INFORMATION LETTER AND INFORMED CONSENT FOR PATIENTS

Title: Determination of Zinc and the Acute phase protein PTX3 in Patients with Sickle Cell disease (ZIP study)

Dear Sir/Madam,

We kindly ask your participation in the above mentioned medical-scientific research. The research will be conducted in the Academic Medical Center Amsterdam and the Slotervaart Hospital. In total 32 patients will participate in this study.

For permission or refusal information from our side and careful consideration on your part are needed. Therefore you receive this written information. Take your time to read this information letter. Before you make a decision, it is important to gain information about the research project. Please read this information letter carefully. Besides this letter, you also received the brochure “Medical-scientific research” from the Ministry of Health, Welfare and Sport. This brochure contains general information about medical scientific research. Please discuss this research project also with your partner, friends or family. Participation is completely voluntary. It is important that you understand all possible risks, possible inconvenience(s) and advantages of participation, leading to a deliberate decision. When you still have questions after reading all the information you can always ask one of the researches named at the end of this information brochure.

1. Background and aim of the research.

In sickle cell patients it can be hard to distinguish between patients who are experiencing a painful crisis and patients who are in pain for another reason. This differentiation is important to make an optimal treatment possible. Pentraxin3 (PTX3) is a marker for tissue damage and zinc is a metal which is a component of human bones and some other tissues. In patients with a painful crisis sometimes tissue- and bone damage occurs. That is why we want to determine the concentration of the above mentioned markers in blood of sickle cell patients who are experiencing a painful crisis.

2. What are the research questions?

We assume that PTX3 and zinc levels in blood are possible markers for disease severity in patients with sickle cell disease. In this study we try to find an answer to the following questions:

- How do PTX3 levels in blood develop during an admission for a painful crisis?
- How do zinc levels in blood and urine develop during an admission for a painful crisis?
- Is there a relation between the concentration of the above mentioned markers and the progress of a painful crisis?

3. How will this study be executed?

Because in sickle cell disease it is not clear when exactly after the start of a painful crisis the levels of PTX3 and zinc rise, we want to draw blood and collect a urine sample at 3 subsequent days. This to investigate how and when the levels of these markers rise in blood and urine and when these levels drop again. Furthermore, together with the researcher, we ask you to fill in a short questionnaire on admission.

What are extra procedures for this research project:

Extra blood extraction
On day 1, 2, 3 and with discharge 3 extra tubes of blood (14 mL) will be drawn. In patients who are admitted over 5 days, preferably at day 5 the same amount of blood will be drawn one extra time. Since you will probably have an iv-line during admission, the blood will be drawn from this line to reduce the inconvenience from the blood extraction as much as possible. If a regular blood extraction was already planned, this will be combined with the blood collection for this study, if possible.
During a visit at the ambulant clinic, at least 4 weeks after the painful crisis, again 14 mL of blood will be extracted. If possible, this will be combined with the regular blood check. No extra venipuncture is needed.

Urine
At day 1 of the admission all patients will be asked to collect their urine produced over 24 hours in a special container. The subsequent days of admission you will be asked to hand in only a urine sample. At the above mentioned visit at the ambulant clinic you will be asked to hand in a 24 hour urine collection again.

Questionnaire
During admission you will be asked to complete a short questionnaire, together with the researcher. This will take approximately 10 minutes.

4. What side-effects can be expected?
A blood extraction may cause bruising.

5. What are possible advantages and disadvantages from participation?
Participation will not give you a direct advantage. The information that will be obtained from this research, will possibly contribute to a better treatment of sickle cell patients in the future. A disadvantage of this research is that at some extra time points some blood will be drawn and that you are asked to hand in a urine sample.

6. What happens if you do not wish to participate in this research?
It is your own decision if you want to participate in this research project. Participation is voluntary. If you do not want to participate there is nothing that you will have to do. You do not have to sign anything. You also do not have to tell why you do not want to participate. We have to ask you to make our decision within few hours, because we have to start the procedures within 24 hours. You will get the same treatment as you would normally get. If you do wish to participate, you can always decide to change your mind and leave the project at any time you want.

