Oral intake and serum levels of ascorbic acid in continuous ambulatory peritoneal dialysis patients

Authors: Su-Lin Lim, Evan JC Lee, Cho-Cho Myint, Kae-Tee Ong, Meng-Eng Tay, Nor Yusuf, Choon-Nam Ong*,

Affiliation: Division of Nephrology, Department of Medicine,
National University Hospital, Singapore.
Dept of Community, Occupational and Family Medicine,
National University of Singapore

Running head: Oral intake and serum ascorbic acid in CAPD

Abstract

Oral intake of ascorbic acid (AA) is essential for optimum health in human beings. CAPD patients have an increased need for ascorbic acid, as there are increased losses through the dialysate, reduced intake due to nausea and loss of appetite, and increased oxidative stress. The optimum intake however is still controversial. Fifty clinically stable patients were studied to determine the relationship between their oral intake and serum ascorbic acid (SAA) levels. The oral intake ranged from 28-412 mg/day. Only one patient had oral intake <60mg/day. SAA ranged from 1-36.17 mg/L. Although there was strong correlation ($p<0.001$, $R^2=0.47$) between intake and SAA, the variation of SAA at any given intake level was wide. Sixty two percent of patients had SAA<8.7mg/L, 40% had SAA<5.1mg/L (below level of healthy population), and 12% had levels <2mg/L (scorbutic). None of the patients demonstrated clinical manifestations of scurvy. Our results show that in CAPD patients, deficiency of ascorbic acid can only be detected reliably with SAA measurements and that oral intake may influence levels of SAA. To maintain the AA in the normal range for healthy adults the oral intake of AA needs to be increased above the US RDA to 80-140mg/day.

Key Words: Ascorbic acid, CAPD, Dietary intake

Introduction

AA is involved in the formation and repair of collagen, development of bones and teeth, amino acid metabolism and the synthesis of hormones (1), wound healing and facilitates iron absorption and utilization in. AA is also an important plasma antioxidant. Patients undergoing CAPD are at great risk to become deficient in AA because of inadequate dietary intake (due to nausea and loss of appetite), altered metabolism in uremia and loss into dialysate (2). Oxidative stress may possibly increase the requirement for AA to maintain normal levels of serum AA. The serum levels of AA have been reported to be low in some studies of dialysis patients (3, 4). Supplementation with AA has been recommended but an optimum dose has yet to be determined as excessive intake of AA may cause hyperoxalemia in dialysis patients (2).

Objective:

We therefore conducted a cross sectional study on clinically stable CAPD patients to determine the relationship between serum ascorbic acid and daily oral ascorbic acid intake.

Patients and methods

Patients: Fifty patients aged 18 years and above who were on peritoneal dialysis for at least 3 months (mean 22 $\pm$ 26 months) were selected for study (Table I). Patients with the following were excluded: current peritonitis or peritonitis within the last 4 weeks, a history of renal calculous disease, a smoking history.

Methods

Measurement of Serum Ascorbic Acid: Venous blood samples of patients were analysed for serum ascorbic acid (SAA) by HPLC with UV detection at 245 nm according to the procedure by L. S. Liau, et.al., 1993 (5).

Oral ascorbic acid intake: Patients were given a 3-day food diary chart with appropriate instructions. On the fourth day, patients were interviewed on their food diaries. Food items and amounts were verified using food models. Dietary AA intake were calculated using NutriGenie Total Nutrition v4.8 software and data for local foods not available in the software were entered based on nutrient analyses from the Singapore Food Facts 1999 and Nutrient Composition of Malaysian Foods - 4th edition (6). All supplements containing AA were taken into account and patients' total AA intakes were then obtained by adding the dietary intake and the oral supplementation of AA.

Statistical methods: Data was analysed by SPSS 10.0 windows. The bivariate correlation coefficient was calculated between SAA and oral AA intake. A p value <0.05 was considered as significant.

Results

Ascorbic acid obtained from diet in our CAPD patients ranged from 7 – 215 mg per day (mean: 67 $\pm$ 51 mg/day) (Table II). Thirty six percent of our patients did not even take 1 serving of fruit per day, 42% consumed 1 serving of fruit and only 22% ate 2 servings of fruit per day (Figure 2). All except 5 patients was on AA supplements of between 50 –360 mg per day (Figure 3). The total oral intake (AA from diet + AA supplements) ranged from 28 to 412 mg/day (Table II). Only one patient had total oral intake less than 60 mg/day.

