Diagnosis and treatment of non-ulcerative dyspepsia syndrome

- Dyspepsia syndrome is determined as pain or discomfort localized in the epigastric area closer to the medial line. Pains localized in the right and left subcostal areas are not regarded as dyspepsia syndrome. A complex of individual unpleasant symptoms being identified as weight and repletion in the epigastrium, as well as nausea and early saturation but not pain, are recognized as the discomfort.

Patients' complaints on admission corresponding to the complex of symptoms in gastric dyspepsia:

- pains in the epigastric area
- gastroesophageal regurgitation and epigastric burning (heartburn)
- anorexia, nausea and vomiting
- early saturation during the meals
- a feeling of «heavy stomach» in the epigastric area
- meteorism, eructation, aerophagia (air swallowing).

- A complex of symptoms in dyspepsia syndrome is to be distinguished from the one in gastroesophageal reflux (heartburn and burning pains in the area of xiphoid process predominate) or in irritated intestine syndrome (pains are associated with defecation and accompanied with disturbances in defecation frequency and stool consistence).

- Depending on the causes triggering dyspeptic disorders, there is **organic** and **functional (non-ulcerative**) dyspepsia.

Organic dyspepsia is recognized if the following markers are highlighted:

- esophageal disease: reflux- esophagitis
- gastric disease: ulcer, cancer, gastritis
- other GIT diseases: chronic pancreatitis, Crohn's disease, pancreas cancer, colon cancer
- other organ's diseases: cardiac, renal, hepatic insufficiency, Addison's disease, toxic goiter, diabetes mellitus, hypo- and hyperthyroidism, hyperparathyroidism
- drug therapy: non-steroid anti-inflammatory drugs, cardiac glycosides, antibiotics
- other causes: alcohol abuse, pregnancy, psychic disorders, depressions, neuroses

- If to exclude the diseases mentioned after a through examination, the patients (in case the dyspeptic complaints proceed more than 12 weeks, roughly a year) are considered to have the syndrome of non-ulcerative dyspepsia.

Classification of functional dyspepsia.

According to **A. Smout et al. (1992)**

- - according to intestinal motility: gastric motility disorders, pylorus motility disorders, gastroparesis, coordination disturbance between stomach and duodenum; - according to evacuation from the stomach: delayed evacuation, accelerated evacuation

<u>According to N. Talley (1991), M. von Oytryve et al. (1993)</u>

- ulcerative-like variant;
- refluxoid variant;
- dyskinetic variant;
- non-specific variant.

- In 20-69% of patients with ulcerative-like variant the duodeno-gastric reflux, delayed evacuation from the stomach, and time prolongation during the passage within the small intestine are to occur. More than a half of patients with dyskinetic variant express poor stomach motility. At the same time, some patients with functional dyspepsia present no harmful changes in motility of esophagus, stomach and duodenum.

Clinical variation of non-ulcerative dyspepsia.

- Depending on the either symptoms predominated in the clinical presentation of non-ulcerative dyspepsia syndrome, **ulcerative-like** and **dyskinetic variants** are distinguished.

Clinical characteristics of various non-ulcerative dyspepsias

Ulcerative-like type

- Pains localized in the epigastric area
- Pains subside soon after taking antacids
- Hunger pains
- Nocturnal pains
- Recurring pains

Dyskinetic type

- Early saturation
- Feeling of repletion in the epigastria area after the meals
- Nausea
- Upper tympania
- Feeling of discomfort, exaggerating after the meals

- If the symptoms presented in patients do not correspond with the underlined variants, then the symptoms are to be associated with **non-specific variant** of nonulcerative dyspepsia. A combination of non-ulcerative dyspepsia with gastro esophageal reflux disease and irritated intestine syndroms are also possible.

Etiology and pathogenesis

- Chronic gastritis usually associated with pyloric helicobacterium (H. pylori), used to be recognized as the cause for dyspeptic disorders, if no signs of ulcerative disease, stomach cancer, cholelithiasis, etc. were revealed in patients with dyspepsia syndrome. However, recent investigations showed **lack of correlation between changes in gastric mucous membrane and dyspeptic complaints,** and a massive amount of patients with chronic gastritis feel quite sound.

- Chronic gastritis associated with H. pylori is frequently revealed in patients with non-ulcerative dyspepsia syndrome. H. pylori eradication (suppression) resulted in inflammatory process suppression in the gastric mucous membrane, however, it didn't favour the disappearance of dyspeptic complaints in most of patients.

