

## **The gastro-intestinal tract in systemic sclerosis**

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Systemic sclerosis (SSc) is a disease abnormality affecting the vessels and the connective tissue. Besides the skin, joints, muscles, several internal organs can also be involved in SSc including the gastrointestinal tract (GI). The internal organ symptoms are complex (different organs can be damaged at the same time to different extent), and heterogeneous (the involvement does not follow the same pattern in a particular patient). Patients with SSc may develop abnormalities of the digestive system from the mouth to the anal canal. The GI complications usually originate from decreased gastrointestinal movements. The increased stiffness and weakness of the muscle in the GI tract leads to decreased movement of food (“dysmotility”). Dysmotility is a term used to describe diseases of the muscles of the gastrointestinal tract (esophagus, stomach, small and large intestines). In patients with SSc, the esophagus-stomach-intestinal movements become „lazy”. The disturbed movements (with other words, diminished peristalsis) is caused by the injury of nerves of the GI system, and also by the weakness and damage of smooth muscles that are responsible of the movements all along the GI system, therefore the muscles in the GI tract are not able to work properly. GI involvement is present in more than 80% of the patients, and both subsets (diffuse and limited SSc) are equally affected.

GI involvement consists of a variety of complaints including heartburn, difficulty in swallowing, nausea-vomiting, bloating, constipation, diarrhea, and abdominal pain. The symptoms can profoundly influence the quality of life. Furthermore, some symptoms can be even life threatening.

The gastrointestinal tract starts with the oral cavity. Decrease in oral aperture caused by the skin involvement around the mouth may cause difficulties in eating. Saliva production is often decreased ending up with dry mouth and throat. A sensation of food sticking in the throat may also occur. Dental decay problems are also often present, therefore effective tooth cleaning is very important in patients with SSc. Because of the decreased ability to mouth opening, it is difficult to keep oral hygiene.

Esophagus is the tube for food travelling between the mouth and the stomach. The esophagus is a commonly involved organ in SSc. Swallowing difficulties are often present in SSc. Symptoms include chest pressure, and a burning feeling after eating. These particular symptoms are caused by the slow movement of food through the esophagus. Furthermore, the narrowing of the lower part of the esophagus can also occur. The lower esophageal sphincter (valve) is a gate which opens to permit food to enter the stomach and then closes to prevent food from coming back up. In patients with SSc, this particular gate between the esophagus and stomach may not close perfectly, and the acid from the stomach can backwash into the esophagus causing a burning pain (“heartburn”). The gastro- esophageal reflux disease /GERD/) in SSc therefore means that the acidic content of the stomach regularly gets backward to the esophagus because of the insufficient closing between the stomach and esophagus. A frequent acid backwash causes inflammation and scarring of the lower portion of the esophagus, ending with a narrowing (“stricture”) of the tube. This particular chronic inflammation and scarring further worsens the swallowing problems. Without therapy, some patients may develop a serious esophagus narrowing. In this case, the patient may even need to have the esophagus dilated periodically to improve swallowing.

Acid production of the stomach can be reduced, and the gastro-esophageal reflux disease can be improved by avoiding the consumption of alcohol, fatty or spicy foods, chocolate, tobacco and caffeine. An upright position after meals, eating small and frequent meals is useful. It is also advised to avoid eating for several hours before bedtime. These particular lifestyle measures prevent or at least decrease acid backwash into the esophagus. Elevating the head of the bed six to eight inches is also helpful. The treatment is to reduce the acid production of the stomach by using proton pump inhibitor or H<sub>2</sub> blocker agents. High doses and long term treatment are often required. Motility-increasing agents might also be occasionally used.

In summary, the overall advices for patients with esophageal involvement are as follows:

#### Lifestyle maneuvers

- Avoid eating 2-3 hrs before bedtime
- Stop smoking
- Elevate the head of the bed
- Minimize reflux producing foods (alcohol, caffeine, citrus juices)
- Try to avoid certain drugs (NSAIDs, anticholinergics, tricyclic antidepressants)
  - Avoid pill induced esophagitis (NSAIDs, bisphosphonates, doxycycline/tetracycline, potassium chloride, ascorbic acid, quinidine, ferrous sulphate)
- „Take you pills at least one hour before bedtime with a full glass of water.”

