INFORMED CONSENT OF THE PATIENT FOR INCLUSION IN THE CLINICAL TRIAL

Study title: Treatment of reflux disease using targeted physiotherapy

Trial participating centres:

1. I. Department of Internal Medicine, Charles University in Prague, Faculty of Medicine and University Hospital in Pilsen, Alej Svobody 80, Pilsen, 304 60, Czech Republic

2. Pavel Kolář´s Centre of Physical Medicine, Walterovo náměstí 329/2, Prague 5 – Jinonice, 158 00, Czech Republic

Patient:……

Birth certificate number:……..

Patient enrolled in the study under number:.....

Dear Madam, Dear Sir,

You have been approached to participate in the above-mentioned clinical study to evaluate the effect of diaphragmatic breathing training on the symptoms associated with gastroesophageal reflux disease (GERD). The diaphragm is a striated (skeletal) muscle that is under partially voluntary control and therefore it can be targeted trained. Improved condition of the diaphragm will not only result in better function in the respiratory system and in correct body posture, but may also improve its function in the so-called antireflux barrier. The diaphragm, together with the lower oesophageal sphincter, plays a crucial role in preventing the return of gastric contents to the oesophagus. According to available data, patients who incorporate diaphragmatic breathing training into the treatment of GERD are more likely to alleviate the associated problems and reduce the consumption of antireflux medication.

Who can participate?

Patients with GERD with persistent symptoms despite lifestyle modification and medical treatment or patients who cannot be taken off antireflux medication because of early return of problems.

What is the purpose of this study?

The aim of this study is to determine the short- and long-term effect of diaphragmatic breathing training on symptoms associated with GERD and to assess whether diaphragmatic breathing improves antireflux barrier function.

How is this study going?

The study will compare the effect of conservative treatment and treatment involving diaphragmatic breathing training. The length of the study is 15 months and consists of 3 months of conservative management (*Control phase*) followed by 3 months of training in diaphragmatic breathing (*Active phase*) and then 9 months of practicing the learned techniques (*Follow-up period*).

The conservative approach (**Control Phase**) consists of regimen measures, i.e. good dietary habits, normal physical activity and medication treatment, which is set to best control your symptoms. At the start of the Control Phase, we will assess your antireflux medication consumption and you will complete two questionnaires about your reflux symptoms and your quality of life. These questionnaires will be completed also at the end of the Control Phase. You will then undergo esophagogastroduodenoscopy (EGDS) to assess the presence of any reflux changes in the oesophageal mucosa, and 2 samples (biopsies) of oesophageal mucosa will be taken to evaluate microscopic reflux changes. Prior to EGDS, any antireflux medication will need to be discontinued for at least 14 days.

Then you will start with diaphragmatic breathing training (**Active Phase**). At the beginning of the Active Phase, two functional esophageal examinations will be performed, i.e. esophageal manometry and 24-hour esophageal pH metry with impedance, to assess the function of the antireflux barrier and the severity of reflux. Antireflux medication will need to be discontinued for a minimum of 14 days prior to the examinations. The diaphragmatic breathing training runs under the guidance of a specialist physiotherapist, and you will attend a total of 6 sessions (1 session per 60 minutes) over 6 weeks. The physiotherapy will follow a pre-determined protocol, as well as the exercises intended for home training. Throughout the Active Phase you will take anti-reflux medication at an unchanged dosage, including the type of medication. At the end of the Active Phase, you will again complete questionnaires regarding your reflux symptoms and your quality of life, and you will undergo a follow-up esophageal manometry and 24-hour esophageal pH metry with impedance after PPI discontinuance.

Active Phase goes on a 9 month **Follow-up period**. Your task during this phase will be to practice diaphragmatic breathing training regularly according to the recommended procedure. During this period you will be allowed to start reducing your antireflux medication. The reduction of medication will be guided by your complaints, the aim will be to reduce the medication to a dose at which your reflux symptoms are still under control or do not worsen. In the Follow-up Period, there will be two check-ups at 3 month intervals where you will again complete questionnaires regarding your reflux disease and quality of life, an assessment of your current PPI consumption and a check-up by a physiotherapist (30 minutes) to assess the correct carrying out of diaphragmatic breathing.