SAA levels ranged from 1.00-36.17 mg/L. Although there was strong correlation ($p<0.001$, $R^2=0.47$) between intake and SAA, the variation of SAA at any given intake level was wide (Figure 1). Sixty two percent of patients had SAA<8.7mg/L, 40%had SAA < 5.1mg/L (below level of healthy Singapore adults), and 12% had levels <2 mg/L (scorbutic). None of the patients however demonstrated clinical signs or symptoms of scurvy.

Discussion

Ascorbic acid has been shown to be essential for health and an important antioxidant in humans (7). It is not synthesised and needs to be obtained from dietary intake (8). It is water-soluble, removed through the dialysate (9) and serum levels have been shown to be low in several populations of CAPD patients (3, 10).

The US Recommended Dietary Allowance (RDA) for AA is 60 mg per day for healthy, non-smoking adults (11). This amount prevents the development of scurvy for about 1 month with a diet lacking in AA (12). Smokers need at least 100mg of AA (1). In our study, we excluded patients who were smokers. The

requirements for AA is increased in many situations such as wound healing and its efficacy is reduced by many drugs (i.e., tobacco and aspirin) (13).

Ascorbic acid obtained from diet in our CAPD patients ranged from 7 – 215 mg per day (mean = 67 mg). Fifty-six percent of our patients had dietary AA intake of less that the US RDA recommendations. Most of our patients have a relatively low intake of fresh fruits, which is the diet's main source of AA. Thirty- six percent did not even take 1 serving of fruit per day (Figure 2). However the total oral intake of AA inclusive of supplements exceeded 60 mg/day for almost all our patients. The optimum daily requirement needed to prevent AA deficiency in CAPD patients is still controversial, as large doses of AA supplementation may lead to hyperoxalaemia (14).

Healthy non-smoking adults in Singapore have SAA levels ranging from 5.1 – 8.7 mg/L(12). The range for normal healthy adults in US is 4 to 15 mg/L (15). Our results show that a large proportion of our CAPD patients have levels of SAA which are low (<5.1 mg/L) when compared to those found in a culturally comparable population without renal failure (16). Possible reasons include:

1. Reduced intake – due to renal failure (loss of appetite, nausea and easy satiety); and inadequate or inappropriate diet preparation. In addition, some patients may still practise some of the pre-dialysis advice of potassium restriction which indirectly limits foods that tend to be high in AA, and boiling of vegetables which destroys AA.

2. Increased loss into the dialysate. Dialysate removal of AA rises with intake (3, 17) and can be as much 10.5 mg/L (3). It has been estimated that 62% of the plasma concentration of AA is lost into the dialysate (3).

Twelve percent of our patient had SAA levels below scorbutic level (<2 mg/L). The finding that none of the patients had signs of scurvy despite low serum AA levels suggests that signs may manifest only late in a deficiency state. This may be because the body normally stores about 1500 mg of vitamin C, and clinical signs of deficiency do not occur until the body pool is less than 300 mg which may take several weeks (1). Our data confirms that early deficiency of ascorbic acid can be detected earlier with SAA measurements.

Studies in normal populations in the US have shown that serum AA levels and oral intake correlate well until the dietary intake reaches 100 –150 mg/day at which point the serum levels plateau at 14 mmol/L (18). In our study, the serum levels did plateau with dietary intake of 100 - 150 mg. On the contrary, we found that patients taking a higher amount of AA continued to show a higher SAA. The data also showed a strong correlation between oral intake of AA and the SAA.($p<0.001$, $R^2 =0.47$). However the variation of SAA at any given

intake level was very wide. This may be due to the lack of precision in our methods of estimating overall intake or may suggest that oral intake is not the only factor influencing SAA.

All our patients except one had total oral AA intake estimated to be above that of the US RDA of 60mg/day. Despite this, 40% of our CAPD patients had serum AA less than 5.1 mg/L. This suggests that the requirement for oral intake of AA for CAPD patients to maintain SAA levels comparable to normal healthy adults should be more than 60 mg/day. From our data, we conclude that this oral intake level of AA should be 90-140 mg/day (fig 1).

References:

1. McDonald A, Natow A, Heslin JA. Vitamin C. Complete Book of Vitamins and Minerals. Illinois: Publications International 1993; 165-176

2. Kopple JD, Massry SG. Nutritional Management of Renal Disease. Baltimore: Williams & Wilkins 1997; 619-656

3. Blumberg A, Hanck A and Sander G. Vitamin nutrition in patients on continuous ambulatory peritoneal dialysis (CAPD). Clinical Nephrology 1983; 20 (5): 244-250.