#### Medication

- Proton pump inhibitors, (±H<sub>2</sub> blockers, or alone); Often higher doses are necessary than usual, usually for lifetime (!)
- Avoid abrupt withdrawal of proton pump inhibitors.

Complaint of gastric (stomach) manifestations includes early satiety, bloating, dyspepsia, nausea, and vomiting. This is caused by abnormal gastric motility and the final outcome is a delayed gastric emptying.

Similar symptoms may be present in patients with small bowel involvement, and furthermore abdominal pain, diarrhea, and weight loss can also occur. Movements of the bowel become „lazy”; the weak bowel muscles do not work efficiently in pushing food through the bowel. Due to the low small bowel intestinal movements, bacteria ascend backward from the large bowel to the originally sterile small bowel. Small intestinal bacterial overgrowth is often present in SSc. These bacteria appearing in the small bowel cause chronic bowel inflammation, diarrhea, and abnormal absorption of the food substances. This condition called „malabsorption” leads to weight loss. Patients may also experience a bloating and abdominal pain. Intestinal pseudo-obstruction (false blockage in the bowels) is a severe condition also caused by severely decreased bowel movements. **Symptoms** include cramps, stomach pain, nausea, vomiting, bloating, fewer bowel movements than usual, and loose stools. This is a severe condition that needs immediate medical intervention.

In case of diarrhea or malabsorption, there is a need to use antibiotics. Supplementary vitamins, calcium and iron may also be necessary. The amount of fatty foods in the diet should be reduced, and the amount of carbohydrates increased. In severe cases, professional help by a dietician may also be required. If the malabsorption is very severe, a long term total parenteral nutrition may also be necessary. This is an effective long-term therapy for intestinal failure. Bone mineral density testing is mandatory because bone loss (osteoporosis) is often a consequence of a poor nutrition and malabsorption.

Large bowel involvement is also a frequent gastrointestinal complication. Constipation and diarrhoea are everyday problems for many SSc patients, symptomatic treatment may be

effective. Patients with SSc often develop anorectal disease. Fecal incontinence is a frequent manifestation of disease. This may be aggravated when patients have diarrhea.

In summary, the overall advices for patients with bowel involvement are as follows:

Lifestyle measures

- Small, frequent meals are important
- Increase fluid intake. Liquids should be emphasized over solid foods
- Avoid excessive high fiber food intake
- Low in fat (fat delays gastric emptying)
- Avoid difficult-to-chew foods (vegetables, fiber)
- Encourage moderate physical exercise
  - Diarrhea: lactose should be avoided, substitution of dietary fat with medium-chain triglycerides

Therapy

- Monthly rotating antibiotics
- Prokinetics before meal
- Treatment of malabsorption
  - Symptomatic treatment of constipation:
    - Bulk laxatives (methylcellulose, polycarbophyl; PEG, sorbitol, avoid mineral oil);
    - Stimulant laxatives (senna, cascara sagrada, aloe, etc.); other symptomatic drugs

Other gastrointestinal manifestations

The most important vessel-related GI disease is the „watermelon stomach” (with other name: gastric antral vascular ectasia /GAVE/). This is a condition caused by abnormally formed vessels in the stomach. The lining of the stomach bleeds, causing it to look like the characteristic stripes of a watermelon when viewed by endoscopy. Watermelon stomach may cause chronic bleeding and as a consequence severe anemia. It is usually treated with endoscopic laser surgery.

Primary biliary cirrhosis is a chronic progressive liver disease characterized by destruction of ducts and finally causing liver cirrhosis. It can be associated with the limited form of systemic sclerosis.

EULAR has recently published the recommendations for the treatment of SSc. The GI system related recommendations are as follows:

-Despite the lack of specific randomized control trials, experts believe that proton pump inhibitors should be used for prevention of SSc-related gastro esophageal reflux, esophageal ulcers and strictures.

