Effect of an Anti-inflammatory Diet on the Nutritional Status and Cytokine Expression of Patients With Locally Advanced Cervical Cancer: A Randomized Clinical Trial.

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INFORMATION AND INFORMED CONSENT FOR THE PATIENT WHO PARTICIPATES IN THE RESEARCH PROTOCOL

Title: Effect of an Anti-inflammatory Diet on the Nutritional Status and Cytokine Expression of Patients With Locally Advanced Cervical Cancer: A Randomized Clinical Trial.

1. **Investigator data.**

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If you have questions about your rights to participate in a research study, you can contact the Research Ethics Committee with Dr. Emma Libertad Verastegui Aviles, President, on tel. 56280400, extension 37015.

2. **Voluntary participation.**

Through this document it is expressed that your participation in this study is voluntary and refusing to participate will not influence the treatment to which you are entitled as an INCan patient. Likewise, the patient will receive an answer to any question, doubt, or clarification about the procedures, risks, benefits, and other matters related to research and treatment.

This consent form may contain words or information that you are not familiar with. Please ask the study doctor or study staff to explain any words or information that you do not clearly understand. You may take a copy, without signatures, of this consent form with you to read it further and consider your participation, as well as to discuss it with your family or friends before making a decision.

It is worth noting the commitment to provide you with updated information obtained during the study.

Your doctor has diagnosed you with cervical cancer. We are inviting you to participate in research to find out if an "anti-inflammatory" diet can help cervical cancer patients

improve their nutrition, reduce some symptoms of gastrointestinal toxicities (caused by cancer treatment) such as diarrhea or constipation, and that your quality of life is better.

This anti-inflammatory diet is a diet that consists of covering all the energy and nutrient needs that each patient needs, personally, to prevent weight loss or malnutrition; In addition, foods that have properties that are known to help reduce inflammation (but studies like this have not been done to prove it) and improve intestinal health, such as fiber and vitamins, will be recommended to reduce intestinal symptoms so that they feel better, can eat what they need and so that they do not become malnourished, and also tolerate treatment better.

It is expected that 156 women with cervical cancer will participate. Your participation is completely voluntary and will not affect your medical care.

3. Justification and purpose of the study.

Because cancer treatment is not selective, some parts of the body can be damaged, such as the intestine; When this occurs, discomfort such as nausea, diarrhea, constipation, inflammation, pain, and other symptoms that together are known as gastrointestinal toxicity can occur, which could also impact the quality with which you do your day-to-day activities (quality of life). We believe that the anti-inflammatory diet, by including foods with nutritional and anti-inflammatory properties, could help reduce intestinal inflammation from being so intense. Another of the benefits of this diet is its high content of soluble fiber, this fiber is particularly special because when it comes into contact with water it forms a kind of gel, so when consumed it could help reduce both diarrhea and constipation, should any occur.

The anti-inflammatory diet is to be compared to a low-residue diet. The low-residue diet consists of reducing the amount of fat, fiber, and lactose (which is the sugar in milk), to avoid diarrhea. This diet will also cover the energy and nutrient needs that each patient needs.

Our main objective is to evaluate the effect of the anti-inflammatory diet, compared to the low-residue diet, on nutritional status, intestinal toxicity complaints, and the amount of some proteins that are produced when inflammation is present and that are measured. in blood and feces (or poop), in patients with locally advanced cervical cancer.

78 patients will be included in the anti-inflammatory diet group and we will compare them with 78 patients receiving the low-residue diet. It should be noted that the group to which you will be assigned is chosen by chance, so we cannot guarantee that you will have one or another diet.

4. Data of the procedure.

Each patient will be evaluated in 5 visits:

1. Two weeks before the start of cancer treatment.
2. At the start of cancer treatment.
3. In the third cycle of chemotherapy.
4. At the end of brachytherapy.
5. 3 months after completing cancer treatment.

