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Review

Indirect calorimetry in nutritional therapy. A position paper by the ICALIC study group

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S U M M A R Y

Background & aims: This review aims to clarify the use of indirect calorimetry (IC) in nutritional therapy for critically ill and other patient populations. It features a comprehensive overview of the technical concepts, the practical application and current developments of IC.
Methods: Pubmed-referenced publications were analyzed to generate an overview about the basic knowledge of IC, to describe advantages and disadvantages of the current technology, to clarify technical issues and provide pragmatic solutions for clinical practice and metabolic research. The International Multicentric Study Group for Indirect Calorimetry (ICALIC) has generated this position paper.
Results: IC can be performed in in- and out-patients, including those in the intensive care unit, to measure energy expenditure (EE). Optimal nutritional therapy, defined as energy prescription based on measured EE by IC has been associated with better clinical outcome. Equations based on simple anthropometric measurements to predict EE are inaccurate when applied to individual patients. An ongoing international academic initiative to develop a new indirect calorimeter aims at providing innovative and affordable technical solutions for many of the current limitations of IC.
Conclusion: Indirect calorimetry is a tool of paramount importance, necessary to optimize the nutrition therapy of patients with various pathologies and conditions. Recent technical developments allow broader use of IC for in- and out-patients.

1. Introduction

Indirect calorimetry (IC) measures the oxygen consumption and the carbon dioxide production, which correspond to the cellular respiration and allows to calculate the energy expenditure (EE) of the whole body [1]. The study of the basic principles started more than 100 years ago mainly by physicists and chemists, from the discovery of gas and its components to the establishment of the

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concept of gas exchange related to combustion [1]. Technical progresses have enabled measurements of oxygen (O_2) and carbon dioxide (CO_2) concentrations, as well as the volume of respiratory gasses and heat production of living organisms. In 1949, Weir derived an equation to calculate EE based on the heat produced when a given substrate was burned and the volume of O_2 needed to burn this substrate and on the protein oxidation derived from urea excretion via the kidney. The EE can be derived from O_2 consumption, CO_2 production and urea excretion [Table 1] [2]. Many proposed formulae deviate minimally from the Weir formula, and are not valid if other substrates such as ketones or pyruvate are oxidized in substantial amounts [5]. The principle that nitrogen is neither utilized nor produced during respiration has enabled calculation of EE without measuring inhaled air volume [4]. This principle, known as the Haldane transformation, has contributed greatly to simplifying the measurement systems as only expiratory gas volume needed to be measured.

Measuring EE was labor-intensive and reserved for laboratory research. It is only in the 1980's, that indirect calorimeters were commercialized for medical use. Their complexity and high cost have limited their use for clinical routine during the last 4 decades. IC was mostly used for metabolic research. Nevertheless, in clinical practice it has been taking hold, and became indispensable in pediatric intensive care units (ICU) [6]. In critically ill adults, half of patients in a mixed medical-surgical ICU had indications for IC [7,8], but were rarely measured.

The assessment of EE requires IC and cannot be predicted by equations [9,10]: a number of predictive equations based on simple anthropometric measures and some including gender, age and minute ventilation have been proposed for clinical use as a surrogate of measuring EE [11]. Unfortunately, many reports have shown that predictive equations are not accurate enough, because patients with acute or chronic conditions have different metabolic characteristics, reflected by highly variable EE. Body composition is also an important modifier of EE because fat free mass accounts for most of EE [12].

Recently, it became clear that both overfeeding and underfeeding can be harmful [13–18] and that optimizing nutrition support to the patients specific needs is an urgent task. IC is the only practical clinical method to measure EE of in- and out-patients [3,19,20] in order to tailor nutrition therapy/support to their specific needs; assuming that the energy target should match EE. However, the calorimeters currently available on the market are not sufficiently accurate [9,21–24], difficult to use, and too expensive to be readily accesible in general hospitals.

Table 1
Equations used for the calculations related to indirect calorimetry [2–4].