-Despite the lack of specific randomized control trials, experts believe that prokinetic drugs should be used for the management of SSc-related symptomatic motility disturbances (dysphagia, GERD, early satiety, bloating, pseudoobstruction, etc.).

-Despite the lack of specific randomized control trials experts believe that, when malabsorption is due to bacterial overgrowth, rotating antibiotics may be useful in SSc patients.

The approach to these GI-related manifestations, we should carefully evaluate the clinical features of a particular patient. History taking is suitable to call the attention to most of

the motility disorders, since esophageal dysmotility, gastroparesis, intestinal bacterial overgrowth, colonic dysmotility or anorectal involvement present typical symptoms. Functional studies (barium swallowing, esophagus manometry, gastric emptying studies, culture of intestinal fluid, H<sub>2</sub> breath test, fat excretion test, colonic transit studies, and anorectal functional tests) are the usual investigations that provide a deeper insight into the GI involvement. Esophago-gastro-bulboscopy, colonoscopy or capsule endoscopy are also used to detect the extent of GI problems in patients with SSc.

In the future, there is also a need to further increase the knowledge of the scleroderma patients about their GI involvement. To achieve this particular goal, a crucial issue that patient's organizations devoted to this particular topic should spread information about the disease in all over the world. Another important aspect of the patient's contribution to improvement of their care is the active participation in the development of different health measurement instrument and scales.

## Dansk oversættelse .

**NB: Der kan være omtale af behandlinger som ikke anvendes i Danmark.**

Sygdommen Systemisk Sklerodermi (SSC) kan give misdannelser der kan få indflydelse på blodkar og bindevæv. Foruden hud, led og muskler, kan flere indvendige organer også være angrebet/involveret samtidig, blandt andet mave tarmsystemet. Symptomerne er komplekse, og flere organer kan blive angrebet samtidig og uensartet. Symptomerne og omfanget/angrebet kan variere fra patient til patient.

Patienter med SSc kan udvikle misdannelser i fordøjelsessystemet, lige fra munden til endetarmen.

Der er ofte nedsat tarmbevægelser som følge af stivhed og svage muskler i mave tarmkanalen, hvilket medfører nedsat bevægelighed for fødevarer. Dysmotility er det ord der anvendes for, at beskrive sygdomme i muskler i mave – tarmkanalen (spiserør, mave, tynd-og tyktarm). Hos patienter med SSc er bevægelserne i fordøjelsessystemet blive "doven". De nedsatte bevægelser er forårsaget af skader på nerver og de glatte muskler i hele fordøjelsessystemet, hvilket bevirker, at fordøjelses systemet ikke arbejder optimalt. Skader på nerver og muskler er til stede i over 80% hos patienter med både diffus og begrænset SSc .

Der kan være forskellige komplikationer i mave tarmsystemet, herunder, halsbrand, synkebesvær, kvalme, opkastning, oppustethed, forstoppelse, diarré og mavesmerter. Hvilket kan have indflydelse på livskvaliteten. Nogle symptomer kan være livstruende.

Fordøjelsessystemet starter med mundhulen. Begrænset bevægelighed af mundåbningen – "karpemund" , kan give spiseproblemer. Nedsat spytt produktion forårsager tør mund og hals. Det føles som om, at maden har vanskeligt ved, at passere spiserøret. På grund af problemer med at åbne munden, er det svært at have en effektiv tandrensning, og der opstår derfor hulle i tænderne. Det er vigtigt for patienter med SSc at holde en god mundhygiejne.