During these visits, you will be asked questions and measurements to find out your nutritional status. Weight, height, waist, and hand strength measurements will be taken; In addition, you will be asked about your diet and the discomforts of gastrointestinal toxicity that you may present.

The following questionnaires will be applied:

1. Subjective Global Assessment Questionnaire Generated by the Patient. This questionnaire will be applied to you to find out if you have had changes in your weight, your diet, and your habits, to evaluate if you are at risk of developing malnutrition. The application lasts 10 minutes.
2. EORTC QLQ-CX24 Quality of Life Questionnaire. This questionnaire will be applied to you to find out if you have had different symptoms specific to cervical cancer and the treatment you are receiving, which affect your life and prevent you from doing the activities you normally do. The application lasts 10-15 minutes.
3. EORTC QLQ-C30 Quality of Life Questionnaire. This questionnaire will be applied to find out if your day-to-day activities have been affected, and if you have had discomfort or difficulties that prevent you from doing the things you regularly do. The application lasts 10-15 minutes.

At visits 1, 3, and 5, a blood sample will be taken to measure some proteins (called cytokines) that the body makes when there is inflammation, and a stool sample (poop) to measure some proteins that the intestine makes when inflammation occurs. In addition, the bacteria that are part of your intestinal flora will be measured.

In this study, tumor samples will not be collected and therefore will not be analyzed, so they will not be used for permanent or immortal cell lines.

What discomfort do these procedures cause?

Measurements of weight, height, waist, and hand strength do not cause any discomfort.

Obtaining a blood sample by venipuncture may cause pain, redness, momentary bleeding, and bruising at the puncture site. In rare cases there may be dizziness or fainting, in a few cases there may be skin infections.

Obtaining the stool sample (poop) will be done when you go to have a bowel movement in the morning and does not cause any discomfort.

Treatment.

Once your doctor decides that you are going to receive your cancer treatment, the investigator determines that you can participate in the study because you meet the requirements, and if you consent, he will begin with an evaluation of your nutritional status by part of the research nutritionist.

What is the study treatment?

The treatment will consist of taking an anti-inflammatory diet. The research nutritionist will provide you with your written diet, which will be designed specifically for your energy and nutrient needs. The nutritionist will talk with you to find out what foods you like and what foods you can get, and will write down in your written diet, several food options that you should include, within those that you can get, that have nutritional properties and that prevent inflammation.

In the case of following the low-residue diet, the nutritionist will also give you a written diet, designed to cover your energy and nutrient needs, where you will consume foods that have very little fiber, little fat, and that do not contain milk or dairy products. of milk.

In both diets, the personal requirements and needs of each patient will be covered and will be calculated in the same way. The group to which you will be assigned is chosen by chance, so we cannot guarantee that you will get one or the other diet.

The diet should be started two weeks before you start your cancer treatment, and continue until 3 months after your cancer treatment is over.

5. Risks of participating in the study.

The diet carries minimal risk. Diarrhea or constipation, softening of stools and sometimes gas could only occur in less than 10% of patients.

6. Benefits of participating in this study.

All the patients in this study will be prescribed an adequate diet to maintain and/or improve their nutritional status, and diet adjustments will be made according to the symptoms that they manifest throughout the treatment.

What are the costs?

There will be no cost to you for your participation in the study and you will not pay for visits to the nutritionist. In the written diet that is given to you, foods that are frequently consumed by Mexicans, that are accessible and low cost, will be recommended.

7. Alternative procedures.

If you decide not to participate in this study, you will continue to receive the cancer treatment that your oncologist considers appropriate for you. If you present gastrointestinal toxicity that prevents you from eating or malnutrition, your doctor will tell you to make an appointment with the nutritionist, this consultation will not be part of the research protocol.

In addition, you or your legal representative will be informed promptly if new information becomes available that may be relevant to your decision to continue participating in this study.