- The recent findings have also exposed **the lack in distinction concerning the hydrochloric acid secretion in health and disease.** No patients having smoking habits, alcohol abuse, tea and coffee preferences, as well as non-steroid
- anti-inflammatory drugs were noted among the mentioned category in comparison with those ones with other gastrointestinal diseases.

- Gastric and duodenal motility disorder proved to be the chief pathogenetic factors of non-ulcerative dyspepsia syndrome. There is a link between the definite dyspeptic complaints and specific motility disorders in the upper parts of gastrointestinal tract

Correlation of various pathological and physiological mechanisms of functional dyspepsia with clinical symptoms.

Mechanisms	*Frequency, %*	*Correlated symptoms*
H. pylori	15-20	Dependency is not detected
Gastroparesis	25-40	Feeling of repletion after the meals, nausea, vomiting
Abnormality in gastric accommodation	40	Early saturation
Heightened sensibility of a gastric wall to the extension.	60	Feeling of repletion, pains on an empty stomach

- Gastric accommodation disorder (accommodation is determined here as capability of the fundic part of the stomach to relax after food absorption) observed in 40% of patients with non-ulcerative dyspepsia, results in disturbances to distribute the food in the stomach and early saturation as well.

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- If stomach evacuates the food well, the cause for the dyspeptic complaints is a heightened sensibility of stomach receptors on the walls to extension (so-called, visceral hypersensitivity).

Diagnosis and differential diagnosis.

- **A complex of symptoms in non-ulcerative dyspepsia is of no specific ground,** therefore, the diagnosis making is based on the exclusion of those diseases, which are of organic dyspepsia origin (firstly, ulcerative disease, stomach ulcer, gastroesophageal reflux disease, cholecystitis and pancreatitis).

- It is essential to take into account secondary motility derangement of the upper parts of the GIT (for example, in diabetes mellitus, Addison's keloid, systemic scleroderma).

- The syndrome of *gastric dyspepsia* in ulcerative disease characterizes with response on food, seasonal character of exacerbation in many patients. Structurally, the syndrome resembles the one in chronic gastritis. Ulcerative stomach disease characterizes with epigastralgia after the food. Time of its origin is noticed to depend on ulcer localization: the lower ulcer is, the later pain occurs. Ulcers of antral part of the stomach resemble those of ulcerative disease of the duodenum.

stomach ulcer

- The diagnostical method of stomach ulcer is an X-ray examination. But in some cases, ulcers may not be revealed, then gastroscopy is to be applied.

Stomach cancer

- Stomach cancer is manifested by gastric dyspepsia, which characterizes with persistence and progression. The gastric dyspepsia is not associated with the food. Most of patients express the whole range of signs, such as, nausea, appetite loss, even anorexia, «bursting» and weight in the epigastrium, vomiting after food intake.
- Some patients may develop gastric dyspepsia followed by stomach cancer. Therefore, the correlation between diet violence, gastric dyspepsia and cancer disappears.

chronic cholecystitis

- Dyspeptic complaints have a more frequent occurrence during the chronic cholecystitis development. Vomiting is presented in 30-50% of patients. In association with hypotonic dyskinesia of the gall bladder, pain and a feeling of weight in the right hypochondrium subside after vomiting.

- During the period of exacerbation, patients complain of nausea, bitter taste, eructation with bitter. Due to the development of secondary duodenitis, gastritis, pancreatitis, enteritis the following signs are presented: heartburn, eructation with «rotten», meteorism, appetite loss and diarrhea.

pancreatic dyspepsia

- is expressed in exacerbation or severe course of the disease. It is manifested by:
- eructation with air (aerophagia) or food eaten;
- nausea, vomiting;
- appetite loss;
- fat food rejection;
- tympania;
- hypersalivation.

Gastric dyspepsia in *chronic gastritis*

- is characterized with the dependency on diet violence. It is presented by tympania and pressure discomfort in the epigastrium, as well as eructation, soon regurgitation. Nausea and vomiting are sometimes to occur. Beside gastric dyspepsia, chronic gastritis is manifested by pains in the epigastrium appeared soon after food intake. Food consistence and character are also of importance.

- As the disease progresses, patients with chronic gastritis have tendency to hyposecretion and reduction in acidity of gastric juice, in some pronounced case the achylic syndrome appears.

- Antral gastritis, gastroduodenitis may resemble ulcerative disease of the duodenum in their clinical manifestations. The disease is frequently accompanied with dyskinesia of biliary and pancreatic ducts and intestines. Gastroscopy and biopsy are essential in contemporary requirements while diagnosing chronic gastritis (it is a clinical morphological diagnosis).

