Title of the study

Efficacy of atorvastatin versus colchicine in reducing myocardial damage biomarkers in patients with rheumatoid arthritis, with severe activity, pilot study.

Name of the Document

Informed Consent Form

Date of the document

July 25, 2018

INFORMED CONSENT FOR THE PATIENT

DEPARTMENT OF RHEUMATOLOGY AND CARDIOLOGY OF THE HOSPITAL CENTRAL “DR. IGNACIO MORONES PRIETO”

TITLE OF THE RESEARCH PROTOCOL		
Efficacy of atorvastatin versus colchicine in reducing myocardial damage biomarkers in patients with rheumatoid arthritis, with severe activity, pilot study.		
NUMBER OF THE REGISTRATION AUTHORIZED BY THE RESEARCH ETHICS COMMITTEE		**PROTOCOL EXECUTION PERIOD**
63-18		01/08/18 - 31/07/19
PRINCIPAL INVESTIGATOR		**PRINCIPAL INVESTIGATOR'S AFFILIATION**
Carlos Abud Mendoza		Department of rheumatology and cardiology Division of Internal Medicine Hospital Central “Dr. Ignacio Morones Prieto”

The Department of Rheumatology and Cardiology of the Hospital Central "Dr. Ignacio Morones Prieto "performs a protocol or clinical research study " Efficacy of atorvastatin versus colchicine in reducing myocardial damage biomarkers in patients with rheumatoid arthritis, with severe activity, pilot study." , This study is authorized for the Committee of Ethics Research of Hospital Central "Dr. Ignacio Morones Prieto” with registration number 63-18 , with the objective of analyzing whether the application of drugs called atorvastatin or colchicine will improve the concentration of cardiac damage biomarker "High sensitivity troponin I" in patients with active and severe rheumatoid arthritis. In this study, 30 patients will be included for each group during 1 year from August 1, 2018 to July 31, 2019 and will be carried out under the supervision of the Rheumatology Department of the Central Hospital "Dr. Ignacio Morones Prieto.

Information for the patient

This study will be performed in the facilities of this hospital as of 01/08/18. The study will be carried out during approximately 12 months in which patients diagnosed with Rheumatoid Arthritis will be invited according to the diagnostic criteria of the American College of Rheumatology and the European League against Rheumatism 2010, with severe activity according to severity scale DAS 28 > 5.1.

You have been selected to participate in this research study because of the type of condition you have, called Rheumatoid Arthritis. In order for you to decide if you agree to participate in this research study, we will ask you to carefully read this informed consent document explaining the purpose, procedures, risks and benefits and privacy rights of the data are obtained from you, so you can make a decision about it. We will ask you to ask Dr. José Alfredo Alvarado Alvarado any doubt or word or term that does not understand or has not been sufficiently clear about this document or any other type regarding this study that you have.

When you have resolved all your doubts about what this research study is about, we will ask you to grant your authorization by your name and signature at the end of this document.

This study consists of taking an echocardiogram and a blood test called high sensitivity Troponin I before being randomly chosen to use a drug called atorvastatin or colchicine, which will take four weeks and it will not be known which of the two possible medications were chosen for you according to the randomization method, afterwards an echocardiogram will be performed again and a new blood sample will be taken for high sensitivity troponin I blood.

Atorvastatin is a drug widely used in many diseases, especially in cardiac diseases, with effect at several points of the inflammation pathway, which is the cause of multiorganic disease in patients with rheumatoid arthritis. Colchicine is another medication used in patients with pericardial inflammation or gout disease, and has been shown to inhibit multiple pathways of immune-inflammatory complexes. The objective of using these drugs in patients with rheumatoid arthritis with disease activity is to assess if they can reduce the concentration of the cardiac damage biomarker called high sensitivity Troponin I, with possible effects in reducing cardiovascular diseases.