8. Patient Responsibilities.

By signing the informed consent, you agree to carry out all the visits stipulated therein, follow the proposed diet, as well as provide true information on what is requested to obtain real results from this research. Finally, if you sign the consent and later decide to no longer participate, you will have the responsibility to inform the principal investigator or one of the collaborators to cancel your next appointment and be able to schedule another patient.

You should not participate in this study if you are pregnant or could become pregnant. A pregnancy test is required before the start of the study in all women who could become pregnant. You must use an effective contraceptive method if you are of childbearing age.

9. Confidentiality.

All information generated from this study will remain confidential. The group of researchers, as well as the monitor, auditor, and regulatory authorities, will have access to your clinical file, for the verification of the study procedures and data. The results will be captured in a database, where you cannot be identified. No one will know the data about you, only the results. We may publish the study results or present them at professional meetings, but your name will not be released or mentioned in any report or publication. Third parties, friends, or relatives of yours can't know about your illness and know other unique things about your age, gender, or illness that could identify you in a publication.

If you have any questions or concerns about your privacy rights, please contact Dr. Emma Libertad Verastegui Aviles, President of the Research Ethics Committee at telephone 01 (55) 5628-0400, extension 37015.

However, the Ethics and Research Committees of the National Institute of Cancerology, as well as the Sanitary authorities (COFEPRIS) may review the original documents and their file to verify the veracity and quality of the information.

10. Compensation.

You will not receive any compensation for your participation. In the event of any side effect of the treatment administered, you will receive medical treatment at no cost to you.

11. Compensation and payment of adverse events.

The National Cancer Institute will not cover medical expenses for injuries unrelated to study treatment or attributable to the natural development of any underlying disease. The National Institute of Cancerology will not provide any other type of compensation. If you suffer any harmful effects or injuries, you should contact your doctor immediately.

12. Termination of the study.

Your participation in the study will end at the fifth visit, which is 3 months after completion of brachytherapy, with an approximate duration of 5 to 6 months. If you or the investigator feel you must leave the study, your participation may be shorter.
You must inform the investigator if you become pregnant during treatment.

13. Contacts.

By signing this consent and agreeing to participate in this research study, you do not waive any legal rights you would otherwise have as a research subject. The signing of this consent does not imply waiving any of your legal rights under Mexican law. If you have doubts or questions about your rights, you can contact the President of the Research Ethics Committee of the National Institute of Cancerology, Dr. Emma Libertad Verastegui Aviles, by phone at 01 (55) 56280400, extension 37015.

If you have any questions about this study or if you become ill during or as a result of the research product, you should immediately call Dr. Lucely Cetina Pérez, at the National Institute of Cancerology, telephone 01 (55) 56280400 extension 12220.

If you have questions about your rights as a research study subject, you can call the Research Ethics Committee of the National Cancer Institute; the telephone at 01 (55) 56280400 extension 37015. The Research Ethics Committee is a group of professionals who evaluate research studies and ensure that your rights and safety are protected. Mexican law requires that a Research Ethics Committee review and approve all research involving the participation of human beings. Review and approval of the study must be done before the study begins. The study will also be continually evaluated as it develops.

Consent.

By signing this consent form, I am indicating that I have read and understand the information contained therein. I have received acceptable answers to all my questions. I voluntarily consent to my participation in the project **"Effect of an anti-inflammatory diet on nutritional status and cytokine expression in patients with locally advanced cervical cancer: a randomized clinical trial."**

I agree to donate any unused samples from my samples for research purposes.

I understand that I will receive a copy of this signed and dated consent form. I confirm that I have received a signed duplicate of the research subject information and consent form.

Printed patient name

patient signature Date

Witnesses:

Printed name of impartial witness Kinship

Witness signature Date

witness address

Printed name of impartial witness Kinship

Witness signature Date

witness address

I certify that, to the best of my knowledge and belief, the subject signing this consent form has received a complete and careful explanation of the research, and that she clearly understands the nature, risks, and benefits of participation.

Printed name of the person in charge of explanation of consent

Signature of the person in charge of the explanation Date of consent