Gastroesophageal reflux disease

- **is a chronic recurrence conditioned by retrograde entrance of food mass into esophagus. Dyspeptic manifestations include the following:**
- Heartburn is recognized as a severe burn in the substernal area, which irradiates upward from xiphoid process. It is accompanied by the reduction of pH in the esophagus lower than 4.0. It is common to bee triggered by a definite food intake, overfeeding, forward incline, physical activity, horizontal position, alcohol and smoking.

- Pains in the epigastrium associated or not with the food taken may occur quite often.
- Vomiting is observed more frequently in comparison with ulcerative or duodenal disease.
- Eructation is accompanied by a bitter or acid feeling in the mouth. Both heartburn and eructation bother mostly in level position and forward inclinations.

Methods of differential diagnosis applied in functional dyspepsia.

- Esophagogastroduodenoscopy
- X-ray examination
- Ultrasonography
- Intragastric and intraesophageal monitoring of pH
- Manometry of the lower esophageal sphincter
- Electrogastrography
- Test course for drug therapy (4-8 weeks)

- Clinical and biomedical blood tests, as well as ultrasound investigations of the abdomen, gastroduodenoscopy and X-ray examination with barium sulfate (ifindicated), computed tomography are carried out.
- If no symptoms denoting motility disorder of the upper parts of the GIT are detected, then electrogastrgraphy, gastric scintigraphy (gamma camera) with technetium and indium isotopes are applied.

- It is supposed to be important to take alarm symptoms or «red flags» into account while making the diagnosis of non-ulcerative dyspepsia. Their presence excludes the diagnosis of non-ulcerative dyspepsia and requires a more profound and thorough diagnostic search to reveal some serious organic disorders.

Alarm symptoms are characterized as follows:

- fever
- anemia
- dysphagy
- leukocytosis
- visible admixture
- accelerated ESR
- blood in feces
- dyspepsia symptoms occurred over the age of 45
- weight loss

Treatment.

The treatment procedures are to be complex and include not only drug administration, but also changes in patient's life style, regimen and feeding habits, psychotherapeutic methods. Common recommendations consist of frequent and partial feeding, heavy and fat food exclusion, smoking and alcohol arrest, non-stroid anti-inflammatory drugs.

- **Antacidic and antisecretory drugs** (H2-blockers and blockers of proton pump) are indicated in ulcerative-like variant of functional dyspepsia.

T. Omeprasoli 20 мg 2 t. a day

T. Qamateli 20 мg 2 t. A day

- Some patients (about 20-25%) may express positive response to anti-helicobacterial eradication therapy. The treatment may have insufficient effect for the vanishing of dyspeptic disorders, but the risk of ulcerative incidence reduces.

Eradication therapy

T. Omeprasoli 20 mg 2 t. a day

T. Clarithromycini 500 mg 2 t. a dayC

T. Amoxicillini 1000 mg 2 t. a day

- The basic means of patients' treatment of a developing dyskinetic variant is supposed to be prokinetic drugs normalizing the motility of GIT. The blockers of dopamine receptor, such as, **metodopramide (Gerucal)** and **domperidone (Motilium)** are recognized in this group of drugs.

The use of metodopramide (especially long-term one) may cause untoward and **side effects** in a great amount of patients (20-30%), which are the following:

- drowse,
- tiredness,
- anxiety
- extrapyramidal responses

- European Motilium investigations in non-ulcerative dyspepsia treatment at doses of 5-20 mg 3-4 times a day during 3-4 weeks, revealed the reduction in complaints, i.e. from 61-85%). Simultaneously with the reduction of intensity in clinical symptoms, patients develop better evacuation from solid and fluid food.
- Side effects in Motilium application are rare to appear (in 0.5-1.8%) of patients). Headaches, general exhaustion are frequently to be observed.

- **Итомед (Itomed)**

итоприда гидрохлорид

50 мг 3 раза в день

side effects:

-лейкопения, тромбоцитопения,

- **гинекомастия, гиперпролактинемия;**
- **диарея**

- **Cyzapride (propulside, coordinacs)** attracts much attention. This drug is quite effective in functional dyspepsia (in 60-90%> of cases). It is to be taken 15-40 mg in a day (5-10 mg 3-4 times a day) during 4 weeks. It should be noted that this drug is more effective in refluxoid, dyskinetic and non-specific forms of functional dyspepsia. But it is less effective in ulcerative-like forms and has perspective action up to 6 months.

Side effects

- of Cyzapride consist of diarrhea; however, there is no need to arrest the drug. Dose to be taken is to reduce.