Cross-Sectional Analyses of Non-Urea Nitrogen Appearance (NUNA) in a CAPD Population

In dialysis patients who are in stable nitrogen balance, it is considered reasonable to estimate dietary protein intake from urea nitrogen appearance (UNA) and direct protein losses (1-5). Such calculations are based on previous measurements of the relationship of total nitrogen appearance (TNA) and UNA in dialysis patients (1-4). Relationships in patients with chronic renal failure not on dialysis (5), or in normal controls (5), are similar to those in dialysis patients. In prospective serial studies, the relationship of TNA to UNA is linear with a slope near 1.0 and an intercept (at a UNA of zero) > 1.0, indicating non-urea nitrogen appearance (NUNA) (5). With increased protein intake, increases in UNA account for almost all increases in TNA, and NUNA remains nearly constant, as reflected by an almost fixed value for TNA UNA (2,5). The ratio UNA/ TNA increases as UNA increases since the equal increments represent smaller percentage increases in TNA (5-7). Estimates of dietary protein intakes from these UNA are usually normalized to standard weight (g/kg st wt/day) and termed the normalized protein equivalent of nitrogen appearance (nPNA) (1).

The purpose of this study was to assess the variability TNA UNA (which is NUNA) in our own CAPD population.

TABLE 1
Population Characteristics

	Mean±SD	Range
Time on CAPD (months)	23±24	1–105
Age (years)	56±13	27–81
Height (cm)	169±10	147–196
Weight (kg)	76±18	44–151
Body surface area (m^2)	1.9±0.2	1.4–2.6
Lean body mass (kg)	44±14	21–75
Lean body mass (%)	58±13	32–92
Total body water (L)	38±8	26–97

TABLE 2
Nutritonal and Adequacy Indices

	Mean±SD
Total serum protein (g/dL)	6.6±0.8
Serum albumin (g/dL)	3.7±0.6
nPNA (g/day/kg standard wt)	0.91±0.21
Kt/V urea	2.0±0.4
Total creatinine clearance[a] (L/wk/1.73 m^2 BSA)	66±23
TNA (g/day)	8.8±3.1
UNA (g/day)	5.9±2.3
TNA – UNA (g/day)	2.9±1.9

nPNA = normalized protein equivalent of nitrogen appearance, TNA = total nitrogen appearance, UNA = urea nitrogen appearance.
[a] Dialysis plus estimated clearance by glomerular filtration.

MATERIALS AND METHODS

In 80 patients on CAPD (43 males and 37 females), we collected 24 hour dialysates and urines, and measured UNA and total Kjeldahl nitrogen therein. The nPNA was calculated as per Randerson formulas (2), which are similar to the Borah equation plus protein losses (3). Fixed estimates of fecal and skin nitrogen losses are incorporated in the formula. We have previously compared Randerson 1 and Randerson 2 formulas in our CAPD patients and find similar results with both (2,8). In Randerson 1: PNA (g/day) = 0.262(UG + 54) + protein losses (g/day). Here UG is urea appearance in μmol/minute. In Randerson 2: PNA(g/day) = 0.301(UG + 52). UGis as above. Protein losses are incorporated as a fixed average 7.3 g/day. In both equations, fecal and skin nitrogen losses are included as an estimated 1.3 g/day (2). In both, PNA was normalized to standard weight (nPNA).

Dialysate effluent, urine, and serum samples were analyzed for concentrations of urea nitrogen, creatinine, and total protein by methods previously described (9,10). Fecal and skin nitrogen losses were neither measured nor estimated, except in the calculation of nPNA via Randerson. Total nitrogen concentrations were measured by the Kjeldahl method (11). Estimated body surface area (BSA), total body water (TBW), residual renal creatinine clearance by glomerular filtration rate (L/wk/l.73 m2 BSA), total weekly creatinine clearances (L/wk/l.73 m2), total weekly Kt/V urea, urea nitrogen appearance (g/day), and lean body mass (kg and percentage body weight) were determined as previously described (8-10) .TN A (g/day) was calculated as the sum of the products of dialysate and urine volumes times their respective total nitrogen concentrations. PNA was normalized to standard body weight calculated as TBW/0.58. TBW was estimated according to Watson *et al.* (12).

Mean ± standard deviations of important outcome measures were calculated. A

RESUL

TS

Table 1 summarizes the population characteristics of the 80 CAPD patients. Table 2 summarizes selected nutritional and adequacy indices. Mean values for indices of nutrition and clearances are similar to those previously reported (8,10). The nPNA from Randerson 1 is shown. Randerson 2 PNA was 0.93 ± 0.22.

Figure 1 shows the relationship of total Kjeldahl nitrogen output (TNA in grams per day) to total urea nitrogen output (UNA in grams per day). Identity and regression lines are shown. There is a very high correlation but substantial scatter around the linear regression line. The intercept of2.44, a mean value of TNA -UNA of2.87 ± 1.9, and a slope of 1.07 support previous reports implying that increases in UNA account for almost all increases in TNA as UNA increases (5). Thus, TNA UNA remains relatively constant as UNA increases as indicated by the near parallelism of the regression and identity lines. Accordingly, there was no significant correlation of TNA UNA (representing NUNA) with nPNA by

