigued.
♦ Suspect when anemia on the blood count.
♦ Confirmed using endoscopy.
♦ Treated with laser coagulation.
Watermelon Stomach
Watermelon stomach

After argon plasma coagulation
Small Intestine

- The small bowel is the part of the gut that absorbs nutrients from food.
- Lack of muscle tone leads to stagnation of food, bacterial overgrowth, diarrhea, cramping, feeling of bloating.
The most frequent cause of diarrhea in SSc is the migration of bacteria, which normally live in the distal (lower) colon, into the small intestine—bacterial overgrowth.

They compete with you for nutrition.
Bacterial overgrowth

♦ Can cause weight loss and inability to gain weight.
♦ Can cause malabsorption of essential vitamins and minerals.
♦ Diagnosed with lactulose or hydrogen breath test.
♦ Suppressing the bacteria with antibiotics often reduces the diarrhea and bloating.
Breath Test

Simren and Stotzer Gut 2006
Some Antibiotics for suppressing bacteria

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dosing schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>♦ Augmentin</td>
<td>875 mg 2x per day</td>
</tr>
<tr>
<td>♦ Cipro</td>
<td>500 mg 2x per day</td>
</tr>
<tr>
<td>♦ Flagyl</td>
<td>500 mg 3 x per day</td>
</tr>
<tr>
<td>♦ Doxycycline</td>
<td>100 mg 2x per day</td>
</tr>
<tr>
<td>♦ Tetracycline</td>
<td>250 mg 4x per day</td>
</tr>
<tr>
<td>♦ Rifaximin</td>
<td>400 mg 2x per day</td>
</tr>
</tbody>
</table>
# Pro-motility agents

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<tr>
<th>Agent</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reglan</td>
<td>10 mg 3-4 x per day</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>250-333 mg 3-4 x per day</td>
</tr>
<tr>
<td>Domperidone</td>
<td>10-20 mg 3-4 x per day</td>
</tr>
<tr>
<td>Octreotide</td>
<td>50 mcg sub q 2 x per day</td>
</tr>
</tbody>
</table>

**NB** Domperidone not approved in USA--can obtain in Canada or Mexico
How to use it?

♦ The antibiotics can be used every 2 weeks ON/ 2-4 weeks OFF.
♦ Some people need initial 4-6 weeks of antibiotics.
♦ Same or different antibiotics are used depending upon the physician’s preference / person’s symptoms.
♦ Take multivitamin and calcium (500 mg) twice a day.
Probiotic therapy

• Probiotics are bacteria that have a beneficial effect in the prevention and treatment of gut problems when they are ingested.
• Lactobacillus has been evaluated with positive results in one study.
• "Live and Active Cultures" seal on the yogurt label.
• Culturelle (http://www.culturelle.com/) 1 capsules 2 x per day
Consider removing foods containing wheat or dairy (lactose) from your diet. If removing wheat and/or dairy products does not provide relief, the adoption of a low FODMAP diet may prove beneficial.

**FODMAP** is an abbreviation for:
- **F**ermentable
- **O**ligosaccharides (fructans and galactans)
- **D**isaccharides (lactose)
- **M**onosaccharides (excess fructose in a food)
- **A**nd
- **P**olyols (sugar alcohols like sorbitol, maltitol, mannitol, xylitol and isomalt)

**WORK WITH A NUTRITIONIST TO ACCOMPLISH THIS**
Pseudo-Obstruction

♦ The bowel is not physically blocked as in true bowel obstruction but has just "had enough" and stops working!
♦ Caused by weakening of the gut muscle.
♦ Causes belly pain, distention, vomiting, and not able to “pass gas”.
♦ Diagnosed by X-ray and CT scan.
♦ NEED TO RULE OUT “REAL” OBSTRUCTION.
Pseudo-Obstruction
Treatment

- Giving small intestine ‘rest’ by staying off fluid and food
- Intravenous (through the veins) fluids
- Pro-motility agents
- Antibiotics (usually associated with bacterial overgrowth)
- Avoid bowel surgery (consult your rheumatologist first)
Octreotide and TPN

- Octreotide can be given during an attack or to prevent recurrent attacks
- Can be given under the skin as 50 mcg at bedtime
- Total parenteral nutrition (food through i/v) may needed temporarily before the gut starts to “move” again
Colon

- Main function is to reabsorb water and salts that have been secreted by the rest of the gut.

- This helps the formation of stools and if the mechanism is impaired may lead to constipation (or diarrhea).
Constipation

- <3 bowels/ week
- Hard or lumpy stools
- Incomplete evacuation
- Straining during bowel movement
 Colon

♦ Constipation

– Caused by weakening of the gut muscle and slow contractions.

– Use of stimulant laxatives - acts on nerve endings in the gut wall that make the muscles in the intestine contract with more force.