4. Ha TKK., Sattar N, Talwar D, et al. Abnormal antioxidant vitamin and carotenoid status in chronic renal failure. Quarterly Journal Medicine 1996; 89: 765-769

5. Liau LS, Lee B.L., New A.L. and Ong C.N. Determination of plasma ascorbic acid by high-performance liquid chromatography with ultraviolet and electrochemical detection. Journal of Chromatography 1993; 612: 63-70

6. Tee ES, Noor MI, Azudin MN, Idris K. Nutrient Composition of Malaysian Foods – 4 th Edition. Kuala Lumpur: Institute for Medical Research 1997.

7. Antos M, Strujic JB, Raos V, Romic Z, Matanovic B. Evidence of antioxidant role of vitamin C in chronic haemodialysis patients. Trace Elements and Electrolytes 1997; Vol. 14, No. 3: 159-161

8. Nishikimi M, Koshizaka T, Ozawa T, Yagi K. Occurrence of humans and guinea pigs of the gene related to their missing enzyme L-gulono-γ- lactone oxidase. Archives of Biochemistry and Biophysics 1988; Volume 267(2):842-846

9. Mydlik M., Derzsiova K., Valek A., Szabo T., Dandar V., Takac M. Vitamins and continuous ambulatory peritoneal dialysis (CAPD). International Urology Nephrology 1985; 17 (3): 281-6.

10. Petridou M, Sinakos Z, Vergoulas G. Effect of ascorbic acid on the haemopoiesis of patients with chronic renal failure receiving CAPD. Nephron 1988; 49:175-176

11. National Research Council. Recommended dietary allowances. 10th ed. Washington DC:National Academy Press, 1989

12. Young VR. Evidence for a recommended dietary allowance for vitamin C from pharmacokinetics: a comment and analysis. Proc Natl Acad Sci USA 1996; 93:14344-14348.

13. Burtis G, Davis J, Martin S. Water Soluble Vitamins. Applied Nutrition and Diet Therapy. Philadelphia:WB Saunders Company 1988:186 –189.

14. Makoff R. Water soluble vitamin status in patients with renal disease treated with haemodialysis or peritoneal dialysis. Journal of Renal Nutr 1991; 1:56-73.

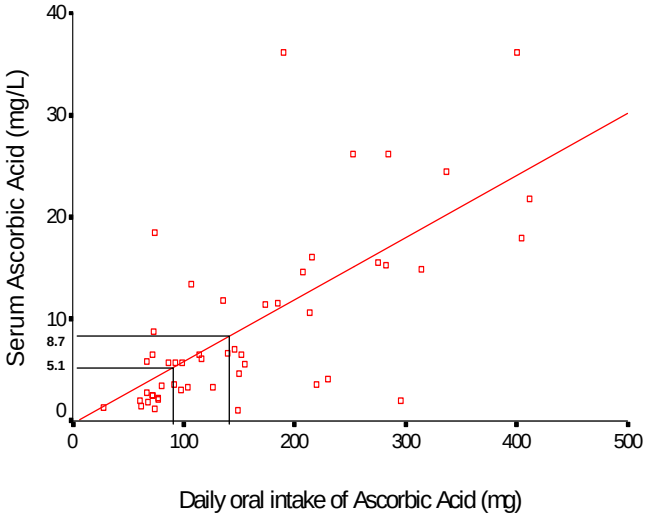
15. Jacob RA. Vitamin C. In: Shils ME, Olson JA, Shike M, ed. Modern Nutrition in Health and Disease. Philadelphia: Lea & Febiger, 1994:432-448.

16. Hughes K, New AL, Lee BL, Ong CN. Plasma Vitamins A, C and E in the General population of Singapore, 1993 to 1995. Annals Academy of Medicine Singapore 1998; 27:149-53.

