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Body water distribution and disease

Abstract The study of body water distribution between extra- and intra-cellular spaces has the potential to improve our knowledge on the mechanisms of disease. A major challenge is that of establishing whether commonly detected subclinical alterations of body water distribution have prognostic or clinical implications.

Key words Body water • Extracellular water • Disease

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Introduction

Total body water (TBW) makes up about 60% of body weight (BW) in the average man (Fig. 1) [1]. Cell membranes separate TBW into extra- (ECW) and intracellular water (ICW), making up 20% and 40% of BW, respectively. ECW can be further separated into interstitial water (IW, 14% of BW), blood water (BlW, 4% of BW), lymphatic water (LW, 1% of BW) and transcellular water (TCW, 1% of BW).

ICW is an index of body cell mass (BCM), i.e. the portion of body mass responsible for energy expenditure [2]. This view is supported, among others, by studies showing that ICW may be a regulator of protein metabolism in health and disease [3, 4].

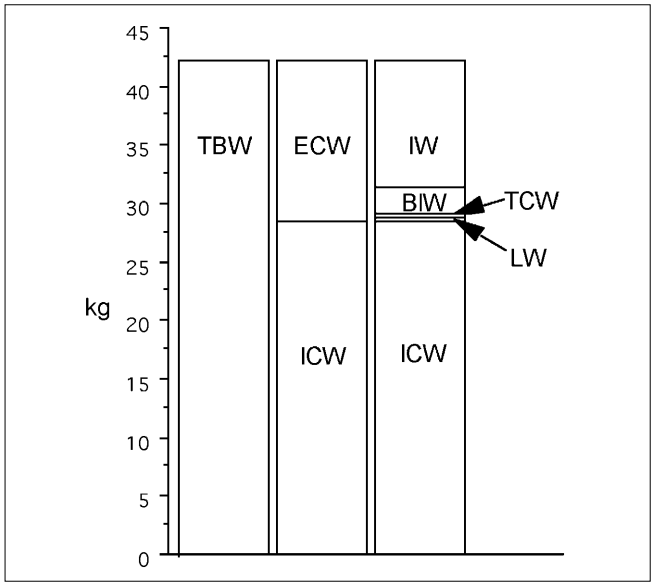

Fig. 1 Body water distribution in the average man. *TBW*, total body water; *ECW*, extracellular water; *ICW*, intracellular water; *IW*, interstitial water; *BlW*, blood water; *TCW*, transcellular water; *LW*, lymphatic water

ECW or the bright side of the moon

There is no doubt that ECW is the water compartment best known by the physician [1]. This is because physicians are specifically trained to detect an expansion of IW (oedema), LW (lymphoedema) or TCW (e.g. ascites). Moreover, physicians are instructed on how to infer a change in BW from parameters such as haematocrit and blood urea nitrogen.

IW is expanded in many diseases with important health implications (e.g. heart failure, liver disease and chronic renal failure) so that clinical assessment of ECW status is rightly emphasised in medical training. For oedema to become apparent, it is calculated that IW must be increased by at least 2.5–3.0 kg [1]. However, the subclinical expansion of ECW is increasingly detected in many disease states even if their clinical significance is not known.

ICW or the dark side of the moon

The theoretical attractiveness of ICW as an index of cell status is counterbalanced by the practical difficulty of assessing it at the patient's bedside. Assessing ICW status will always be difficult in clinical practice but the real challenge, as we understand it, is to be able to show that deviations of ICW:TBW and ICW:ECW have direct health implications.

Clinical examples

Some examples of altered body water distribution follow, with a discussion on their potential health implications.

Obesity

TBW is higher and TBW:BW lower in obese than in normal-weight subjects. However, whether body water distribution (BWD) differs in obese and normal-weight individuals has been the subject of some controversy until recently. Waki et al. have shown that obese women have a greater ECW: TBW than normal-weight women, and we found this to be the case also in obese children of both sexes [5–7]. The greater adipose tissue of obese subjects may contribute to their higher ECW: TBW ratio because the ECW: ICW ratio of adipocytes is greater than that of other cells [8]. However, other explanations must be sought because ECW expansion persists after weight loss [9], even when the loss is massive [10]. Is this expansion of ECW:TBW clinically relevant? For example, does it contribute to the risk of hypertension in obese subjects [11]? This is surely one of the questions that will help establish the clinical relevance of the study of BWD in the near future.

Duchenne muscle dystrophy

Duchenne muscle dystrophy (DMD) is characterised by a progressive loss of muscle tissues and by their replacement with adipose and connective tissues. We found that DMD children have a lower TBW:BW, a higher ECW:TBW and a lower ICW:TBW ratio than healthy controls [12]. The simplest explanation is that the lower ICW reflects a lower amount of muscle tissues and the higher ECW a higher amount of connective and adipose tissues. However, BCM may also be involved *as a whole* because DMD children have lower values of total body potassium and energy expenditure than control children [13, 14].

Liver cirrhosis (early stages)

It is well known that ECW undergoes expansion in the late stages of liver cirrhosis because of an increase in IW and/or TCW. Because there was some evidence that ICW could also be expanded [15], we were interested in studying ICW status in the early stages of liver cirrhosis [16]. We found a greater ICW:TBW ratio in Child-Pugh B patients than in Child-Pugh A patients and controls. This may be an early sign of cell dysfunction in liver cirrhosis, possibly linked to a defective activity of the Na-K ATPase pump, but further studies are needed to ascertain whether it has prognostic or clinical relevance.

Conclusions

The study of BWD between extra- and intra-cellular spaces can potentially improve our knowledge of disease mechanisms. This may in turn increase our ability to treat disease and benefit our patients. A major challenge will be that of establishing whether commonly detected subclinical alterations of BWD have prognostic or clinical implications.

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