Pergamon

PII: S0969-8043(97)00229-7

Appl. Radiat. Isot. Vol. 49, No. 5/6, pp. 671–672, 1998

Printed in Great Britain
0969-8043/98 $19.00 + 0.00

Determination of Total Body Water by IVNAA and ^{40}K Counting in Young Normal and Growth Hormone Deficient Adults

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Introduction

Of the many techniques that are available for the measurement of total body water (TBW), isotopic dilution using D_2O is generally regarded as the standard reference method. More recently, an alternative method of determining TBW has employed both total body chlorine (TBCl), as measured by *in vivo* neutron activation analysis (IVNAA), and total body potassium (TBK), determined by ^{40}K counting, which are markers of extra-cellular water (ECW) and intra-cellular water (ICW) respectively (Yasumura *et al.*, 1983; Mitra *et al.*, 1993). However, the use of this method has so far been limited to normal adults. In this study, we aimed to validate further the use of TBCl by IVNAA and of TBK by ^{40}K counting as a measure of TBW by presenting: (1) cross-sectional data from groups of young normal and growth hormone deficient (GHD) adults; (2) longitudinal data in GHD adults before and after a six-month period of treatment with recombinant growth hormone (rhGH).

Subjects and Methods

Thirty-six young normal adults (24 males, 12 females) aged between 18 and 30 years were recruited for the study. In addition, thirty-nine GHD adults (27 males, 12 females) were selected from a larger study of the effects of rhGH on body composition.

TBW was determined by two methods. First, the D_2O dilution technique was used as previously described (i.e. TBW(D_2O)) (Wong *et al.*, 1995). Second, TBW was calculated as the sum of ECW, as determined from the IVNAA measurement of TBCl, and ICW, as determined from the ^{40}K counting of TBK (i.e. TBW(Cl + K). In particular, ECW was calculated as $(0.876 \times 0.95 \times 0.93 \times TBCl/100\ mmol\ l^{-1})$, where 87.6% of TBCl is associated with the ECW (Edelman, 1961), 0.95 is the Donnan equilibrium factor, 0.93 corrects for protein content of plasma (Cheek *et al.*, 1957) and 100 mmol l^{-1} is assumed as the plasma chloride concentration (Yasumura *et al.*, 1983). Similarly, ICW was calculated as $(0.00833 \times 0.75 \times 0.962 \times TBK)$, where 0.00833 is the ratio of body cell mass (BCM) to TBK, 0.75 is the assumed ratio of ICW to BCM (Moore *et al.*, 1963) and 96.2% is the proportion of TBK associated with the ICW (Edelman, 1961).

Comparisons between TBW(D_2O) and TBW(Cl + K) were expressed using the statistics of Bland and Altman (1986), Pearson's correlation coefficient and the Student's paired t test. Descriptive statistics are expressed as mean ± standard error of mean (SEM).

Results

Table 1 shows no significant differences between TBW(Cl + K) and TBW(D_2O) in GHD adults before (0 m) and after (6 m) a six-month period of GH treatment, although a significant bias (+ 1.25 l) was observed between the two methods in young normal adults. Dividing them into males and females, there is good agreement for the young normal females; however, for males, a significant bias was found in young normal males. Table 2 shows that both methods of measuring TBW agreed and demonstrated a significant increase in TBW following a six-month period of rhGH treatment.

Discussion

The main finding of this study is that TBW, as determined from the sum of TBCl and TBK, demonstrates good agreement with the D_2O dilution technique when applied to both young normal females and GHD adults pre- and post-treatment.

Notably, we observed that TBW(Cl + K) demonstrated significant bias when applied to young normal males. This finding contrasts with previous studies

Table 1. Cross-sectional data comparing TBW(Cl + K) with TBW(D_2O) in young normals and GHD adults pre- and post-rhGH treatment

	Young normals			GHD adults	
	Combined	Males	Females	GH at 0 m	GH at 6 m
Bias (l)	+1.25	+1.87	+0.01	+0.58	−0.75
95% CI (l)	+2.15 to +0.36	+3.01 to +0.74	+1.44 to −1.41	+2.04 to −0.89	+1.64 to −3.13
t test	<0.05	<0.01	NS	NS	NS
r^2	0.91	0.79	0.69	0.81	0.56
p value	<0.0001	<0.0001	<0.001	<0.0001	<0.001
SEE (l)	2.68	2.80	1.79	4.45	5.80

Table 2. Longitudinal data showing values of TBW(Cl + K) and TBW(D_2O) pre- and post-6-month rhGH treatment ($n = 39$)

	Value at 0 m		Value at 6 m		
Variable	Mean	SEM	Mean	SEM	*p* value[a]
TBW(D_2O) (l)	37.33	1.61	39.63	1.79	< 0.001
TBW(Cl + K) (l)	37.91	1.60	39.76	1.33	< 0.05

[a]Comparison between TBW values at 0 and 6 months by Student's paired *t* test.

that show agreement between TBW(Cl + K) and TBW as determined by the tritiated water dilution method in normal adults (Yasumura *et al.*, 1983; Mitra *et al.*, 1993). In part, this discrepancy may relate to the methods used to determine ICW. For example, Yasumura used population-specific equations to convert measurements of TBK into values of ICW whereas the present study employed published constants relating TBK to ICW. Alternatively, this bias may also reflect the inappropriateness of using the BCM to TBK ratio (i.e. 0.00833) to determine ICW in young normal males. A subsidiary analysis of data, which included measurements of body composition by dual energy X-ray absorptiometry and total body nitrogen by IVNAA, revealed that the BCM to TBK ratio is significantly reduced in young normal males (i.e. 0.0077 versus 0.0083, $p < 0.05$). No such difference was noted for young normal females (i.e. 0.0081 versus 0.0083, $p > 0.05$). At a body composition level, this reduced ratio of BCM to TBK most probably reflects an increased proportion of body fat-free mass consisting of potassium-rich skeletal muscle. It may also reflect an age and sex related increase in potassium concentration in fat-free mass (Cohn *et al.*, 1980, 1983).

Conclusion

This study affirms that TBW can be determined from measurements of TBCl and TBK. Two limitations are observed in this study. Our method of calculation relies on fixed constants which may need to be altered, especially for young normal males. Secondly, the TBCl measurement technique as implemented in our laboratory has a precision of ± 9%; this is adequate for group studies, but not for measurements on individuals.

Acknowledgement—We would like to thank Pharmacia & Upjohn Pty Ltd for sponsorship.

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