As part of this study, we will also ask you to sign your acceptance to participate, at the end of this document and give us your authorization to review your clinical record and collect some information necessary to complete this investigation, such as your age, weight, which was the exact diagnosis of your disease, the data referring to the studies that have been carried out, the laboratory analysis (blood count, protein-C reactive, erythrocyte sedimentation rate and albumin), as part of your diagnosis and treatment.

Benefits for the patient

The patient will not obtain an additional benefit, direct or immediate additional to the benefit implicit in the treatment of his condition. However, their participation in this clinical research study will contribute in a very important way to determine if the medicine called atorvastatin or colchicine could cause less cardiovascular complications in similar patients in the future.

Potential risks and discomfort for the patient and compensation

The medicine called atorvastatin, like any other medicine, can cause the following complications, among others:

1. Allergic reactions
2. Diarrhea
3. Neuromuscular and skeletal pain
4. Insomnia
5. Nightmares
6. Urticaria
7. Hyperglycemia
8. Nausea
9. Elevation of liver enzymes

The medicine called colchicine like any other medicine, can produce the following complications, among others:

1. Diarrhea
2. Nausea
3. Abdominal pain
4. Neuromuscular pain
5. Vomiting
6. Fatigue
7. Headache

The risk of death or hospitalization in patients taking the medication will not be greater than the risk that occurs without it. Therefore, the procedures that will be carried out in this study to the patient will not have an additional risk to the already established and considered for his illness.

Any complication of those previously described or any other that may arise in the patient during and after the intervention that will be used in this research study will be attended immediately by the medical personnel participating in this study and who have the necessary training.

It is important that you are clearly aware that you will not receive any payment for participating in the study, but neither will it generate an additional cost.

If you decide to agree to participate in this clinical research study, you will agree to apply the drug atorvastatin or colchicine according to the group chosen by a randomized method.

The researchers responsible for this study will provide you with an original signed copy of this informed consent document.

Participation or withdrawal

You have been invited to participate in this study because you have a diagnosis of rheumatoid arthritis with active disease. If you agree to participate in this research study, we will ask you to carefully read this document of informed consent and to ask all the necessary questions to the responsible investigating physician, Dr. Carlos Abud Mendoza or the associate researcher Dr. José Alfredo Alvarado Alvarado , so you can solve your doubts. When you no longer have any doubts about what will be done in this study, we will ask you to sign your acceptance to participate, at the end of this document.

You are free to refuse to participate in this research study; but if you decide to participate, at any time and without giving any explanation, you can revoke or cancel your participation and the consent you now sign. Your decision to participate or not will not affect in any way the medical treatment you receive in this hospital for your illness.

Privacy and confidentiality

The personal and medical information you provide for this study will be strictly confidential and will be used only by the research team of this project and will not be available for any other purpose. This information will be combined with that of other participants to carry out the present study. In order to maintain anonymity, you will be assigned an identification code for the use of your data.

The results of this study may be published for scientific purposes in special journals aimed at medical personnel, nurses, chemists and researchers related to the area of health in order to know if the use of the drug atorvastatin or colchicine in patients with diagnosis of rheumatoid arthritis with disease activity is beneficial for the patient. The results of this study may also be presented at scientific meetings in which the new findings of this study and other studies related to health and the treatment of patients with the same diagnosis are discussed. The clinical data of all the participants will be presented anonymously and in such a way that you or any of the patients participating in this study can not be identified.

In accordance with the General Law for the Protection of Personal Data in Possession of Obligated Subjects and the Personal Data Protection Law of the state of San Luis Potosí, your personal data may not be processed, transferred or used for purposes not expressly described in this document, to unless it is strictly necessary for the exercise and fulfillment of the attributions and obligations expressly provided for in the regulations governing the actions of the researchers responsible for the study; comply with a legal mandate; are necessary for reasons of public safety, public order, public health or safeguarding the rights of third parties.

