

## Evaluation of Zn and Fe in diets of patients with chronic renal failure

D. I. T. Fávoro,<sup>1\*</sup> D. Mafra,<sup>2</sup> V. A. Maihara,<sup>1</sup> L. Cuppari,<sup>3</sup> M. B. A. Vasconcellos,<sup>1</sup> S. M. F. Cozzolino<sup>2</sup>

<sup>1</sup> Laboratório de Análise por Ativação Neutrônica (LAN - CRPO) – IPEN/CNEN-SP. Caixa Postal 11049, 05422-970, São Paulo, Brasil

<sup>2</sup> Faculdade de Ciências Farmacêuticas, Departamento de Alimentos e Nutrição Experimental, Universidade de São Paulo, SP, Brasil

<sup>3</sup> Universidade Federal de São Paulo, Departamento de Nefrologia, UNIFESP, São Paulo-Brasil

(Received July 21, 2003)

Having in mind the importance of Fe and Zn content in the diets of nondialyzed patients with chronic renal failure, diets of 39 patients with ages varying from 18 to 79 years under a conservative treatment were analyzed by INAA. The 24-hour recall method was used for sample collection. The content of proximate composition was also determined. The average daily dietary intake was compared to the new recommended values by the Food and Nutrition Board. It was observed that the diets were deficient for these elements and, therefore, there should be a nutritional follow-up to avoid possible negative effects.

### Introduction

Subnormal plasma zinc levels have been reported in patients with chronic renal failure (CRF), but it is not clear at present whether a low concentration of plasma zinc is indicative of zinc deficiency in uremia, because the zinc concentration of erythrocyte is frequently reported to be elevated.<sup>1,2</sup> Zinc depletion was suggested to play a role in the pathogenesis of some uremic symptoms, e.g., impotence (testicular atrophy), immunological impairment and abnormalities of taste.<sup>1</sup>

Many factors could lead to zinc deficiency in uremia such as a decrease in dietary intake and intestinal absorption, as well as an excretion increase. Anemia is another problem found in these patients. Erythropoietin and iron deficiencies are some of the causes of anemia in patients with CRF. Initiating anemia therapy at an earlier stage in the course of kidney diseases can bring potential benefits to patients.

Pre-dialysis chronic renal failure should be actively treated, but much less attention has been given to the role of iron replacement in these patients, in whom iron stores are low. Low iron stores are probably caused by a combination of Fe intake reduction, low protein diets which contain low animal protein and low iron content, reduced gastrointestinal absorption of iron, phosphate binders and histamine 2-blockers, increased gastrointestinal blood loss, proteinuria, and reduced bone marrow use of oral iron.<sup>3,4</sup>

There are many mechanisms that can cause the progressive loss of renal function and due to these complex factors, it is more difficult to evaluate the impact of dietary manipulation. But, advances in clinical nutrition that emphasize studies of diet are basic to assess the progress of renal disease.

The early control of protein intake is important because its metabolic degradation produces nitrogenous wastes. Energy and the other macronutrients intake are

emphasized because of the adverse effects of decreased food intake on nutritional status.<sup>5–7</sup>

In the CRF disease the protein intake and some minerals as potassium should be controlled. Dietary therapy is also very important, especially when the disease is present at a more advanced stage when the capacity of the kidney to excrete dietary excess and metabolic by products is too low. In this step, the nutrition becomes one of the most difficult problems for the patient, since it is necessary to introduce some nutrients limitation and this implies in avoiding some favorite foods.<sup>8</sup>

The findings show that early nutritional intervention may delay or even prevent rapid progression of renal diseases in some patients. Therefore, patients' diets should be accurately assessed. This can be performed mainly by software programs, food composition tables or direct analysis of the diets.

In the present work, diets of 39 patients (25 male and 14 female) with chronic renal failure in a pre-dialysis stage, with ages ranging from 18 to 79 years, undergoing a conservative treatment, were analyzed. Fe and Zn concentrations were determined by instrumental neutron activation analysis. The 24-hour recall method was used for sample collection and the content of proteins, lipids and carbohydrates were also analyzed in the diets. This study aims at assessing these elements content and also diets proximate compositions of this group.

### Experimental

#### *Sample collection and preparation*

The protocol for the study with these patients was approved by the São Paulo Hospital (UNIFESP) Research Committee. After giving their informed consent, thirty nine nondialyzed patients with CRF were selected in this study during the period of October 1999

\* E-mail: defavaro@curiango.ipen.br

to April 2000. In Table 1 the characteristics of these patients are shown. The dietary prescription for them was to consume 0.6 g protein/kg/day and 35 kcal/kg/day.

