PROTOCOL SUMMARY

Title:	Monthly administration of high dose vitamin D3 in hemodialysis patients: A prospective study over nine months and review of the literature.
Objectives and Outcome	To assess the safety of a large dose of VD3 over nine months and its effects on the levels of calcium, phosphorus, alkaline phosphatase, 25(OH)D, 1,25(OH)$_2$ D, and iPTH
Measures:	Mean serum iPTH, 25(OH)D, 1,25(OH)$_2$D, serum calcium, serum phosphorus, and alkaline phosphatase.
Population:	Patients will be recruited over one month and then followed prospectively for nine months
Number of Sites:	Single-Centre Study
Study Duration:	The study will be conducted over nine months

Principal Investigator: Dr. Adnane Guella, Senior Consultant Nephrologist, University Hospital Sharjah, Department of Nephrology, adnane.guella@uhs.ae

Signature: 

08.07.2019

1.Study information

1.1 Scientific Title

Monthly administration of high-dose vitamin D3 in hemodialysis patients

1.2 Ethics Approval

Ethical approval is to be obtained from the Research Ethics Committee of the University Hospital of Sharjah (PO Box 72772, Sharjah, United Arab Emirates; +971(6) 505 8555; adnane.guella@uhs.ae).

The responsible investigator and all the involved personnel in the study have the responsibility to report any changes in the research activity and unexpected risks. Further, no change can be made to the protocol without prior ethical approval from the responsible committee. The study will be carried out according to the protocol and with the principles of the current version of the Declaration of Helsinki.

1.3 Clinical Trial Registration

The study is intended to be registered in the ISRCTN registry.

1.4 Declaration of Interest

The investigator certifies that he has no affiliation with or involvement in any organization or entity with any financial interest, or non-financial interest in the materials investigated in the study

1.5 Study Sites

The single-center single-arm interventional study will be conducted at the University Hospital Sharjah, United Arab Emirates.

1.6 Study Design

Interventional, Non-randomized study

1.7 Patient Information and Informed Consent

To guarantee understandability of the information, the principal investigator will provide clear and detailed information about the: research purpose and objectives; name and institution of researchers; voluntary nature of participation (with no penalty for those who refuse or withdraw participation from the study); duration of the study; actions taken to protect personal data (confidentiality, anonymity, and privacy); participants' right to freely withdraw participation before initiation of the survey with no penalty; and option to be informed about the global results. Participants will be informed about their entitlement to obtain additional information and clarification of any aspect related to the study through the email or phone number of the principal investigator. The information will be provided to the research participants through a Study Information Sheet written in simple and understandable terms that will be presented to all potential participants. All study materials will be provided in English and Arabic so that participants can choose the language of their preference. The information sheet will be pilot-tested to ensure understandability, and any necessary changes will be made in accordance.

1.8 Participant Privacy and Confidentiality

The investigator affirms and upholds the principle of the participant's right to privacy.
The anonymity of each participant shall be guaranteed when presenting data or publishing it in scientific journals. All data and information collected/ obtained from this study shall remain confidential, and disclosure to third parties is prohibited. For data verification purposes, only authorized representatives of the principal investigator may require or have direct access to the data of the medical records related to the study.

1.9 Early Termination of the Study

The sponsor- investigator and competent authorities may terminate the study prematurely according to certain circumstances such as ethical concerns when the safety of the participants is at risk or early evidence of harm of the intervention.

1.10 Amendments to the Protocol

Suggestions regarding study protocol changes are allowed to direct collaborators in the study and approved by Dr. Adnane Guella before being submitted to the Research Ethics Committee.

2. Background and Rationale

2.1 Background

Hemodialysis is a procedure where a dialysis machine and a special filter called an artificial kidney, or a dialyzer, are used to clean the blood. Hemodialysis patients are usually low in vitamin D3 (VD3) and active VD3. However, they rarely receive VD3. Instead, they are typically prescribed active vitamin D because the kidneys can no longer activate VD3. The compliance to active VD treatment is not good, and it is thought to cause vascular calcifications (mineral deposits on the walls of the arteries and veins). Hemodialysis patients also frequently have high levels of intact parathyroid hormone (iPTH), which causes damage to the bones. The usual treatment given is active VD and calcimimetics (drugs that mimic the action of calcium on tissues). Studies have shown that VD3 is very beneficial for dialysis patients. It can restore the VD3 store and decrease the blood level of iPTH. Other studies showed that it could lead to increased levels of active VD, but there is no published guideline on which treatment to follow to reach these targets. This study aims to use large doses of VD3 (also used in other studies) over a long period, assess the safety of such a practice, and observe the effects on bones.