Transport af mad fra mund til mave sker gennem spiserøret. Ved SSc er der ofte problemer i spiserøret, synkebesvær, trykken for brystet og en brændende fornemmelse efter at have spist. Årsag til symptomerne er, den langsomme bevægelse af mad gennem spiserøret. Der kan også være en forsnævring i den nederste del af spiserøret. Lukkemuskelen i det nederste af spiserøret åbner for, at maden kan komme ned i maven, og derefter lukker den, for at maden ikke skal komme op igen. Hos patienter med SSc er der ofte problemer med, at lukkemuskelen ikke lukker helt, syre fra maven giver sure opstød, en brændende fornemmelse "reflux". De hyppige sure opstød kan give kronisk betændelse og arvæv hvilket forværrer synkebesværet. Uden behandling kan der udvikles en alvorlig forsnævring af spiserøret.

Ved for høj syreproduktionen og sure opstød/Reflux kan det hjælpe, at undgå alkohol, fed og krydret mad, chokolade, tobak og koffein. Sid oprejst efter et måltid, spis flere små måltider.

Spis ikke før sengetid. Hæv hovedgærdet i sengen.

De generelle råd er;

- Undgå at spise 2-3 timer før sengetid.
- Stop rygning.
- Løft sengens hovedgærdet.
- Begræns sure opstød/Reflux, undgå alkohol, koffein, citron saft, fed og krydret mad.
- Undgå medicin af typen NSAID Kodimagnyl, Ascorbin syre m. flere se på indlæssedlen.
- Tag dine piller mindst 1 time før og med et glas vand.
- Syredæmpende medicin skal ofte gives i højere doser end normalt.
- Ved ophør med syredæmpende medicin skal det sket gradvis.

De fleste patienter med Reflux klager over, tidlig mæthed, oppustethed, fordøjelses vanskeligheder, kvalme og opkast.

Lignende symptomer kan være til stede ved problemer med tyndtarmen, her er det desuden mavesmerter, diarré og væggtab kan forekomme. Musklerne i tarmen bliver svage/dovne og arbejder ikke effektivt, men at presser fødevarerne gennem tarmen.

På grund af de langsomme/dovne tarmbevægelser, kan bakterier bevæge sig "baglæns", fra tyktarm til tyndtarm. Høj vækst af bakterier i tyndtarmen er ofte til stede ved SSc. Bakterier i tyndtarmen kan forårsage, kronisk maveinfektion, diarré og unormal optagelse af mad, denne tilstand kan medføre væggtab. Der kan også forekomme, oppustethed, mavesmerter, kramper, kvalme, opkastning og afføring færre end normalt, og løs afføring. Tilstanden er alvorlig og kræver medicinsk behandling. Der kan være behov for, at bruge antibiotika, suppleret med vitamin tilskud i form af, kalcium og jern kan være nødvendigt. Mængden af fede fødevarer i kosten bør reduceres, og mængden af kulhydrater bør øges. I svære tilfælde kan det være nødvendigt med professionel hjælp af en diætist. I svære tilfælde kan det være nødvendigt med streng diæt.

Tab af knoglemasse/osteoporose er ofte et resultat af dårlig ernæring/fødeoptagelse, og derfor bør der foretages obligatorisk undersøgelse for osteoporose.

Komplikationer i tyktarm, forstoppelse og diarré er hverdagens problemer for mange SSc patienter, og symptom behandling skal være effektiv. Afførings inkontinens ses ofte, og det forværes når patienten har diarré.

De generelle råd er;

- Små og hyppige måltider.

- Øget vædskeindtagelse.
- Undgå fiberrig kost.
- Lavt fedtindtag.
- Undgå mad med højt fiberindhold.
- Vær fysisk aktiv.
- Undgå mælkesukker/laktose.

#### Behandling.

- Behandling med antibiotika, hvor arten af det aktive stof ændres hver måned.
- Før måltid medicin mod for megen mavesyre.
- Behandling af forstoppelse.
- Behandling af fordøjelses besvær.

#### Andre symptomer fra maven:

- " Vandmelon" mave ( gastric antral vascular ectasia/GAVE) årsagen er misdannelser i mavens slimhinder. Misdannelsen kan give blødninger, hvilket ved endoskopi ses som de karakteristiske striber på vandmelon.

Vandmelon mave kan forårsage kronisk blødning og medføre alvorlig blodmangel, der normalt behandles med endoskopisk laser kirurgi.