Stature and weight were used in the Body Mass Index (BMI) ( $\text{weight}/\text{stature}^2$  in  $\text{kg}/\text{m}^2$ ) to describe levels of body composition in adults group. Each patient completed a 24 hours food records. Before the collection of food records, each patient underwent a standardized session on how to keep food records, including instructions on how to estimate the portion sizes. After this, all patients' meals were prepared in the Laboratory of Experimental Nutrition from the food records, mixed and homogenized in a domestic blender. After this, the diets were freeze-dried and again mixed and homogenized.

#### Determination of the proximate composition

The diets were analyzed for their moisture content at 105 °C, fixed mineral residue (550 °C), protein (micro Kjeldahl method) and ether extract (Soxhlet method), according to the methodology of the AOAC (1990).<sup>9</sup> The carbohydrate amount was obtained as the difference between total dry weight and the sum of protein, fat and ash content.

#### Instrumental neutron activation analysis (INAA)

INAA was used to determine Fe and Zn concentrations in 39 diets of patients with CRF. Fe and Zn synthetic standards were prepared from SPEX CERTPREP standard solutions. The analytical procedure was already described in previous work.<sup>10</sup>

*Validation of the methodology:* The reference materials Typical Diet (SRM NIST 1548<sup>a</sup>), Peach

Leaves (SRM NIST 1547) and Orchard Leaves (SRM NIST 1541) were used for checking the precision and accuracy of the method.

## Results and discussion

The results obtained for dietary data of the diet samples analyzed are shown in Table 2 and are discussed below:

#### Proteins

It has been shown that a protein-restricted diet can ameliorate many uremic symptoms and certain CRF complications.<sup>11,12</sup> In general, protein intake of 0.6 to 0.8 g/kg/day can make renal failure develop more slowly, as well as avoid uremic toxin accumulation. In this study it was verified that 74% of the patients consumed more than 0.8 g protein/kg/day with 26%, showing an intake higher than 1.0 g protein/kg/day. The others (22.2%) followed the dietary prescription and only one patient presented an intake of 0.56 g protein/kg/day.

#### Energy intake

Many authors concluded that 35 kcal/kg/day is the energy intake recommended for patients with CRF in a pre-dialysis stage.<sup>8,13</sup> KOPPLE<sup>8</sup> showed that these patients have a daily intake of 24 to 27 kcal/day and even those under treatment did not achieve the recommended energy intake. In this study it was also observed that 70% of the patients consumed less than the recommended value with the following distribution: 50% between 20–30 kcal/kg/day, 20% less than 20 kcal/kg/day, 12% between 30–35 kcal/kg/day and 18% more than 35 kcal/kg/day.

Table 1. Characteristics of patients with CRF compared to the normal values

Data	Uremics patients, mean $\pm$ sd (range)	Normal values, (range)
Age females (years) (14)	50.5 $\pm$ 17.2	
Age males (years) (25)	58.6 $\pm$ 14.4	
Creatinine clearance ml/min/1.73 m <sup>2</sup>	34.6 $\pm$ 13.3 (14 – 62)	90 - 130
Serum creatinine mg·dl <sup>-1</sup>	2.7 $\pm$ 1.1 (1.3 – 5.6)	0.5 – 1.2
Hemoglobin g·dl <sup>-1</sup>	11.7 $\pm$ 1.6 (7.8 – 14.7)	> 12
Hematocrit, %	35.8 $\pm$ 4.6 (24 – 45)	> 37
Ferritin, ng/ml	84.6 $\pm$ 67 (5 – 246)	> 100
BMI kg/m <sup>2</sup>	25.3 $\pm$ 4.5 (20.5 – 41.6)	18 – 25

Table 2. Comparison between dietary intake of the patients with CRF and recommendations<sup>8</sup>

Energy/Nutrient	Patients	Recommendation <sup>8</sup>
Energy, kcal/day	1444 ± 409** (799 – 2427) ***	–
Energy, kcal/kg/day	26.2 ± 7.7 (13.7 – 39.7)	30 – 35
Proteins, g/kg/day	0.89 ± 0.2 (0.4 – 1.4)	0.6 – 0.8
PNA,* g/kg/day	0.96 ± 0.26 (0.55 – 1.66)	0.6 – 0.8
Carbohydrates, %	64.4 ± 7.9 (46.3 – 81.2)	The rest of kcal
Lipids, %	20.4 ± 7.0 (7.1 – 36.7)	30

\* PNA: Equivalent of protein nitrogen appearance.

\*\* Mean ± standard deviation.

\*\*\* Extreme values.

### Lipids

The lipid contents of the diets contributed with low caloric percentages (20.4%), with the extreme values of 7.1 to 36.7%, which led to in a caloric percentage adequacy below the recommended value of 30%. Dietary protein cannot be considered alone because when protein is limited, it is important that enough

calories are consumed. MONTEON et al.<sup>14</sup> showed that an adequate calorie supply is critical for CRF patients who have protein-restricted diets.

### Carbohydrates

The average intake of carbohydrates was 64.4%, ranging from 46.3 to 81.2%.

Three reference materials from NIST were analyzed by INAA according to the *z*-criteria. The standardized difference or *z*-value was calculated according to BODE.<sup>15</sup> If  $|z| < 3$  means that the individual result of the control sample (reference material) should be in the 99% confidence interval of the target value. In both cases *z* values ranged from –1 to 0.5, indicating a good precision and accuracy of the results.

The average concentration values obtained by INAA were: for the male group: Fe – 17.2 ± 5.8 (9.0–28.4) and Zn – 18.1 ± 5.9 (9.3–30.5) mg·kg<sup>-1</sup> and for the female group: Fe – 18.4 ± 7.7 (11–37) and Zn (15.9 ± 4.7 (11–27) mg·kg<sup>-1</sup>. The average daily dietary intake obtained was 6.3 (±2.8) mg Fe/day and 6.6 (±2.6) mg Zn/day for the male group whereas for the female group, 6.0 (±2.0) mg Fe/day and 5.2 (±1.2) mg Zn/day.

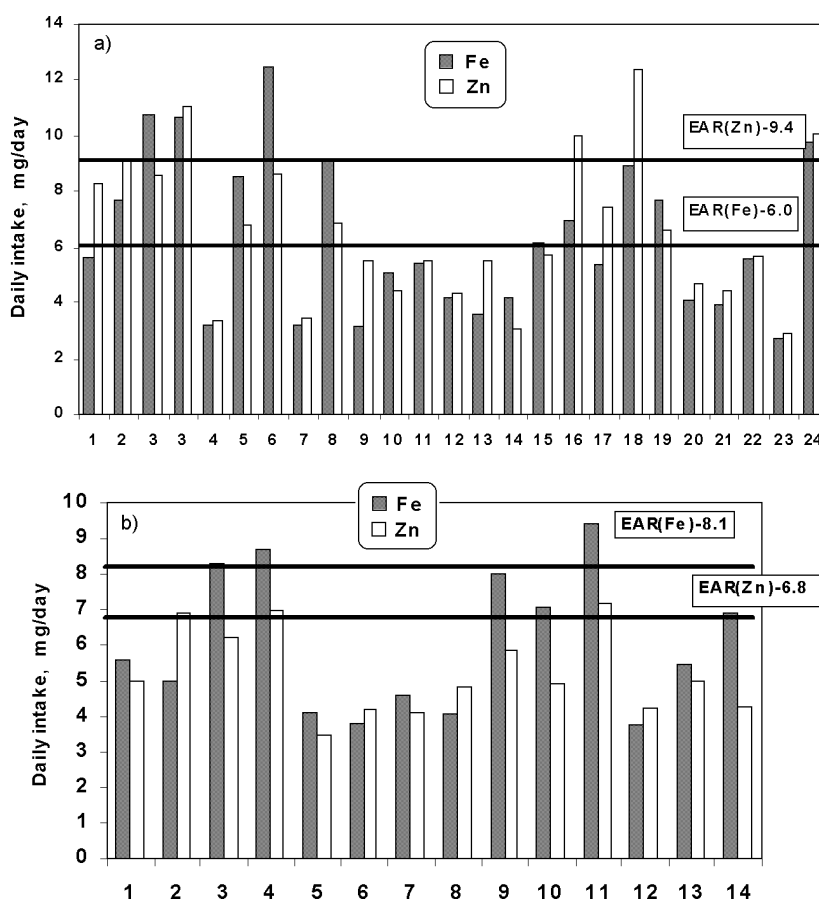


Fig. 1. Daily intake (in mg/day) compared with EAR values for Fe and Zn, for male (a) and female (b) groups

Figure 1 shows the daily intake values compared with the new EAR<sup>16</sup> (Estimate Average Requirement) values for Fe and Zn, in both groups. It could be verified that in the female group the adequacy was obtained only for 21.4% of the diets for Fe and Zn. For the male group the adequacy was 44% for Fe and 16% for Zn. It was observed that the diets showed to be deficient for these elements and therefore there should be a nutritional follow-up to avoid possible negative effects.

