身體組成的測量: 病弱兒童的需要

Body composition measurement: the challenge in the unwell child

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The assessment of body composition in the unwell child presents a significant clinical and technological challenge. The effect of disease adds to the complex series of changes in body composition that occur during normal growth and development. To assess the progress of disease or the effect of therapy, repeat measurements of body composition in a single patient may be desirable. However, repeat studies using some methods may not be appropriate due to the potential risks associated with repeated radiation exposure in this young age group. The ability to accurately detect changes in body composition between studies depends on the precision of measurement. Unfortunately, there may be a reduction in precision of measurement with smaller patients when the ability for detecting small changes is of particular relevance. Adequate and correctly timed fluid samples required for dilution studies may be difficult to obtain in the unwell infant and child. New equations or modification of 'adult' equations need to be devised to interpret raw data and these need to be validated in patients of different ages and sizes and in children with different diseases states. Specific challenges related to some common and uncommon paediatric diseases are discussed.

Introduction

The assessment of body composition in the unwell child requires special consideration due to the complexity of normal changes in body composition throughout the spectrum of paediatrics. Patients may range in size from the 600 premature infant to the 60 kg adolescent. This represents a difference of magnitude of 100-fold within this patient group. The potential for such a wide difference in patient dimensions presents an enormous technical challenge. Equipment designed for the more 'homogeneous' adult population may require significant modifications to adapt to patients of such varying sizes.

Body composition in childhood is dynamic; changing in the normal child as a part of growth and maturation. At no time in life is this more dramatic than in the preterm infant. Total body water (TBW) represents approximately 72% of total body weight (BWT) in the 1.2 kg premature infant, at term this has decreased to 69% and by adulthood decreases further to 60%[1,2]. In addition, the proportion of extracellular fluid (ECF) and intracellular fluid (ICF) changes from 42% and 27% of BWT, respectively, at birth to 27% and 38% at 10 years in males[1]. Mineral content increases from 3.2% of BWT to 4.1% BWT over the first 10 years of life[1]. For adults to remain weight-neutral during disease may be considered optimal, however, for children in whom growth and weight gain is expected, weight neutrality may represent a failure of appropriate nutritional management. Therefore, repeat measurements of body composition need to be interpreted with consideration of changes in body composition expected for a normal child over the intervening time period. New equations or modifications of 'adult' equations need to be devised to interpret raw data and these need to be validated in patients of different ages and sizes, and in children with different disease states.

Diseases in childhood may effect normal growth and body composition in a disease specific or non-specific manner. Children with growth hormone deficiency have poor linear growth from infancy with an appropriate weight-for-height ratio or even mild obesity. However, in children with malabsorption, weight and fat stores frequently decline prior to a deceleration in linear growth. Body composition analysis may provide an additional clue to the type of underlying disease process and may be helpful in monitoring the effects of therapy. As some diseases of childhood are similar to diseases in adults, information available from the adult population may be helpful in interpreting paediatric data. However, there are also some diseases that are unique to childhood, such as inborn errors of metabolism and congenital diseases, where little information about body composition is available.

Difficulties using the currently available methods in the unwell child

The results of body composition analysis from the unwell child needs to be interpreted with reference to data obtained from normal children of the same age, sex and/or physical characteristics. However, there is a paucity of reference data for body composition in the normal child. This lack of reference data is due to a number of significant ethical, practical and theoretical problems encountered when using the currently available techniques in normal control children.

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To assess the progress of disease or the effect of therapy, repeat measurements of body composition in a single patient may be desirable. However, when using some modalities repeat studies may not be possible in children due to the increased risk of repeated radiation exposure. Dual-energy X-ray absorptiometry (DEXA), computerized tomography and neutron capture analysis are all methods which involve the exposure of the subject to a dose of ionizing radiation. While this dose is usually minimal (<0.2 mSV or equivalent to a few weeks to months of normal background radiation), repeated studies increase the risk associated with such a radiation dose. There is very limited information to guide the clinician as to the safety of ionizing radiation in the infant and young child. The International Commission on Radiation Protection does not specify a specific radiation dose limit for children[3]. However, it is estimated that the risk of cell changes leading-to cancer induction or genetic injury may be two to three times higher for children than for young adults[3]. Given these higher risk estimates and the lack of evidence for a dose threshold, it is prudent to employ discretion when considering repeat measurements in children by methods using ionizing radiation.

The ability to accurately detect changes in body composition between repeat studies depends on the precision of measurement. This is of particular importance in young patients where the difference between measurements may be very small. Unfortunately, there also may be a reduction in the precision of measurement in smaller patients due to a number of technical factors. For example, the theoretical standard error for measurement of total body potassium (TBK) for a 2000 second counting period in preterm infants is reported to be 19.9% for a 1 kg infant and 11.9% for a 2 kg infant[4].

All methods of body composition analysis require some level of patient cooperation. Some methods require the child to remain motionless for a specific time period. This may be impossible for some children, particularly toddlers, children with behavioural problems or those children with a intellectual disability. Even the most cooperative child when well, may be difficult to study when tired and unwell. Assistance from a parent may be invaluable. The technician must be flexible and be prepared to try again at another time or on another day if necessary.

Techniques measuring dilution space using stable isotopes require the collection of timed fluid samples in volumes that are adequate for analysis. Blood collection is often difficult and distressing for young children and their parents. Even small volumes of 5–10 mls of blood may be of hemodynamic significance in a sick, dehydrated or anaemic infant. Urine samples are a suitable alternative although clean samples of adequate volumes and at appropriately times intervals may be difficult to obtain.

Some specific challenges in the unwell child

The nature of the challenge in the unwell child can be illustrated by examples of common and uncommon diseases of childhood in which body composition analysis may be helpful in the clinical management or may contribute to the understanding of disease pathophysiology.

Cystic fibrosis

Cystic fibrosis is the most common fatal genetic disease of Caucasians. It occurs in 1 in 2500 live births in Australia with a carrier frequency of 1 in 25[5]. The disease manifests as chronic suppurative lung disease, pancreatic insufficiency and failure to thrive. Changes to the approach to nutritional management have contributed to improved morbidity and prolonged life expectancy[6]. Early recognition of changes in body composition and nutritional intervention may further efforts to improve the outcome in these patients. However, there has been some concern over the most appropriate technology to use to measure body composition in this population.

In 1989 the cystic fibrosis gene was identified as a single amino acid deletion on chromosome 7 resulting in an abnormal ATP binding domain on the cystic fibrosis transmembrane conductance regulator[7]. This results in abnormal chloride transportation across the cell membrane. Whether this defect also effects the flux of other chemicals and water within and between cells is currently being investigated. Therefore the validity of methods such as (TBK) measurement, bio-electrical impedance and isotope dilution have been questioned.

Within the cystic fibrosis population there is a wide range of severity and rate of progression of the disease. The co-factors resulting in this clinical diversity have not yet been defined. Therefore, recognition of the major clinical phenotypes in cystic fibrosis should be considered in the interpretation of body composition data[8].

Neonatal screening for cystic fibrosis has provided an opportunity to assess changes in body composition with the development of manifestations of the disease. Infants with cystic fibrosis have a normal birth weight but by diagnosis at age 6–9 weeks there is a reduction in the rate of weight gain, linear growth, total body fat and TBK, compared with normal control infants (personal data[9]). Body composition abnormalities including a decrease in body fat and nitrogen are detected in older malnourished patients with cystic fibrosis[10]. A mild decrease in total body nitrogen was also detected in a small number of normally nourished cystic fibrosis patients when compared to normal controls[10].

Cerebral palsy

Cerebral palsy is a non-progressive motor disability caused by damage to the central nervous system occurring during pregnancy, at birth or soon after birth. It is the most common cause of physical disability world-wide. Disturbances in nutritional status in these patients often fall at two opposite ends of the nutritional spectrum. There is high incidence of chronic undernutrition in children with cerebral palsy, particularly in the more severely disabled. This usually is the result of difficulties experienced in chewing and swallowing food, with some children taking up to 2 hours to eat a small meal with assistance. At the other end of the spectrum are problems of overnutrition and obesity. This problem is more prevalent in children with mild to moderate disabilities who have minimal exercise despite a normal or increased food intake. In both cases the abnormal nutritional status has implications for the clinical care and ambulation of these patients. Despite this, very little is known about the body composition and energy requirements of patients with cerebral palsy.

Body composition measurement by anthropometry has been problematic in this population due to physical deformities affecting the measurement of linear height. This not only has implications on assessing growth but also interpreting results of other methods of body composition analysis such as bioelectrical impedance. Knee-height measurements may be a suitable alternative although this may be affected by

limb contractures in some patients[11]. In the only study to report body composition using a method other than anthropometry, Bandini et al. found an increase in the extracellular water/TBW ratio using the isotope dilution in a small group of adolescents with cerebral palsy[12].