7. Privacy:
Only a few other people are able to look into your data. These individuals/agencies are, for example: employees of the research team, members of the Medical Ethics Committee of the AMC and the Inspection for Health care. Besides that, designated employees of the AMC will monitor all study data and will be allowed access to personal data. All research data will be handled according to the 'Wet Bescherming Persoonsgegevens' (Dutch Data Protection Act). All research data and bodymaterial/blood that is collected during this research will be assigned a code number. This is to make sure that your personal data will not be used in research documentation. Furthermore is it not possible to retain personal data from a possible future publication of research results. Only the researcher who holds the key to the code knows who the person behind the code number is.

After closure of the research your medical data will be kept up to 20 year. It is possible that we will use research data and/or stored body material/blood in the future for research that is not defined in this protocol, but is in line with this research. This can only be done if the Medical Ethical Committee again gives its permission to perform this research.
All stored body material is kept with a maximum of 15 years after closure of the project. If you do not give permission for the storage of this material for future research the material will be destroyed after this research is finished. This will not influence the further participation of this research.

8. Are there extra costs/is there compensation when you decide to participate in this research?

Participation in this research will not give you extra costs. No compensation is given for participation and travel costs.

9. Approval

This research project was approved by the Medical Ethical Committee of the AMC. For this research the applicable current international guidelines will be observed accordingly.

10. Insurance

The Medical Ethical Committee of the AMC has given exemption for this research from the obligation to take out insurance to cover damage caused by this research to a test person. The reason for this derogation is that the Committee considers that this research for the test person is without any risk.

11. Is there anything else you want to know?

For more information about this research you can ask your doctor or one of the researchers of the Academic Medical Center: Dr B.J. Biemond and Dr Schimmel tel: 0205665785

Independent physician
If you doubt about participating in this research you can consult an independent physician, who is not involved in this research, but who is an expert in the field of this research. Furthermore, if before or during the research you have questions that you rather not ask your treating physician, you can contact the independent physician: prof dr S. Middeldorp, tel 020-5665976

Complaints
If you are not satisfied with the research or the treatment you can report this to your physician. If you do not prefer this, you can contact: department patient information of the academic Medical Center: tel 020-5663355

12. Informed consent

If you decide to participate in this research, we kindly ask you to sign the informed consent. By signing this form you agree to participate in this research. After this you can still decide to end your participation. Your physician will also sign this form and thereby confirms that you are well informed about the research and that you received this information letter.

Attachments

- General brochure medisch-wetenschappelijk onderzoek met mensen (medical-scientific research with humans)
- Informed consent (duplicate)

Attachment 2 **DECLARATION OF CONSENT**

for participation in the clinical study:

Zinc and the acute phase protein PTX3 in sickle cell disease

I have read the patient information sheet. I understand the information. I have had the opportunity to ask additional questions. My questions have been answered satisfactorily. I have had enough time to decide if I will participate.

By signing this informed consent I give my permission for participation in the above mentioned medical scientific research.

I know that my participation in this study is voluntary. I can decide to withdraw from the study at any time without stating my reasons.

I understand that some persons will have access to my data. These persons are mentioned in this patient information letter.

I give my consent to use my data for the purposes listed in this information letter.

I give my consent to storage of my data for a period of a maximum of 20 years after closure of the study.

I do /I do not give * to preserve my body material/blood for a maximum of 15 years after the end of this research for possible supplementary future scientific research.

***Please strike out what is not applicable**

Name patient: Signature: Date : __ / __ / __
I hereby declare that I have fully informed this patient about the study mentioned above. If, during the study, information emerges which may affect the consent of the patient I will inform him/her promptly. Name physician: Signature: Date: __ / __ / __

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