At the end of the Follow-up period, you will complete questionnaires regarding your symptoms and your quality of life for the last time and your current antireflux medication consumption will be assessed. Then you will undergo an final examination, i.e. EGDS including an esophageal biopsy, esophageal manometry and a 24-hour esophageal pH metry with impedance. This concludes the study for you.

What are the potential risks of the study?

The risks to the patient from this study are minimal. You will undergo several invasive examinations (i.e., EGDS, esophageal manometry, and 24-hour esophageal pH metry with impedance) during the study. The overall risk resulting from EGDS as the most invasive of the above mentioned procedures is 0.11%. The questionnaire always takes a maximum of 5 minutes to complete.

It will not be possible to identify you from the biological material and medical data provided for research purposes. Your personal data will be handled in accordance with the applicable data protection laws of the Czech Republic. Participation in the clinical trial may be terminated at any time without affecting further treatment and all further treatment will be carried out in a completely standard manner.

Responsible physician for the I. Department of Internal Medicine of the University Hospital Pilsen: MUDr. Karel Balihar Ph.D., balihar@fnplzen.cz, +420 377 103 322, 234

Responsible physician for Pavel Kolář´s centre of Physical Medicine: MUDr. Lucie Zdrhová, lucie.zdrhova@cpmpk.cz, +420 222 204 304

Responsible physician for the Department of Hepatogastroenterology IKEM (providing esophagogastroduodenoscopy): prof. MUDr. Jan Martínek, Ph.D., coordinator: adela.ryantova@ikem.cz, endoscopy IKEM, +420 26136 2617

PATIENT DECLARATION

1. I, the undersigned, agree to participate in the study. I am over 18 years of age.

2. I have been fully informed about the purpose of the study, its procedures, and what is expected of me. The doctor responsible for the study has explained to me the expected benefits and possible health risks that could occur during my participation in the study and how he/she will proceed if any adverse events occur. I acknowledge that the study is a research activity.

3. I have informed the study physician of all medications I have taken in the last 28 days and those I am currently taking. If any medication is prescribed by another physician, I will inform him/her of my participation in the clinical trial and will not take it without the consent of the study physician.

4. I will cooperate with my physician in my treatment and will inform him/her immediately if any unusual or unexpected symptom occurs.

5. I understand that I can discontinue or withdraw from the study at any time without affecting my future treatment. My participation in the study is voluntary.

6. Upon enrollment in the study, my personal data will be kept in full confidentiality in accordance with the applicable laws of the Czech Republic. My original medical records will be available for inspection by representatives of the sponsor, independent ethics committees, and foreign or local competent authorities (in the Czech Republic, the State Institute for Drug Control) for the purpose of verifying the data obtained. For these cases, the confidentiality of my personal data is guaranteed. In the actual conduct of the study, personal data may only be provided to entities other than those mentioned above without identifying information, that is, anonymous data under a numerical code. Also for research and scientific purposes, my personal data may only be provided without identifying data (anonymous data) or with my explicit consent.

7. All participants in the clinical trial are insured in accordance with the applicable laws of the Czech Republic. Please contact the investigating physician in case you suffer a personal injury as a result of your participation in the clinical trial. Adequate medical care will be provided and reimbursed. You have the right to reimbursement and compensation for personal injury under applicable law. If you experience unexpected symptoms or harm, or if you require medical treatment, seek emergency medical attention immediately and notify the investigating physician.

8. My participation in the study involves the ensuring of highly specialised physiotherapy under more favourable conditions than is usual in clinical practice.

9. I understand that my name will never appear in reports about this study. I, in turn, will not oppose the use of the results from this study.

10. I have received a signed copy of this informed consent.

Signature of the patient:

Signature of the physician in charge of this study:

Date: