Clinical research informed consent form

Title of the study: Characterization of esophageal motility functions and evaluation of prokinetic effectiveness in mechanically ventilated critically ill patients: high-resolution manometry study

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Name and Surname: .....

Identification number: .....

Dear Sir, dear Madam,
We would like to offer you participation in the above-mentioned study. The aim of this study is to assess the degree of esophageal movement impairment, which often accompanies critically ill patients and the effect of a commonly used drug (metoclopramide) on this disorder.

Impaired motility and weakening of the lower esophageal sphincter with backflow of gastric content into the esophagus affects 50-60% of critically ill patients on mechanical ventilation. The cause of this disorder is unclear and is probably associated with impaired organ function caused by the underlying disease with the participation of previous illnesses, medication and other factors. The consequences of this disorder are poor intake of nutrition administered through a tube into the stomach and its backflow to the esophagus, deterioration of nutritional status, easier microbial colonization of the stomach, higher risk of gastric mucosal damage and possibly aspiration of gastric content into the lungs with development of pneumonia. These consequences lead to longer hospital stays and higher mortality. According to previous studies, it is certain that impaired esophageal motility in critically ill patients is completely different from other disorders such as esophageal reflux disease or regurgitation (backflow) of gastric contents, which occurs to a small extent after eating in healthy individuals. One of the possible treatment options for this disorder, which is widely used in critically ill patients but also in patients with digestive problems, is the administration of a drug to improve the motility of the esophagus and stomach - metoclopramide. This drug is the only one in its class available in the Czech Republic that can be administered intravenously, and therefore is frequently used in intensive care in this indication. In healthy individuals, it increases the closing ability of the lower esophageal sphincter and improves forward esophageal motility, however, these data were obtained on fasted subjects. In critically ill patients, metoclopramide improves gastric motility, but the effect on the esophagus and the ability to prevent backflow of gastric contents into the esophagus and possibly into the lungs have not been studied.
The study follows 2 main paths - assessment of esophageal function firstly in critically ill patients on mechanical ventilation and secondly in healthy volunteers in similar conditions in terms of body position and amount of gastric contents as in critically ill patients. Of course, we address you to participate as a healthy volunteer.

How is the study performed?
In the beginning, we will discuss with you your health condition, motivation and eligibility to enter the study. If you agree, the nurse will take a blood sample for basic laboratory tests and

insert a flexible cannula into a superficial vein in your arm. In women of childbearing potential, hCG will be tested to rule out potential pregnancy. You should be fasted for at least 4 hours before the study. Then a special thin catheter (3 mm in diameter) will be inserted through your nose into the stomach. It will be able to measure pressure in the esophagus and the backflow of fluid or air to the esophagus. Subsequently, we will evaluate the function of your esophagus in the supine position with the upper half of the body raised to 30-40% slope, at first on an empty stomach then after ingesting the study meal and then after applying the above-mentioned drug into a vein to improve gastric motility. The study meal consists of nutrition drinks (2x125mL, various flavors available). The estimated duration of the entire study is approximately 60 minutes.

How will you profit from the study?
The first part of this study overlaps with a standard manometric examination of the esophagus, which is able to evaluate the anatomy and function of your esophagus, including the detection of possible axial hiatal hernia. The result of this examination will be provided to you, including a treatment recommendation in the event of any pathology found, and if interested, you will be provided with an explanation of all the findings from different phases of the examination. Discomfort resulting from the insertion of a venous cannula, esophageal catheter and administered study drug (in the case of a completed study) will be compensated by a financial reward of CZK 2,000.

Are there any risks associated with the study?

1 / The risks associated with venous cannula insertion and blood collection are very small, especially with short-term insertion and include discomfort during insertion, the possibility of hematoma or a very small risk of infection.

2 / The risks posed by introduction of a manometric-impedance catheter are again minimal, they include dyspepsia due to nasopharyngeal irritation during catheter insertion. Nosebleeds or nasopharyngeal injuries are not described as the catheter is very soft, but cannot be completely ruled out.

3 / The risk of administering 1 dose of 10 mg metoclopramide into a vein is very small. With the usual therapeutic doses of metoclopramide, side effects are rare and mild and transient. The development of side effects depends on the dose and the overall duration of treatment. Fatigue, drowsiness, restlessness may occur frequently (approximately 10% of patients). Uncommonly, insomnia, headache, confusion, dizziness or mental depression, indigestion, urticaria and dry mouth may occur. Rarely (0.2% of patients), extrapyramidal side effects occur and, in most cases, manifest as acute dystonia. Symptoms may include involuntary movements of the limbs and facial muscles, torticollis, ocular crisis, tongue crawling, trismus, bulbar type speech, opisthotonus, and in rare cases, stridor with dyspnoea. These reactions occur mainly in younger women, in whom the daily dose of metoclopramide is between 30 and 40 mg. The risk of extrapyramidal side effects is reduced if the total daily dose of metoclopramide does not exceed 0.5 mg / kg body weight, i.e. 35 mg / day in a 70 kg human. Symptoms consistent with parkinsonism and tardive dyskinesia may occur, especially in elderly patients who are taking higher doses over a long period of time. Haematological disorders, hypersensitivity reactions, neuroleptic malignant syndrome and urinary incontinence have been reported rarely, but again include long-term drug administration.

All obtained results will be used anonymously and the data will be handled in accordance with the valid laws of the Czech Republic on personal data protection. If the results of the study are published, none of the included subjects will be recognizable from the published data. Participation in this study is entirely voluntary and can be terminated at any time without

the need to provide a reason for withdrawal. If you have any further questions or concerns after reading this information, your questions will be answered at any time.

I attest that the above facts have been communicated and explained to me by the doctor, that I have understood them and that I have had the opportunity to ask additional questions which have been answered by the doctor. By signing this document, I declare that I understand its content and that I agree to the anonymous processing and publication of data obtained during the study.

Signature of subject entering the study: ……..

Signature and name of informing doctor: ....……

In Pilsen, date: …… time: ……..