Restriction in protein intake is one of the factors that promote abnormalities in mineral concentration, vitamins and essential aminoacids in patients with CRF, since the main source of proteins such as meat also contributes with micronutrients. HIDA et al.<sup>17</sup> studying patients with different levels of CRF, found that protein intake of 20 g/day, even though adequate for essential aminoacids, did not meet the recommendation regarding vitamins A, B<sub>1</sub>, B<sub>2</sub>, B<sub>6</sub> and also Ca, Fe and Zn. They concluded that there was a need of micronutrient supplementation even though protein intake recommendation was achieved.

MAFRA et al.<sup>18</sup> showed that absolute iron deficiency could occur on nondialyzed patients, and that there is an abnormal distribution of zinc in these patients. The low intake of these minerals can lead to deficiency in uremia.

A low protein diet reduces zinc and iron intake and is correlated with meat consumption. Zinc supplementation may be recommended for patients with proven zinc deficiency, however, it is questionable for all chronic renal failure patients. Iron supplementation is recommended to correct anemia, and according to the stage of the disease, the combination of erythropoietin as adjuvant therapy is necessary.

### Conclusions

The results from the dietary analysis of the present study showed that predialysis patients consumed less than 50% of the recommended values for zinc and iron. With the low dietary intake reported for zinc and iron by these patients, they may be in a steady state of negative zinc and iron balance. In addition, further studies with uremic patients should evaluate the effect of both, zinc and iron supplementation together on mineral balance.

\*

The authors would like to thank the financial support given by FAPESP from Brazil.

### References

1. T. ZIMA, V. TESAR, O. MESTEK, K. NEMECEK, *Blood Purif.*, 17 (1999) 187.
2. L. M. BLENDIS, M. AMPIL, D. R. WILSON, J. KIWAN, J. LARANCHE, M. JOHNSON, C. WILLIAMS, *Am. J. Clin. Nutr.*, Bethesda, 34 (1981) 2658.
3. D. S. SILVERBERG, M. BLUM, Z. AGBARIA, D. SCHWARTZ, A. A. ZUBKOV., T. YACHNIN, A. IAINA., *Kidney Intern.*, 55, Suppl. 69 (1999) 79.
4. D. S. SILVERBERG, M. BLUM, Z. AGBARIA, V. DEUTSCH, M. IRONY, D. SCHWARTZ, R. BARUCH, T. YACHININ, *Clin. Nephrol.*, 55 (2001) 212.
5. J. A. BETO, *J. Am. Diet. Assoc.*, 95 (1995) 898.
6. T. A. IKIZLER, R. M. HARIM, *Kidney Intern.*, 50 (1996) 343.
7. A. L. STEIBER, *J. Renal Nutr.*, 9 (1999) 84.
8. J. D. KOPPLE, *Nutritional Management of nondialysed patients with chronic renal failure*; in: *Nutritional Management of Renal Disease*, J. D. KOPPLE, S. G. MASSRY (Eds), Williams and Wilkins, Maryland, 1997, p. 479.
9. Association Official Analytical Chemists. *Official Methods of Analysis of the AOAC*, 15th ed., Assoc. Off. Agric. Chem., Washington, 1990.
10. D. I. T. FÁVARO, V. A. MAIHARA, D. MAFRA; S. A. SOUZA, M. B. A. VASCONCELLOS, M. B. C. CORDEIRO, S. M. F. COZZOLINO, *J. Radioanal. Nucl. Chem.*, 244 (2000) 241.
11. B. M. BRENNER, T. W. MEYER, T. H. HOSTETTER, *N. Eng. J. Med.*, 307 (1982) 652.
12. W. E. MITCH, *Kidney Intern.*, 57 (2000) 38.
13. W. E. MITCH, *Am. J. Clin. Nutr.*, 67 (1998) 359.
14. F. J. MONTEON, S. A. LAIDLAW, J. K. SHAIK, J. D. KOPPLE, *Kidney Intern.*, 30 (1986) 741.
15. P. BODE, *Instrumental and Organizational Aspects of a Neutron Activation Analysis Laboratory*, Interfaculty Reactor Institute, Delft University of Technology, Delft, The Netherlands, 1996, p. 147.
16. Food and Nutrition Board, *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium and Zinc*, National Academy of Sciences, Washington, 2001.
17. M. HIDA, H. FUJI, T. SATOH, *Nippon Jinzo Gakkai Shi*, 36 (1994) 740.
18. D. MAFRA, L. CUPPARI, S. M. F. COZZOLINO, *J. Renal Nutr.*, 12 (2002) 38.