RANDOMIZED CLINICAL TRIAL FOR THE EVALUATION OF THE EFFECTS OF CHOLECALCIFEROL SUPPLEMENTATION ON THE PARATHYROID HORMONE IN HEMODIALYSIS PATIENTS

INFORMED CONSENT

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Vitamin D enters the body through food intake or via the skin by exposure to sunlight, and goes through the first step in its activation process to 25 Vitamin D (the form which is used to measure Vitamin D deposits) in the liver. The last step in its activation process takes place in the kidney where it takes on its active form, 1-25 vitamin D.

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The main function of vitamin D is to facilitate the entry of calcium and phosphorous through the intestine, to be subsequently deposited in the bones. A deficiency of vitamin D is associated with rickets in children and osteoporosis in adult populations. In a population on dialysis it is the deficiency of the active form that leads to an increase in the parathyroid hormone (PTH) and to secondary hyperparathyroidism.

In some published studies it was found that there was a correlation between the lack of vitamin D and some illnesses such as diabetes, osteoporosis and risk of fractures, higher frequency of some types of cancer and more severe cardiovascular disease (events such as myocardial infarction).

25 vitamin D is very stable (with a half-life longer than 2 weeks) and suitable for evaluating vitamin D sufficiency. It has been found that levels of 25VD are inversely related to those of the parathyroid hormone (PTH), and its supplementation has been associated with a decrease in levels of PTH in patients with Chronic Kidney Disease, although these results have not been uniform in patients on hemodialysis (HD).

Usual treatment for secondary hyperparathyroidism in dialysis has been with active forms (calcitrol) and/or analogous forms of vitamin D (paricalcitol). Both of these, but especially the use of calcitrol, increase the risk of hyperphosphatemia and of greater progression of vascular calcifications.

The aim of the study is to evaluate whether a 12-week course of cholecalciferol brings about the normalization of decreased levels of vitamin D and a reduction in the increase in PTH. A secondary aim is to evaluate whether this treatment improves anemia or reduces the need for erythropoietin.

The study will take place at the dialysis centre of CASMU-IAMPP, located at Av. Luis Alberto de Herrera 2421.

In this study the patients on HD who agree to participate will be selected at random to receive the treatment with the drug being researched (cholecalciferol) or with a placebo (that is, medication with the same characteristics as the drug but without its effects). The patients will have the same chances of receiving the active treatment as the placebo. Neither the patient nor the doctor will know which type of treatment the former is receiving. The intention of this treatment is to treat simultaneously the low levels of vitamin D (lower than 30 ng/ml) and the high levels of PTH (higher than 300 ng/ml).

The medication will be administered in the form of 1 tablet during dialysis (at each dialysis session) for 12 weeks, the only difference being the medication received, thus ensuring that at the end of the follow-up the differences observed will be due only to the drug used.

Checks will be made monthly by measuring levels in blood of: hemoglobin, calcium, phosphorous, PTH and erythropoietin doses. At the beginning and at the end of the study the following will be checked: alkaline phosphatase, CRP, vitamin D and iron deposits, and measures of quality of life (by means of auto-administered protocol SF36).

During the course of the study, your doses of calcitrol and paricalcitol will not be modified.

For your safety, treatment will be halted if you present levels of plasma calcium higher than 10.5 mg/dL on two occasions.

The risks of using cholecalciferol are minimal as there is a large difference between doses used for this treatment and those that are toxic. Among possible

undesirable effects of the treatment, it is occasionally found that there is an increase in levels of calcium and phosphorous in the blood.

If there were to be a complication considered associated to the treatment, you will be attended to at the same institution where the study is being carried out, at no cost to you.

We invite you to participate in this study from which you could potentially benefit, if you receive the active treatment, by presenting the desired effect of an increase in vitamin D and decrease in PTH.

If you agree to participate, you must know that there will be no financial cost to you and that you will not receive any financial remuneration or compensation for taking part in the study.

You must also know that your participation is voluntary and that your refusal to take part will not compromise the attention you receive.

You must also know that you can decide to halt your participation in the study at any time and without explanation. The principal researcher can decide to exclude you from the study without your consent if guidelines are not followed, and this will not compromise the attention you normally receive either.

After being notified of the possibility of your participation in the study, you will have a period of 15 days to think it over, consult your family or trusted doctor.

In case of any doubts both before or during the study, you or your relatives can consult Dr Laura Solá at the following telephone number: 24870421 ext. 4102, or by e-mail to lsola@casmu.com.

Confidentiality

If you agree to the data from your evaluation being included in the collection of the information for a global study of all the population, it will be stored confidentially according to current legislation. Your identity as well as any information obtained in regard to this evaluation will be confidential.

Once it has been entered into the study, your identity will be exchanged for an auto-generated number for later handling of the information.

Individual data will not be published, and the only ones who will have access to it will be those monitoring the study, the members of the Ethics Committee, delegates of the Ministry of Public Health and the researchers.

The undersigned agrees to the study being carried out and that related data will be kept in safekeeping by the team of Dr Laura Solá and used strictly for the purposes described above.

I have understood the proposal and agree to participate in the study administering 25 vitamin D.

Yes / No

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PARTICIPANT'S SIGNATURE DOCTOR'S SIGNATURE

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PRINTED NAME AND ID PRINTED NAME AND ID

Date: ☐☐ / ☐☐ / ☐☐☐☐

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