Any other use that is required for the use of your data or analysis or management of your samples and / or results of the analyzes described in this document, must be informed and requested with due justification to the Committee of Research Ethics of this Hospital, who will determine the pertinence of the application and, where

appropriate, authorize a different use for your data, samples and / or products derived from your samples and / or results. Always in accordance with national and international legislative guidelines and norms and for the benefit and protection of the integrity of the participating actors.

There are Mexican institutions or organizations such as the Ministry of Health, the Federal Commission for the Protection against Health Risks (COFEPRIS), the National Commission of Bioethics (CONBIOETICA) or even the Research Ethics Committee (CEI) of this hospital, which are in charge to monitor the good handling of your samples and the personal and medical data that you and the other patients have authorized to be used in conducting research studies such as this one. These institutions or organizations may request at any time to the researchers of this study, the review of the procedures carried out with their information, with the purpose of verifying that they are used correctly and ethically; so they can have access to this information that has been previously assigned with an identification code, when they require it.

Ethical Considerations:

This study is considered minimal risk because the medical researchers responsible for this study will apply the drug atorvastatin or colchicine. However, it is important that you know that the risk due to this intervention will be the same for you if you decide not to participate in this research study, since the fact of having Rheumatoid Arthritis represents a high risk of presenting cardiovascular complications.

The medical researchers who carry out this research study are part of the assigned doctors who apply this medicine to multiple patients for different diseases. So you can be confident that the medical staff that will work with you is perfectly trained.

We will ask for your authorization to review your clinical file to obtain some important information that we have previously discussed (blood count, protein-C reactive, erythrocyte sedimentation rate and albumin), so at the end of this document we will ask for your authorization.

We will also ask you if you want the researchers responsible for this study to inform your treating physician that you have agreed to participate in this research study and that your results are included in your clinical record.

You will be given a copy of this informed consent, signed by the responsible researcher where you include your contact information and the data of the Research Ethics Committee of this hospital to clarify any questions that may arise.

Commitment to answer questions and doubts:

In case you have doubts about this research study, you can contact the following people at any time:

Dr. Carlos Abud Mendoza

Department of Rheumatology

Central Hospital "Dr. Ignacio Morones Prieto "

e-mail: c_abud@hotmail.com

Dr. José Alfredo Alvarado Alvarado

Department of Internal Medicine

Central Hospital "Dr. Ignacio Morones Prieto "

Tel. 4441565378

e-mail: alfredo_alvarado290@hotmail.com

If you have any questions regarding your rights and obligations to participate in this study, you can contact:

Dr. Emmanuel Rivera López

Chairman of the Research Ethics Committee Central Hospital "Dr. Ignacio Morones Prieto "

Av. Venustiano Carranza 2395, Col. University Zone San Luis Potosí, S.L.P., C.P. 78290

Tel (444) 8 34 27 01, Ext. 1710

Declaration of the acceptance of informed consent

1. It has been clearly explained to me that I have a diagnosis of Rheumatoid Arthritis, with severe activity of the disease, with a higher risk of cardiovascular disease due to this pathology.

2. The intervention that will be applied during the study has been clearly explained to me. They explained to me in detail that I will receive treatment with the medicine called atorvastatin or colchicine, according to the group to which I am randomly chosen.

3. I declare that I have been fully informed about the possible risks and discomfort that I may have when participating in this study.

4. I understand that whoever participates in this study will not generate a greater risk than the one already established for my illness.

5. I declare that I have asked all my doubts to the doctor who explained to me what the study is about and he has answered me clearly and I have been satisfied with the answers he has given me.

6. I have been explained that I can withdraw my consent and terminate my participation in this study at any time and without affecting my right to receive the present and future medical attention required in this hospital.

7. I affirm that I am 18 years of age or older and am legally authorized to give this consent.

8. I declare that I ACCEPT voluntarily and without being pressured or obligated to give my written consent to participate in this study.

