Gender, Degree of Obesity, and Discrepancy Between Urea and Creatinine Clearance in Peritoneal Dialysis

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Abstract. The effect of gender and degree of obesity on the size indicators V, used to normalize urea clearance (Kt/Vur), and body surface area (BSA), used to normalize creatinine clearance (Ccr), in peritoneal dialysis was studied by: (1) mathematical comparison of the formulae used to estimate V (Watson and Hume) with the Dubois formula used to estimate BSA in peritoneal dialysis; and (2) comparison of percent deviation of BSA (ΔBSA%) and V (ΔV%) from ideal weight estimates in 933 clearance studies performed in actual patients (555 in men and 378 in women on continuous ambulatory peritoneal dialysis). V was estimated by the Watson formulae and BSA by the Dubois formula in these studies. ΔBSA% and ΔV% were stratified in 10% increments in deviation of body weight from ideal (ΔW%) in these studies. Mathematically, the relationship between V and BSA is not linear. In the same subject, as obesity develops (ΔW% increases) and BSA increases in a linear manner, V increases exponentially. In addition, there are substantial differences in the relationship between V and BSA caused by gender. For the same height and BSA, men have a larger V than women. In the clearance studies performed in actual continuous ambulatory peritoneal dialysis patients, the difference between ΔV% and ΔBSA% increased significantly (P < 0.0001) from the wasted to the obese subjects by one-way ANOVA in both men and women. Normalization of urea and creatinine clearances by different size indicators creates two types of mathematical distortion in the relationship between the two clearances. One distortion is caused by the degree of obesity. The second distortion is caused by gender. Use of the same size indicator to normalize both urea and creatinine clearances would eliminate these distortions. (J Am Soc Nephrol 9: 497–499, 1998)

It is currently recommended that both urea and creatinine clearance should be used in the clinical assessment of peritoneal dialysis (PD) adequacy. The lowest acceptable clearances have increased. Earlier weekly targets were 1.7 for total Kt/Vur and 50 L/1.73 m² of body surface area (BSA) for creatinine clearance (Ccr) (1). Recent guidelines have set the weekly targets at 2.0 for Kt/Vur and 60 L/1.73 m² for Ccr (2) in continuous ambulatory peritoneal dialysis (CAPD) and at higher levels in intermittent forms of PD (2). Maintenance of both clearances above the target levels is prudent (3). The two clearances are mathematically coupled (4) and are highly correlated (5,6). However, discrepancies have been reported.

When the older clearance targets were used, discrepancies between Kt/Vur and Ccr were found in approximately 20% of the studies. The identified physiologic causes of these discrepancies were the type of peritoneal transport and the residual renal clearance: Subjects with low peritoneal solute transport type and Kt/Vur above the target value are at risk of Ccr below the target value, whereas subjects with substantial residual renal function and Ccr above the target value are at risk of Kt/Vur below the target value (6,7).

Using the newer targets, a discrepancy between the two clearances was reported in approximately 30% of the studies (8). Residual renal function was again identified as one cause of the discrepancy. In addition, the degree of obesity (the deviation of body weight from ideal weight) appeared to cause discrepancies between the two clearances (8). The development of obesity may either cause changes in peritoneal and/or renal function or produce different mathematical effects on the size indicators V and BSA. In this report, we studied the effects of developing obesity on V and BSA. A linear relationship between V and BSA would eliminate mathematical distortion as a potential cause of discrepancy between the normalized urea and creatinine clearances.

Materials and Methods
We performed a mathematical comparison between V and BSA and an analysis of the relationship between V and BSA from actual clearance studies in CAPD patients. The mathematical relationship between V and BSA was derived as follows: The general form of the anthropometric formula for V is (9–11):

\[ V = k_1 + aA + bH + cW, \]  

(1)

where A is age, H is height, and W is weight, and the coefficients a, b, and c plus the constant k₁ are gender-specific. The coefficient a differs from zero only in the Watson formula for men (10). From equation 1:

\[ W = (V - k_1 - aA - bH)/c. \]  

(2)
The formula for BSA is as follows (12):
\[
\log BSA = d(\log W) + f(\log H) + k_2, \tag{3}
\]
from which
\[
W = \{BSA/(H^2 10^{23})\}^{1/3} \tag{4}
\]
From equations 2 and 4:
\[
V = c\{BSA/(H^2 10^{23})\}^{1/3} + aA + bH + k_1. \tag{5}
\]
Equation 5 obtains the following specific forms for the Watson anthropometric V (10) and the Dubois BSA (12):
For men:
\[
V = 0.3362\{BSA/(71.8456H^{0.725})\}^{1.3529} - 0.09516A + 0.1074H + 2.447 \tag{6}
\]
For women:
\[
V = 0.2264\{BSA/(71.8456H^{0.725})\}^{1.3529} + 0.1069H - 2.097 \tag{7}
\]
The corresponding forms of equation 5 for the Hume V (11) and the Dubois BSA (12) are as follows:
For men:
\[
V = 0.296785\{BSA/(71.8456H^{0.725})\}^{1.3529} + 0.192786H - 14.012934 \tag{8}
\]
For women:
\[
V = 0.183809\{BSA/(71.8456H^{0.725})\}^{1.3529} + 0.344547H - 35.270121 \tag{9}
\]
Equations 6 and 7 were plotted assuming the same height in men and women (170 cm) and a change in BSA from weight gain secondary to developing obesity, not edema (9), from 1.3 to 2.5 m². In addition, the age of the male subjects was set at 50 yr.
The patient studies consisted of 933 clearance studies, 555 in men and 378 in women on CAPD. In these studies, V was computed by the Watson formulae (10), BSA by the Dubois formula (12), and ideal weight by the Hamwi method (13). After calculating percent deviations from ideal weight conditions in weight (ΔW%), BSA (ΔBSA%), and V (ΔV%), ΔW% was stratified by 10% increments. The differences between ΔBSA% and ΔV% among the stratified ΔW% groups were compared by one-way ANOVA separately in men and women.

Results

Figure 1 shows the mathematical relationship between V and BSA (equations 6 and 7). This relationship is not linear. In the same subject, a linear increase in BSA secondary to developing obesity (increase in ΔW%) is accompanied by an exponential increase in V. In addition, there are substantial differences between V and BSA caused by gender. For the same height and BSA, V is larger in men than in women.

Figure 2 shows ΔBSA% and ΔV% in 933 clearance studies. ANOVA disclosed that the difference between ΔV% and ΔBSA% increases progressively as ΔW% increases (P < 0.0001 in both genders). Thus, the relationship between V and BSA differs between subjects with different degrees of obesity. The difference between ΔV% and ΔBSA% became large in very obese subjects: At a ΔW% of 133% in a man, ΔV% was 70% and ΔBSA% was 48%. Despite the differences shown in Figure 2, high degrees of correlation were found between V and BSA (r = 0.939) and between ΔV% and ΔBSA% (r = 0.983).

Discussion

The size indicators V and BSA used to normalize urea and creatinine clearance, respectively, are computed from mathematical formulae in PD. Therefore, the relationship between V and BSA can best be shown by a mathematical comparison of the formulae. Using this method, we showed that the relationship between V and BSA is not linear and is affected by the degree of obesity (ΔW%) and by gender (Figure 1). As obesity develops, the increase in V is disproportionately greater than the increase in BSA. The result is that obesity causes a relatively smaller decrease in normalized Ccr than in Kt/Vurea. Two reports support this conclusion. In a study of 24 obese subjects with average ΔW% equal to 55%, Kt/Vurea was 28% lower, but Ccr was only 19% lower than their respective values calculated at ideal weight (14). A recent editorial reported similar results (15). The relationship between V and BSA is different between men and women, creating a second distortion in the relationship between the normalized clearances (Figures 1 and 2).

High correlation coefficients have been reported between V
and BSA (11,16) and were found in this study. Despite these high correlations, normalization of urea clearance by V and creatinine clearance by BSA creates a mathematical distortion of the relation between Kt/V_{cr} and C_{cr}. The use of different size indicators for urea and creatinine clearance in PD is based only on precedent. A plea for a unified size indicator was made in recent guidelines (2). The rate of elimination of any substance from the body, including urea and creatinine, is determined by the ratio of its clearance (K) to its volume of distribution (V), i.e., by K/V, not K/BSA (17). Urea V is equal to body water (18), whereas creatinine V is considered equal to body water (19). Although the evidence that creatinine V is equal to body water in PD is not definitive, we suggest that expressing creatinine clearance as Kt/V_{cr} offers a practical advantage over C_{cr} normalized by BSA, because it will eliminate the mathematical distortions in the relationship between urea and creatinine clearance caused by BSA.

Acknowledgment

This work was supported by the Albuquerque Veterans Affairs Medical Center.