Study protocol 170485. Approved on 29/06/2017 by UNIQUE ETHICAL COMMITTEE OF THE PROVINCE OF FERRARA, ITALY

Characteristics of INTESTINAL DYSFUNCTION in patients with MULTIPLE SCLEROSIS. Effectiveness of the TRANSANAL IRRIGATION PROCEDURE with the PERISTEEN DEVICE in the treatment of constipation and disease-related anal incontinence.

COVER PAGE

STUDIO 170485. CARATTERISTICHE DELLA DISFUNZIONE INTESTINALE IN PAZIENTI CON SCLEROSI MULTIPLA: EFFICACIA DELLA PROCEDURA DI IRRIGAZIONE TRANSANALE CON IL DISPOSITIVO PERISTEEN NEL TRATTAMENTO DELLA STIPSI E DELLA INCONTINENZA ANALE CORRELATA ALLA MALATTIA
29 June 2017

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INFORMED CONSENT FORM

This Informed Consent Form is for men and women who attend Multiple Sclerosis and Colorectal Outpatient Clinic 2 at the University Hospital of Ferrara, Italy and who we are inviting to participate in research on neurogenic bowel. The title of our research project is:
Characteristics of INTESTINAL DYSFUNCTION in patients with MULTIPLE SCLEROSIS. Effectiveness of the TRANSANAL IRRIGATION PROCEDURE with the PERISTEEN DEVICE in the treatment of constipation and disease-related anal incontinence.

PART I: Information sheet

We are doing research on intestinal dysfunctions in patients with Multiple Sclerosis. I am going to give you information and invite you to be part of this research. You do not have to decide today whether or not you will participate in the research. Before you decide, you can talk to anyone you feel comfortable with about the research.

There may be some words that you do not understand. Please ask me to stop as we go through the information and I will take time to explain. If you have questions later, you can ask them of me, the study doctor or the staff.

Purpose of the research

MS (Multiple Sclerosis) is the most common neurological disease involving disabilities in young adults, with Central Nervous System involvement in both the brain and spinal cord. In a recent review, its incidence in the United Kingdom is estimated at 7 new cases per 100,00 inhabitants per year, with a prevalence of about 100,000 patients. Bowel symptoms, in particular constipation and faecal incontinence, affect more than two thirds of MS patients, and have a significant impact on patients' quality of life (QoL) by significantly limiting their social, occupational and emotional life.

Recently, bowel management based on Transanal Irrigation (TAI) has also been proposed in patients with MS, but TAI efficacy on intestinal transit time and patient's compliance with TAI have not been defined yet.

The aim of this study is to assess the prevalence, characteristics, severity and impact on the Quality of Life of intestinal disorders in patients who consecutively refer to the neurological clinic for the diagnosis and treatment of Multiple Sclerosis at Ferrara University Hospital, Italy.

Secondary objectives are to correlate the severity and characteristics of constipation and fecal incontinence with intestinal transit time and the type of feces evacuated; to evaluate the costs in terms of the precautions (diapers, traverses, drugs, medicated enemas, etc.) and the time dedicated to the evacuation, to study the composition of the intestinal microbiota in MS patients in relation to the type of bowel characteristics, comparing it with the profile of the healthy population of the same region of origin, Emilia-Romagna, Italy. Finally, we will register how these items change in relation to the use of transanal irrigation (TAI).

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Type of Research Intervention

The type of research is observational.
We will assess the severity of bowel dysfunction in patients, like you, affected by Multiple Sclerosis, using questionnaires, diaries and imaging. We will study your intestinal microbioma just recording some fecal samples. Then we will propose a validated treatment for neurogenic bowel that is transanal irrigation (TAI) with a device called Peristeen.

Participant selection

We are inviting all adults with Multiple Sclerosis who attend Multiple Sclerosis Outpatient Clinic to participate in the research to assess and cure intestinal dysfunction correlated to Multiple Sclerosis.

Voluntary Participation

Your participation in this research is entirely voluntary. It is your choice whether to participate or not. Whether you choose to participate or not, all the services you receive at this clinic will continue and nothing will change. If you choose not to participate in this research project, you will be offered the treatment that is routinely offered in this clinic/hospital for Multiple Sclerosis, and we will tell you more about it later. You may change your mind later and stop participating even if you agreed earlier.

If you have a severe intestinal dysfunction you will undergone a X ray transit study and clinical questionnaires to measure the impairment of bowel function intended as constipation or fecal incontinence. X ray transit study is safe with no side effects. Then we will study your intestinal microbioma by fecal samples. Moreover, you will be offered a treatment consisting in bowel lavage from the anus, defined transanal irrigation (TAI). This treatment is safe with no side effects reported in other studies. It has been tested successfully in many diseases, such as spinal cord injury or low anterior resection syndrome after surgery rectal tumours.

Procedures and Protocol

The type of research is composed by two phases. The first phase is observational: we will assess the prevalence, characteristics, severity and impact on the Quality of Life of intestinal disorders in patients with Multiple Sclerosis. In this phase we will administer you two self-filling questionnaires: PacQol (Patient Assessment of Constipation Quality of Life) and NBD (Neurogenic Bowel Dysfunction Score).

