DOCTORAL THESIS

SUMMARY

MINERAL AND BONE DISORDERS AND CARDIOVASCULAR RISK IN PATIENTS WITH CHRONIC KIDNEY DISEASE

Scientific Coordinator:
Univ. Prof. Dr. Eugen Moța

PhD Candidate:
Vladu Iulia-Daniela

Craiova, 2012
I. INTRODUCTION

Chronic kidney disease (CKD) has an increasing prevalence both in Romania and worldwide. Today we can speak about a 'endemic prevalence' of BCR globally. Despite growing concerns of the medical community, the figures on the incidence and prevalence of CKD in stages predialitice [1-3] remain unknown. United States reported a prevalence of 12-13% [4] of BCR, although other estimates (for the period 1999-2004) go up to 15.3% [5]. Today it is considered that 1 in 10 Romanian suffering from this disease and nearly 10,000 receiving renal replacement therapy (TSFR) with a growth rate of 7.2% over the previous year, in Dolj was a decrease by 4.1% prevalence of hemodialysis (HD) in 2011 compared to 2010 [6].

Mineral Bone disease is a common complication of chronic kidney disease [30.31] and covers a wide range of disturbances of mineral metabolism that occur in this clinical context and consequences both bone and extraosseous defined by one or more of the following entities: abnormal serum Ca, P, PTH and vit. D abnormalities's turnover, mineralization, volume, linear growth or bone hardness and vascular or soft tissue calcification [31.32].

The idea of the present thesis is based on the premise outlined above and I aimed to analyse and evaluate the impact of mineral metabolism disturbances on cardiovascular risk in patients with chronic kidney disease. The objectives of the thesis are based on assessing,
determinating the prevalence and correlations between serum calcium, phosphate, vascular calcification, traditional risk factors and other variables in patients with chronic kidney disease in order to assess behavioral risk factors in patients with BCR in relation to general population. It is also useful therapeutic strategy addressed both in prevention and in reducing cardiovascular risk and vascular calcifications.

II. PERSONAL RESEARCH

II.1. Mineral and bone metabolism and cardiovascular risk factors in patients with chronic kidney disease

The main aim of this study was to establish the prevalence of mineral and bone metabolism disorders (hypocalcemia, hyperphosphatemia, secondary hyperparathyroidism, valvular and vascular calcification) and cardiovascular risk in patients with chronic kidney disease.

II.1.2. Material and methods

This is a prospective, observational, longitudinal study based on data centralized after obtaining written informed consent, personal medical history, complete clinical examination, lumbar spine profile radiography highlighting abdominal aortic calcifications, ECG at rest, cardiac and carotid vessels ultrasound, biological determinations (complete blood count, creatinine, urea, calcium, phosphorus, intact parathormone, in patients with chronic kidney disease in different stages Nephrology Clinic Clinical Emergency County Hospital Craiova. A total of 271 patients were included in this study and they were divided into the following groups:
- A: 3-5 stage CKD patients (n = 100)
- B: hemodialysis patients (incident and prevalent) (n = 100)
- C: continuous ambulatory peritoneal dialysis patients (n = 19)
- D: control group, subjects without chronic kidney disease (n = 52).
Each group was divided into 2: patients with and without diabetes mellitus and the sex ratio was 1:1.
II.1.3. Results and discussions

The mean age of the patients included in the study was 60.43±13.20 years and the patients were evenly distributed. Of the whole study group, 18.45% of the patients had serum phosphorus >5.5mg/dl and 26.94% had calcium <8.5mg/dl and 33.95% of the patients had iPTH lower than 65pg/ml. All patients in the control group had iPTH in target whereas only 34% of the patients in CKD stages 3-5 not on dialysis had iPTH in target.

100% of the patients in the control group, 96% of the patients with CKD not yet on dialysis, 84.21% of DP patients and 78% of the HD patients had CaXP<55mg/dl. Evaluating the number of CKD-MBD biochemical parameters in target (Ca,P,CaXP, PTH) the prevalence I found was: no DP patient had all 4 parameters in target- whereas 10.53% of the patients had no parameter in target. The most important findings are found in the figures below and are in agreement with data found in literature.

Figure 19, 20 and 22. Seric values for seric calcium, phosphorus and iPTH

Figure 29. Number of parameters in target and Figure 30. Prevalence of vascular and valvular calcifications
III. CONCLUSIONS

1. The prevalence of changes in mineral and bone metabolism parameters in the patients in this study is similar to data found in literature (72.14% and 47.03% vascular and valvular calcification among people with chronic kidney disease).
2. Mineral and bone metabolism parameters had a significant impact on mortality (especially vascular calcification (OR = 9.1, p <0.0001), valvular calcification (OR = 6.7, p <0.0001) and hyperphosphataemia (OR = 2.4, p = 0.025)).

3. Cardiovascular risk score QRISK2-2012 is a predictor for vascular calcification in chronic kidney disease patients.

4. Age> 60 years, diabetes, inflammation (risk generated by CRP), high blood pressure, CKD stage and renal replacement therapy are predictors for vascular calcification.

5. Among diabetic patients with HbA1c values below 7% showed the lowest prevalence of vascular calcifications (42.86%), the values of HbA1c≥ 7.5% - prevalence of vascular calcifications was higher.