Many patients with cerebral palsy have an asymmetrical pattern of body composition that may require special consideration. A patient with a spastic hemiplegia may have wasted limbs on one side of the body or a patient who is wheelchair bound may have a well-developed upper body but wasted lower limbs.

In addition to their physical deformities many patients with cerebral palsy have additional disabilities such as intellectual disabilities that may make techniques requiring significant patient cooperation difficult. Patients with involuntary choreiform movements may be unable to remain motionless for the time required for satisfactory DEXA, TBK or total body nitrogen measurements.

Preterm Infants

The adaptation of the currently available methodology to accurately measure infants as small as 500 g is an enormous challenge. Due to their extreme prematurity, most of these infants have multisystem disorders, are ventilated and may require drug therapy. This is also an age when very rapid changes in body composition occur with normal growth.

To identify if the weight loss observed during the first 2 weeks of life in preterm infants weighing < 1500 g is due to changes in fluid balance or caused by catabolism, Bauer et al. used a combination of deuterium, sucrose and Evan's blue dilutions in clinically stable preterm infants requiring ventilatory support[13]. In these patients ECF volume decreased while plasma volume remained unchanged suggesting that fluid loss occurred only from the interstitial volume. There was no evidence of catabolism. As birth weight was regained fluid balance was positive but no increase was observed in body solids despite the presence of high nitrogen retention. Measurement of total body potassium in preterm infants using a whole body counter has been reported[2,4]. Dual-photon absorptiometry, using ^{153}Gd in a whole body scanner has been used to measure lean body mass in preterm infants[14]. In small-for-gestational-age and appropriate-for-gestational-age preterm infants lean body mass was the same (104% and 103%, respectively) and no fat was detected. By term, appropriate-for-gestational-age infants had 87% lean body mass or an average of 452 g fat compared to small-for-gestational-age infants who had a lean body mass of 98% corresponding to an average of 48 g fat.

Preterm infants given routinely recommended energy intakes of greater than 110 kcal/kg/day (protein:energy ratio ≤2.7 g/100 kcal) gain weight faster than infants of the same gestational age who remain in utero[15]. The effect of the type of nutrition provided (parenteral nutrition versus enteral nutrition, breast milk versus formula feeds) and the method of nutrition delivery (nasogastric versus oral, demand versus continuous, hourly or two hourly) on body composition in preterm infants remains poorly understood.

Congenital syndromes

Children with specific congenital syndromes, such as chromosomal abnormalities, may have different growth expectations and body composition profiles when compared with the normal reference population. This may be particularly relevant in those syndromes which are accompanied by major organ system abnormalities, such as cardiac disease in children with trisomy 21.

Endocrine diseases

Growth hormone influences body composition via a number of potential mechanisms. It has metabolic effects including anabolic activity thought to be mediated by IGF-1, stimulation of insulin production and a lipolytic effect[16]. This interesting and complex hormone has been used therapeutically in a number of clinical disorders. A group of children (6.5–12.4 years) with subnormal spontaneous growth hormone secretion were studied during the first year of treatment with synthetic growth hormone replacement using total body potassium, bromide dilution, anthropometrics and dual photon absorptiometry[16]. Over this period height velocity almost doubled from 3.8 cm/year to 7.1 cm/year. The percent body fat decreased from 18.4% to 16.2% during the first 6 months of therapy but then stablized suggesting that resistance had developed to the lipolytic effect of growth hormone. Bone mineral density increased but no increase in ECF volume was detected. Due to its anabolic effect, the use growth hormone has been tested in patients receiving intravenous nutrition to encourage nitrogen retention[17]. Accurate measurement of body composition changes will help determine the future of growth hormone for this clinical indication.

Inborn errors of metabolism

This unusual group of inherited disorders result from an absence or defect of a metabolic pathway causing an excess of a precursor substrate and/or a deficiency of the product of that pathway. The clinical manifestations of these diseases vary according to the specific pathway affected. Management of these diseases often involves diets excluding particular dietary substrates. The effect of these severely restrictive diets on specific compartments of body composition is unknown.

Conclusion

The measurement of body composition in the unwell child presents a significant challenge in terms of technical, theoretical, practical and ethical considerations. As these problems are addressed we can look forward to important advances in our understanding of the effect of disease in this age group.

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