If PacQol score will result ≥ 32 you will be sent to the surgical clinic for the second phase. During this phase you will undergo a number of visits varying from 1 to 4 depending on your willingness to continue the study. Further questionnaires will be given you to evaluate the disease status; if you will consent to the continuation of the study, you will be given 7-days food diary, evacuation diary, radiopaque markers, stool collection container and appointment date for plain abdominal X-ray which may coincide with the appointment for examination number 2 (visit 2 or 3). Radiopaque

markers Intestinal Transit Study will be performed by ingestion of 10 markers for 6 days at the same time and execution of a plain abdominal X-ray on the 7th day. You will be asked to collect a fecal sample in a container during the last week before the following inspection at Visit 2.
During the second visit, the outcome of the plain abdominal X-ray will be discussed, the completed diaries will be collected, and the faecal sample will be stored at -20 C° and subsequently sent to the Laboratory of the Department of Pharmacy and Biotechnology of the University of Bologna, Italy for the analysis of the intestinal microbiome composition.
In case of severe intestinal dysfunction (resulted from questionnaires, and Transit Study) you will be offered the adoption of transanal irrigation (TAI) as a way to manage your own evacuation, replacing any other measure used until that moment (suppositoires, enemas) with the exception of the possible intake of macrogols and/or prebiotics and/or probiotics which instead can be continued. This treatment will be proposed to all patients with severe impairment of intestinal function.
The TAI training with Peristeen will be carried out at the surgical clinic of the Surgical Department of the Ferrara University Hospital, Italy, by the personnel involved in the study, usually in a single session, but more sessions may be necessary.
During the following 4 weeks, you will continue to use the Peristeen at home according to the instructions provided by the training staff collecting a stool sample each week. During the last of the four weeks of TAI use you will be asked to repeat the compilation of food diary, evacuation diary, the radiopaque markers Transit Time, and collection of the stool for microbiota analysis. The appointment for the radiography could coincide also in this case with the following visit (visit 3 or 4). During the last visit the outcome of Transit Time X-ray will be discussed, completed diaries and stool samples will be collected, and PAC-QoL questionnaire will be submitted to you if you will complete the study pathway. You will be asked about overall satisfaction of TAI treatment with Peristeen by means of a numerical assessment from 0 to 10. Finally, any your comment will be noted as well any events that might be related to TAI irrigation with Peristeen will be recorded.

The healthcare workers will be looking after you and the other participants very carefully during the study. If there is anything you are concerned about or that is bothering you about the research please talk to me or one of the other researchers.

Duration
The research takes place over 4 weeks in total. During that time, it will be necessary for you to come to the hospital 3 or 4 times for outpatient visits, collection of diaries, fecal samples, training of transanal irrigation, and transit studies with x-ray.
We would like to meet with you 3 months after your last clinic visit for a final check-up.
In total, you will be asked to come 3/4 times to the clinic in 1 month. At the end of 3 months, the research will be finished.

Side Effects
No unwanted effects are expected.

Risks
No risks are expected by participating in this research, except for the risk that transanal irrigation will not be efficacy in you case.

Benefits

If you participate in this research, you will have the following benefits: a solution to your intestinal problems. There may not be any benefit for you, but your participation is likely to help us find the answer to the research question.

Reimbursements

You will not be given any other money or gifts to take part in this research.

Confidentiality

With this research, something out of the ordinary is being done in your community. It is possible that if others in the community are aware that you are participating, they may ask you questions. We will not be sharing the identity of those participating in the research.
The information that we collect from this research project will be kept confidential. Information about you that will be collected during the research will be put away and no-one but the researchers will be able to see it. Any information about you will have a number on it instead of your name. Only the researchers will know what your number is and we will lock that information up with a lock and key. It will not be shared with or given to anyone except Dr Simona Ascanelli.

Sharing the Results

The knowledge that we get from doing this research will be shared with you through community meetings before it is made widely available to the public. Confidential information will not be shared. There will be small meetings in the community and these will be announced. After these meetings, we will publish the results in order that other interested people may learn from our research.

Right to Refuse or Withdraw

You do not have to take part in this research if you do not wish to do so and refusing to participate will not affect your treatment at this clinic in any way. You will still have all the benefits that you would otherwise have at this clinic. You may stop participating in the research at any time that you wish without losing any of your rights as a patient here.

Alternatives to Participating

If you do not wish to take part in the research, you will be provided with the established standard treatment available like bowel care with enemas or suppositories.

Who to Contact

If you have any questions you may ask them now or later, even after the study has started. If you wish to ask questions later, you may contact any of the following: Simona Ascanelli, simona.ascanelli@unife.it

This proposal has been reviewed and approved by regional ethical Committee, which is a committee whose task it is to make sure that research participants are protected from harm. If you wish to find about more about the Ethical regional Board, contact Marco Voci, m.voci@ospfe.it.

PART II: Certificate of Consent

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked, have been answered to my satisfaction. I consent voluntarily to participate as a participant in this research.

Print Name of Participant_____

Signature of Participant _____

Date _____
Day/month/year

If illiterate
A literate witness must sign (if possible, this person should be selected by the participant and should have no connection to the research team). Participants who are illiterate should include their thumb-print as well.
I have witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Print name of witness_____ **AND** **Thumb print of participant**

Signature of witness _____

Date _____
Day/month/year

Statement by the researcher/person taking consent
I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands the surgical procedure will be done.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.
A copy of this ICF has been provided to the participant.

Print Name of Researcher/person taking the consent_____

Signature of Researcher /person taking the consent_____

Date _____
Day/month/year