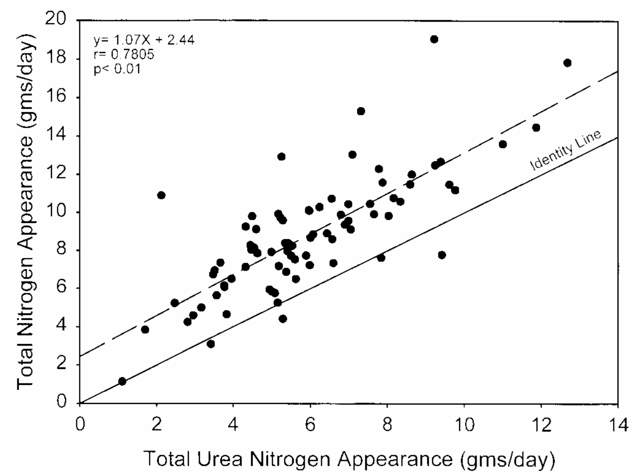

Figure 1 — Total urea nitrogen appearance (TNA) is related to urea nitrogen appearance (UNA). Both are in g/day. The linear regression (broken) and identity lines are shown.

either calculation. There were also no significant correlations of NUNA with components of NUNA, such as creatinine and protein losses, suggesting unpredictable variable proportions of NUNA substances from patient to patient. There was a significant positive correlation ofNUNA with total Kjeldahl nitrogen losses (r = 0.69, p < 0.0001) compatible with the slope of 1.07 in Figure 1, suggesting some very small increases in NUNA as UNA and TNA increase.

DISCUSSION

We have recently compared nPNA calculated by Randerson to that calculated by multiplying total Kjeldahl nitrogen output by 6.25 (8). This previous report found that nPNA calculated from urea kinetics and protein losses in CAPD patients was highly correlated with PNA calculated from Kjeldahl nitrogen output.

The standard deviation for TNA UNA of 1.9 implies a potential variation of more than (1.9 x 6.25) or 11.9 grams ofPNA per day at a given UNA in onethird of the population on CAPD. Based on the average standard weight of 65.5 kg (mean TBW of 38/0.58), this represents a variation of more than 11.9/65.5 = 0.18 g/kgfornPNA, normalized to standard body weight. Thus, some caution is necessary in calculating PNA and nPNA from UNA based on unpredictable variations in NUNA from patient to patient. Reports with less variation of NUNA probably include serial measurements ofNUNA at varying protein intakes in the same patient rather than cross-sectional single measurements per

Our linear regression results are consistent with NUNA remaining nearly fixed as UNA increases, as reported by others even though ours is a crosssectional study (5). The use of standard formulas to calculate PNA from UNA (based on previously determined relationships of TNA to UNA) is subject to some error based on variation ofNUNA from patient to patient, accounting for scatter around linear regression lines. The error in nPNA is of a magnitude >0.18 g/kg standard body weight in over one-third of the CAPD patients. Thus, the average nPNA of 0.91 calculated from UNA could be associated with a true value more than 1.09 or less than 0.73 in one-third of patients. NUNA in each patient represents a summation of creatinine nitrogen, protein nitrogen, urate nitrogen, amino-acid nitrogen, and other non-urea nitrogen outputs that seem to have different proportions of each from patient to patient, since there were poor correlations of NUNA with individual components of NUNA in our cross-sectional study. Also, protein intake and increased UNA result in only slight increases in NUNA (TNA to UNA linear regression slope = 1.07).

Talha H. Imam [1]

Harold L. Moore [1,2]
Karl D. Nolph [1,2]
Ramesh Khanna [1,2]
Zbylut J. Twardowski [1,2]

Division of N ephrology [1]
Department of Internal Medicine
Dalton Cardiovascular Research Center [2]
University of Missouri-Columbia

Columbia, Missouri, U.S.A.

REFERENCES

1. Kopple JD, Jones MR, Keshaviah PR, *et al.* A proposed glossary for dialysis kinetics. *Am J Kidney Dis* 1995; 26:963-81.
2. Randerson DH, Chapman GV, Farrell PC. Amino acid and dietary status in CAPD patients. In: Atkins RC, Thomson NM, Farrell PC, eds. Peritoneal dialysis. Edinburgh: Churchill Livingstone, 1981:179-91.
3. Borah MF, Schoenfeld py, Gotch FA, Sargent JA, Wolf son M, Humphreys MH. Nitrogen balance during intermittent dialysis therapy of uremia. *Kidney Int* 1978; 14:491-500.
4. Keshaviah PR, Nolph KD. Protein catabolic rate in CAPD patients. *ASAIO Trans* 1991; 37:M400-2.
5. Grodstein G, Kopple JD. Urea nitrogen appearance, a simple and practical indicator of total nitrogen output. *Kidney Int* 1979; 16:953.
6. Bargman JM. The rationale and ultimate limitations for urea kinetic modeling in the estimation of nutri tional status. *Perit Dial Int* 1996; 16:347-51.
7. Blumenkrantz MJ, Kopple JD, Moran JK, Grodstein GP, Coburn JW. Nitrogen and urea metabolism during continuous ambulatory peritoneal dialysis. *Kidney Int* 1981; 20:78-92.
8. U sha K, Moore HL, Nolph KD. Protein catabolic rate in CAPD patients: comparison of different techniques. In: Khanna R, ed. Advances in peritoneal dialysis. Toronto: Peritoneal Dialysis Publications, 1996; 12:284-7.
9. Nolph KD, Moore HL, Twardowski ZJ, *et al.* Crosssectional assessment of weekly urea and creatinine clearances in patients on continuous ambulatory peritoneal dialysis. *ASAIO J* 1992; 38:M139-42.
10. Nolph KD, Moore HL, Prowant *B,et al.* Cross-sectional assessment of weekly urea and creatinine clearances and indices of nutrition in continuous ambulatory peritoneal dialysis patients. *Perit Dial Int* 1993; 13:178-83.
11. KjeldahlJ. Neue method zur bestimmung des stickstoffs in organischen körpern. *Zeitschrift fur Analystische Chemie* 1883; 22:366-82.
12. Watson PE, Watson ID, Batt RD. Total body water volumes for adult males and females estimated from simple anthropometric measurements.Am *J Clin Nutr* 1980; 33:27-39.