Calculations of O_2 consumption and CO_2 production
$VO_2 = (Vi \times FiO_2) - (Ve \times FeO_2)$
$VCO_2 = (Ve \times FeCO_2) - (Vi \times FiCO_2)$
Haldane transformation
Assumption based on the concept that N_2 is constant in inspired and expired gas
$Vi = [FeN_2/FiN_2] \times Ve$
$FeN_2 = (1 - FeO_2 - FeCO_2)$
$FiN_2 = (1 - FiO_2 - FiCO_2)$
If $FiCO_2$ of 0.03–0.05% is ignored,
$VO_2 = [(1 - FeO_2 - FeCO_2) \times (FiO_2 - FeO_2) \times Ve]/(1 - FiO_2)$
Weir's equation
$EE = [(VO_2 \times 3.941) + (VCO_2 \times 1.11) + (u\,N_2 \times 2.17)] \times 1.44$

VO_2: O_2 consumption (L/min), VCO_2: CO_2 production (L/min), Vi: inspired volume (L), Ve: expired volume (L), FiO_2: fraction of inspired oxygen, FeO_2: fraction of expired oxygen, FeN_2: fraction of expired nitrogen, FiN_2: fraction of inspired nitrogen, EE: energy expenditure (kcal/d), uN_2: urinary nitrogen (g/d).

An ongoing initiative supported by two major academic organizations (i.e. The European Society for Clinical Nutrition and Metabolism (ESPEN) and The European Society for Intensive Care Medicine (ESICM)) was launched to develop a new indirect calorimeter. The goals were defined by a bottom-up approach with the aim of developing an accurate, easy-to-use and affordable indirect calorimeter for the use of the scientific and medical community.

This review aims at summarizing the scientific background supporting IC in order to optimize nutrition therapy for critically ill patients and other patient populations. It features a comprehensive overview of the technical concepts, the practical application and current developments of IC.

2. Technical concepts

2.1. Calorimetry: the basics

IC measures inspired and expired gas exchanges to calculate EE. This is possible because heat production is tightly correlated with O_2 consumption (VO_2) and CO_2 production (VCO_2) according to the type of energy substrate [20,25].

The conditions of the subjects during IC must be defined as they deeply influence the results. For healthy individuals, basal energy expenditure (BEE) is measured in a resting state that is free of physical and psychological stress, a thermally neutral environment, i.e. at temperature ranges where energy used for the body temperature maintenance is minimal, and a fasting state, i.e. no oral intake for more than 10 h prior to the measurement, to avoid the EE related to physical activity and diet-induced thermogenesis (DIT) [Table 2]. DIT is defined as the production of heat related to substrate oxidation during energy uptake. Resting energy expenditure (REE) is defined as the sum of BEE and DIT, and total energy expenditure (TEE) as the sum of REE and activity induced energy expenditure (AEE) [1,25]. By definition, BEE measurements must be conducted in conditions that are unfeasible for diseased individuals [Table 3]. In clinical practice, REE or TEE reflects the patient energy needs. For patients in the ICU, measured EE should be considered as TEE. If physical activity becomes a standard routine ICU care in the future, then this statement must be revised.

2.2. How is EE measured?

IC requires the measurement of inspired and expired O_2 and expired CO_2 concentrations, as well as the volume of expired gas per minute to calculate the VO_2(L/min) and VCO_2(L/min) [28]. Then VO_2 and VCO_2 are used to calculate the EE(kcal/day) using the Weir's equation [Table 1] [2,20,28,29].

In a mechanically ventilated patient, the gas sampling is obtained from the circuit connecting the endotracheal tube to the ventilator, and measured by using either the breath-by-breath analysis [Fig. 1 a] or the analysis using a mixing chamber [Fig. 1 b] [Table 4]. In spontaneously breathing subjects, a ventilated canopy hood or a fitted face mask is used to collect the inspired and expired gas [Fig. 1c] [28]. Air leaks of respiratory gases alter the accuracy of the measurements and should be avoided.

For measurements using the canopy without O_2 enrichment, VO_2 and VCO_2 can be calculated as a difference between the O_2 concentration in ambient air and the measured O_2 and CO_2 concentration in the expired gas, collected by the canopy. For measurements in mechanically ventilated conditions or using the canopy with O_2 enrichment, the measurements are more complex. Breath-by-breath systems measure the exhaled gas volume and the O_2 and CO_2 concentration transitions, and integrate the product of instantaneous expired gas concentrations with instantaneous expiratory flow over time. A mixing chamber system measures the