17. Shah G.M., Ross E.A., Sabo A., et al., Ascorbic Acid Supplements in Patients receiving Chronic Peritoneal Dialysis. American Journal of Kidney Diseases 1991; XVIII (1): 84-90

18. Sauberlich HE. Vitamin C status: Methods and findings. Ann NY Acad Sci 1975; 258:438-450

Figure 1: Scatter plot & Correlation of serum levels with dailv oral intake of Ascorbic Acid



p<0.001, R square =0.47

Figure 2: Fruit consumption per day among CAPD patients

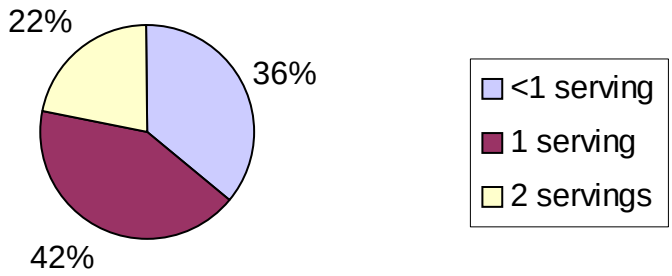


Figure 3: Ascorbic Acid supplements in CAPD patients

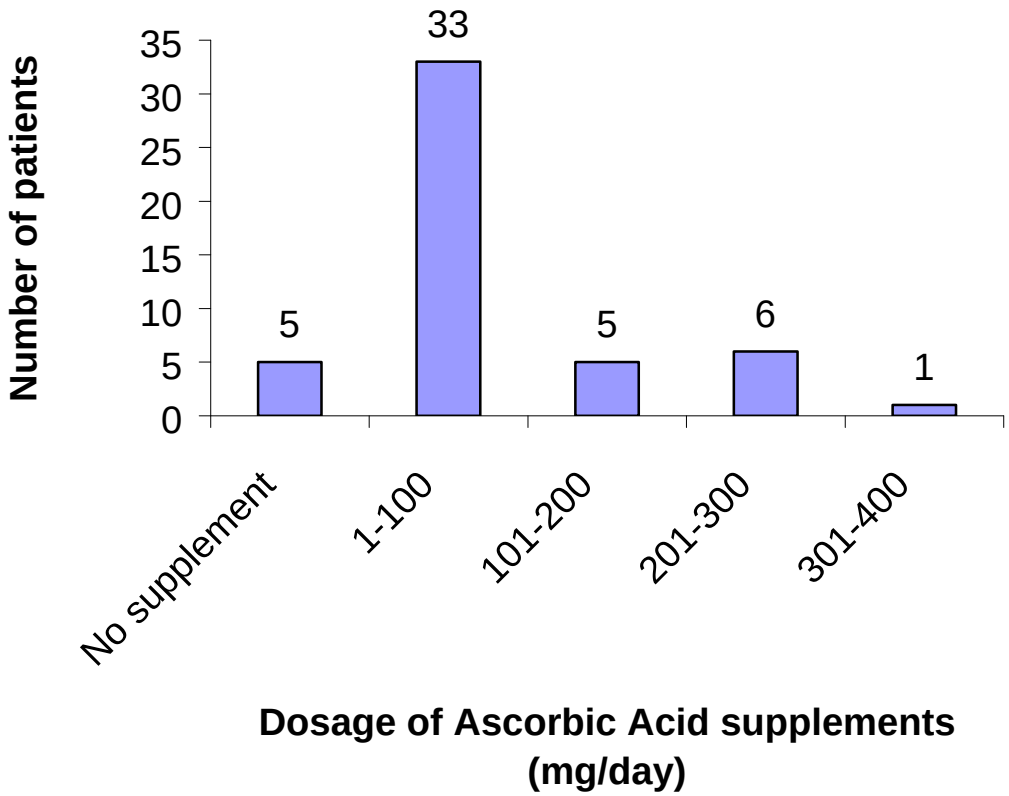


Table I: Patient demographics

Age (mean ± SD years)	60.84 ± 11.03 years
Age range (years)	(36 – 81)
Sex (Male : Female)	24 : 26
Diabetic status (yes: no)	32 : 18
Causes of Renal Failure	Diabetes Mellitus - 64%
	Glomerulonephritis - 26%
	Others - 10%
Duration on CAPD	22 ± 26 months
Racial distribution	
(Chinese:Indian:Malay)	38 : 5 : 7

Table II: Oral intake and serum levels of Ascorbic Acid

Parameters	**Range**	**Mean ± SD**
Ascorbic acid from diet (mg/day)	7 – 215	67 ± 51
Ascorbic acid from supplements (mg/day)	50 – 360	93 ± 83
Total ascorbic acid intake (mg/day)	28 – 412	160 ± 100
Serum ascorbic acid (mg/L)	1.00 -36.17	9.44 ± 8.80