9. I have been told that the personal and clinical information that I have consented to provide will preserve my privacy and that it will be used only for the purposes of this study. The results of this study could be published for academic purposes and as support for clinical practice. The data related to my privacy will be handled in a

confidential manner since a code assigned to maintain my anonymity and the confidentiality of all my data will be used.

10. The researchers participating in this project have committed to provide me with the updated information obtained during the study at the time they request it, and they will give me a signed copy of this informed consent document.

Access to the patient's clinical file and use of clinical data

You are requested to indicate your agreement or disagreement so that the researchers responsible for this project can review your clinical file and use the clinical data that are described therein, anonymously for this research protocol whose objectives and procedures have been explained. Mark your answer with an X:

____ Yes, I give my authorization to the researchers participating in this project for the use of the data in my clinical file in the research that they have explained to me.

____ I do not give my authorization to the researchers participating in this project for the use of the data in my clinical file in the research they have explained to me.

Authorization for the use of clinical data

You are asked to indicate your agreement or disagreement so that the researchers responsible for this project can use the clinical data anonymously to carry out this research protocol, whose objectives and procedures have been explained to you and which you freely and volunteer has provided, Mark with an X your answer:

____ Yes, I give my permission to the researchers who participate in this project to use my clinical data in the research they have explained to me.

_____ I do not give my authorization to the researchers participating in this project for the use of my clinical data in the research they have explained to me.

Authorization to inform the attending physician of my participation in this research study and for the results to be included in your clinical file.

You are asked to indicate your agreement or disagreement so that the researchers responsible for this research study inform your treating physician, Dr. (a)

_____, who has agreed to participate in this study with the registration number 63-18 by the research ethics committee of this hospital and so that the results obtained are included in their clinical file so that they can be used as a reference for subsequent treatments. Mark your answer with an X:

____ Yes, I give my authorization to the investigators to inform the attending physician of my participation in this research study and to include their results in their file, in accordance with the aforementioned and how they have explained me.

____ I do not give my authorization to the investigators to inform the attending physician of my participation in this research study and to have their results included in their file, in accordance with the aforementioned and explained to me.

Through this document of informed consent, I agree to participate in the research project entitled "Efficacy of atorvastatin vs colchicine in reducing myocardial damage biomarkers in patients with rheumatoid arthritis with disease activity, pilot study" registered before the Research Ethics Committee of the Hospital "Dr. Ignacio Morones Prieto ".

PATIENT'S NAME	PATIENT ACCEPTANCE SIGNATURE
DATE OF OBTAINING INFORMED CONSENT	

NAME OF LEGAL REPRESENTATIVE (if necessary)	SIGNATURE OF ACCEPTANCE OF THE LEGAL REPRESENTATIVE
DATE OF OBTAINING INFORMED CONSENT	RELATIONSHIP
ADDRESS/CONTACT TELEPHONE OF THE LEGAL REPRESENTATIVE	

WITNESS NAME 1	SIGNATURE OF THE WITNESS 1
DATE	RELATIONSHIP
ADDRESS/CONTACT TELEPHONE OF THE WITNESS 1	

WITNESS NAME 2	SIGNATURE OF THE WITNESS 2

DATE	RELATIONSHIP

ADDRESS/CONTACT TELEPHONE OF THE WITNESS 2

_____

(name and signature of who obtains the informed consent)

DR. CARLOS ABUD MENDOZA		**DR. JOSÉ ALFREDO ALAVARADO ALVARADO**
MAIN INVESTIGATOR RESPONSIBLE FOR THE RESEARCH PROTOCOL **DEPARTMENT OF RHEUMATOLOGY** **HOSPITAL CENTRAL "DR. IGNACIO MORONES PRIETO"**		**RESEARCH ASSOCIATE** **DEPARTMENT OF INTERNAL MEDICINE** **HOSPITAL CENTRAL DR. IGNACIO MORONES PRIETO**