2.2 Study Hypothesis (Study Rationale)

Administration of Vitamin D3 in a large dose for an extended period may prevent the administration of active vitamin D, which is known to cause vascular calcification. Moreover, this practice may stimulate endogenous production of 1,25 dihydroxy vitamin D3 [1,25(OH)2 Vit D3]. Its effect on reducing intact parathormone (iPTH) was reported; however, the target level of serum level of cholecalciferol to obtain a decrease in iPTH is not established.

2.3 Risks/ Benefits

The benefits include replenishment of vitamin D3 stores. There are no potential risks expected.

3. Study Objectives:

3.1 Overall Objectives

To find out whether a simple regimen using a very large dose of VD3 given orally once monthly over a long period of 9 months would benefit the safety and control of SHPT.

4. Study Outcomes & Procedures

4.1 Primary outcome measure

Measured at 0, 3, 6, and 9 months:

1. Serum levels of 25(OH)VD measured using the LIAISON® 25 OH Vitamin D assay
2. Serum levels of 1,25(OH)2 VD measured using the LIAISON® XL 1,25 Dihydroxyvitamin D assay
3. Serum levels of iPTH measured using the Atellica IM PTH assay

4.2 Secondary outcome measures

Measured at 0, 3, 6, and 9 months:

1. Serum calcium measured using the Atellica® CH Calcium (Ca) assay
2. Serum phosphorus measured using the Atellica™ CH Inorganic Phosphorus (IP) assay
3. Serum alkaline phosphatase measured using the Atellica™ CH Alkaline Phosphatase, concentrated (ALP_2c) assay

5. Study Population

5.1 Eligibility Criteria

Participants fulfilling the following inclusion criteria are eligible to be included in the study

1. Hemodialysis patients
2. On dialysis for more than one year
3. Not on active Vitamin D
4. Not on calcimimetics

Participants fulfilling the following exclusion criteria will lead to the exclusion of the patients from the entire study

1. Tertiary hyperparathyroidism
2. Ongoing debilitating condition (e.g., cancer)

5.2 Recruitment.

The study participants will be pre-selected at the University Hospital Sharjah registration office and the Dialysis Unit record system.

5.3 Criteria for Withdrawal

Participants in this trial are free and have the right to accept or refuse to participate. Whether they choose to participate or not, the way they receive medical care will continue to be the same, and their relationship with their physician will not be affected by any means. Any participant who wishes to withdraw from the study can leave without prior notice or agreement. Participants withdrawing from the study will be given various instructions for ending their participation, including how to stop the study medications safely and who to contact in case of concerns or questions. For that, the principal investigator's email and telephone number will be provided so that the participants can contact him. The withdrawn patient will not be replaced.

6. Study Intervention

6.1 Study Intervention

Hemodialysis patients with secondary hyperparathyroidism and not on either active VD3 or calcimimetics are included in the study to receive a large oral dose of vitamin D3 (300,000 units) every month for nine consecutive months post-dialysis. Serum levels of 25(OH)VD, 1,25(OH)2 VD, calcium, phosphorus, alkaline phosphatase, and iPTH are measured at the start and every three months until the end of the study.

6.2 Compliance with the Study Intervention

In case of non-compliance proceeds, the participant shall be excluded from the study and the data.

7. Results and Publications

The datasets generated or analyzed during the current study will be available upon request from Dr. Adnane Guella (guella@gmail.com). Data will be available for one year from the date the study has ended by email. All the blood investigations studied can be available for sharing and consent from participants—planned publication in a high-impact peer-reviewed journal.

8. Funding & Support

No funding to declare. This research will not receive any specific grant from the public, commercial, or not-for-profit funding agencies.

9. Trial participating Centre

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10. Sponsor Details

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