– Liberal use of fluids.

– Avoid high-fiber diet and bulk-forming laxatives; may make constipation worse.

– Take medication every other day to maintain a healthy bowel regimen.
Stimulant Laxatives

♦ Laxatives
  ♦ Colace
  ♦ Dulcolax
  ♦ Senna
  ♦ Milk of Magnesia
  ♦ Lactulose
  ♦ Amitiza

♦ Dosage
  ♦ 100 mg once-twice/day
  ♦ 10-15 mg once a day
  ♦ 2-4 tablets once a day
  ♦ 30-60 mg/day
  ♦ 15-30 ml/day
  ♦ 8-24 ucg twice a day

Do not use these laxatives if symptoms of bowel obstruction!!
Diarrhea

- Can be “paradoxical” diarrhea, where diarrhea occurs around an impaction—usually painful.
- Usual diarrhea treated in usual manner, with bulk agents, anti-motility agents and careful bowel rest, using clear liquids (careful about dehydration, in this case).
Rectum

◆ Stool incontinence occurs in up to a third of patients.
◆ Weakening of the rectal muscle and poor control over rectal sphincter.
◆ Biofeedback therapy- strengthen the rectal muscle by volunteer squeezing of the muscle.
◆ Bulk agents such as Citrucel.
◆ Anti-diarrheal agents such as Imodium.
Sacral nerve stimulation

- Low-level electric stimulation
- Using electrodes to the nerves in the sacrum
- Done under general anesthesia
Table 2. FREQUENCY OF EPISODES OF INCONTINENCE

Episodes of Incontinence to Solid or Liquid Stool During a 7-Day Period

<table>
<thead>
<tr>
<th>Patient</th>
<th>Pre-stimulation</th>
<th>With Temporary Stimulation Before Permanent Stimulation</th>
<th>With Permanent Stimulation at a Median of 16 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>15</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>58</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>11</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Prospectively recorded on the diary card during a 7-day test period. Two patients had minor passive soiling: the patient with daily soiling is shown in the table, and the other patient had minor soiling once a month only and no episodes during the diary card period.

Malouf 2000
Liver plays an important role in detoxification of drugs in our body.

About 10% of patients may have liver involvement—Primary Biliary Cirrhosis. Usually occurs 10-15 years after Scleroderma onset.

Symptoms: Itchy skin and fatigue.

BUT 39% HAVE no symptoms.
Primary Biliary Cirrhosis

♦ **Diagnosis:** Increase bilirubin, decrease albumin, and increase alkaline phosphatase.
♦ **Blood test for anti-mitochondrial and anti-smooth muscle antibody.**
♦ **Treatment:** Ursodeoxycholic acid 500-1,000 mg three-four times/day.
♦ **May need liver transplantation.**
Scleroderma Gastrointestinal Tract 2.0 Instrument

- Captures gut involvement in people with SSc.
- 34-item instrument for clinical care and clinical trials.
- Takes approximately 8 minutes to complete.
- SSC-GIT has 7 scales
  - Reflux
  - Distension/Bloating
  - Diarrhea
  - Constipation
  - Fecal Soilage
  - Emotional well-being
  - Social functioning

The UCLA SCTC GIT 2.0 Questionnaire

Before beginning the UCLA SCTC GIT 2.0 Questionnaire, please answer a few questions about yourself. Providing your name and/or email address is optional, and will only be used to contact you in the future regarding updates to this instrument or about new surveys. By providing us with your email address, you indicate that you would like to receive such updates.

Name (optional):

Email address (optional):

Age:

Gender:

I am a:

Submit and Start Survey
The UCLA SCTC GIT 2.0 Questionnaire

Your total GIT score is **0.911**. Your individual section scores are detailed in the table below and after each section in the questionnaire.

[Click here](#) for a printable version of your results.

<table>
<thead>
<tr>
<th>Category</th>
<th>Your Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reflux</td>
<td>0.13</td>
</tr>
<tr>
<td>Distension/Bloating</td>
<td>3</td>
</tr>
<tr>
<td>Sollage</td>
<td>0</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>2</td>
</tr>
<tr>
<td>Constipation</td>
<td>0.25</td>
</tr>
<tr>
<td>Social Function</td>
<td>0.87</td>
</tr>
<tr>
<td>Emotional Well-Being</td>
<td>0.33</td>
</tr>
<tr>
<td>GIT Score</td>
<td>0.91</td>
</tr>
</tbody>
</table>
Conclusions

♦ Scleroderma frequently effects the gut.
♦ Symptoms can be distressing and can cause impairment of person's quality of life.
♦ Good tests are available to find the location and extent of involvement.
♦ Appropriate treatments are very effective.
SUPPORT

◆ Scleroderma Foundation
◆ NIH
UNIVERSITY OF MICHIGAN
SCLERODERMA PROGRAM

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