6. Patients treated with vitamin D had:
- Over 100% increase in serum levels of vit. D
- Sustained decrease of serum iPTH, more than 30%,
- Normalization of all parameters TMO-BCR for 26.67% of patients
- Decrease proteinuria/24h and
- Decrease in CRP.

7. Lumbar simple profile radiography and echocardiography are explorations cost-effective for detecting vascular calcification, implicit in patients with increased cardiovascular risk.

### IV SELECTED REFERENCES


Curriculum vitae

Name: Vladu Iulia - Daniela
Address: Craiova, Dolj, Romania
E-mail: Vladui@yahoo.com
Nationality: Romanian
Date of birth: 18 September 1984
Gender: Female

Occupation:
- October 2009-present: Nephrology PhD student at the University od Medecine and Pharmacy Craiova
- January 2010-present: Nephrology resident at Emergency County Hospital Craiova

Education and training:
- 2003-2009: Faculty of Medecine, University of Medecine and Pharmacy Craiova
- 2008: Erasmus student - Faculte de Medecine Paris Decartes , 6 months
- 2010: 17th Budapest Nephrology School
2011 7 months training in Service de Nephrologie, Hopital Bicatre, France : POSDRU grant ‘New trends in the diagnostics and treatment of glomerulonephritis’, Praga, Cehia, (ERA-EDTA grant)

2012 Romanian Nephrology Society
2012 European Renal Association - European Dialysis and Transplant Association (ERA-EDTA)

**Scientific activity**

**Languages**

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**Understanding**

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**Personal skills and competences**

Microsoft Office: Word, Excel, Power Point; Adobe Reader

**Other competences and aptitudes**

Participation in the Logos Radio Craiova - 2005-2007, empathy, team spirit, desire to work, perspicacity

**Driving license**

B

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**SCIENTIFIC ACTIVITY**

**Articles:**


**Presentations (oral and poster) at national and international congresses:**


5. Therapeutic options in hemodialysis patients with high cardiovascular risk- Vladu I., D. Mary, C. Grauntanu, C. Vaduva, E. Mota, Le14eme international congress for medical students and young doctors, Timisoara 2010

6. Proteinuria as a cardiovascular risk factor in patients with type 1 diabetes Grauntanu C., M. Bicu, C. Vaduva, S. Zaharie, Dena M., O. Jercan, Vladu I., M. Mota, Mota E., Days of the University of Medicine and Pharmacy Craiova 2010

7. Screening in the general population (World Kidney Day 2010) compared to the late presentation to nephrologists of patients with chronic kidney disease, Dena M., C. Grăunţanu, C. Vaduva, Vladu I., M. Tudor, C. Militaru, Mota E. Days of the University of Medicine and Pharmacy Craiova 2010

8. The evolution of anemia in hemodialysis patients, Jercan O., C. Militaru, C. Grauntanu, C. Vaduva, D. Alexandru, Vladu I., E. Mota, Days of the University of Medicine and Pharmacy Craiova 2010


10. Analysis of the social impact of sport in replacement therapy in renal function, A. Arcereanu, C. Vaduva, Vladu I., E. Mota, Days of the University of Medicine and Pharmacy Craiova 2010

11. Glucose tolerance in hemodialysis patients vs patients with renal transplantation- C.Vaduva, C. Grauntanu, Vladu I., Dena M., D.Cana-Ruiu, E. Mota, Days of the University of Medicine and Pharmacy Craiova 2010

12. Cardiovascular risk was the beginning of dialysis, S. Zaharie, Vladu I., E. Mota, Days of the University of Medicine and Pharmacy Craiova 2010

13. The prevalence of disorders of bone and mineral metabolism associated with chronic kidney disease at the initiation of dialysis- Vladu I., M. Mota, Mota E., Annual Congress of the Romanian Medical Association, Bucharest 2010

14. Analysis of the social impact of sport in replacement therapy in renal function, A. Arcereanu, C. Vaduva, Vladu I., E. Mota, Days of the University of Medicine and Pharmacy Craiova 2010

15. Glucose tolerance in hemodialysis patients vs patients with renal transplantation- C.Vaduva, C. Grauntanu, Vladu I., Dena M., D.Cana-Ruiu, E. Mota, Days of the University of Medicine and Pharmacy Craiova 2010

16. Cardiovascular risk was the beginning of dialysis, S. Zaharie, Vladu I., E. Mota, Days of the University of Medicine and Pharmacy Craiova 2010

17. The prevalence of disorders of bone and mineral metabolism associated with chronic kidney disease at the initiation of dialysis-Vladu I., M. Mota, Mota E., Annual Congress of the Romanian Medical Association, Bucharest 2010


24. The impact of haemoglobin levels on patients with diabetes and renal impairment. D Cana-Ruiu, M Dena, N Istrate, Vladu I, E Mota. World congress of Nephrology, April 8-12, 2011, Vancouver, Canada


Participation at national and international congresses:

1. Certificate of Proficiency in English, University of Cambridge, Local examination syndicate, Bucharest, 2002
5. Certificate of attendance in the workshop-'Methodes analyzing DNA and RNA and their applications in the field of medicine’, Craiova, 2007
9. Diploma of Erasmus student Faculty of Medicine Paris 6 months, France, 2008
11. Certificate of participation at meetings ‘National Romanian Congress of Nephrology, Dialysis and Transplantation’, 2010
12. Certificate of attendance at the 17th Budapest Nephrology School, 2010
15. Certificate of attendance at Nefrocardia, Timisoara, 2011