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Original article

Validation of ventilator-derived VCO_2 measurements to determine energy expenditure in ventilated critically ill children

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SUMMARY

Background & aims: Indirect calorimetry (IC) is considered the gold standard to determine resting energy expenditure (REE) but its availability in PICUs worldwide is limited. Ventilator-derived VCO_2 could potentially improve the possibility of performing REE measurements. We investigated whether ventilator-derived VCO_2 values are comparable to IC-derived VCO_2 values and can clinically be used in clinical practice to determine REE.

Methods: VCO_2-values were simultaneously collected in mechanically ventilated children from IC (Deltatrac®) and Servo-I® ventilator on a minute base over at least 10 min period of steady state. REE was calculated using the modified Weir formula (for IC) or REE = 5.5*VCO_2 (L/min)*1440 (for the Servo-I values) and compared with frequently used predictive equations by Schofield and the WHO to calculate REE.

Results: Measurements were performed in 41 children; median age 2 years. The mean relative difference between VCO_2 measured by IC and Servo-I® was 15.6% ($p = 0.002$), and limits of agreement in the Bland–Altman analysis were wide. Comparable measurements, defined as a difference ≤10% between IC and Servo-I® VCO_2 values, were seen in 18 (44%) children, but this proportion was 70% in children ≥15 kg. In this group, REE could be accurately predicted using Servo-I® derived VCO_2 values and this method was superior to the use of predictive equations. The Servo-I® derived VCO_2 values were not sufficiently accurate for the large proportion of children weighing <15 kg.

Conclusions: In children ≥15 kg, VCO_2 measurements of the Servo-I® seem sufficiently accurate for use in clinical practice and may be used to determine energy expenditure in the future.

1. Introduction

Adequate nutritional support is essential in the care of children admitted to the paediatric intensive care unit (PICU) to prevent the negative consequences of underfeeding and overfeeding [1,2]. Measurement of resting energy expenditure (REE) through indirect calorimetry (IC) is the preferred method to determine energy requirements in critically ill children. Predictive equations by Schofield [3] and the World Health Organization (WHO) [4], which are based on weight and/or weight/height, do not accurately predict REE in critical illness [5,6]. Mechanically ventilated children are at greater risk of not meeting nutritional needs [7]. In this group, IC can be performed by measurement of O_2 consumption (VO_2) and CO_2 elimination (VCO_2) using metabolic monitors; from this REE is calculated using the modified Weir formula (REE (kcal/day) = [3.941*VO_2 + 1.106*VCO_2]*1440 [8]). Worldwide, measurement of REE is limited, because IC is only available in 14% of the PICUs [9]. Recently, we have shown that REE can be calculated from only the VCO_2 values derived from IC instruments in critically ill children by the following formula: REE = 5.5*VCO_2 (L/min)*1440 [10].

Abbreviations: PICU, paediatric intensive care unit; IC, indirect calorimetry; REE, resting energy expenditure; VCO_2, carbon dioxide production; WHO, World Health Organization.

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Modern ventilators are also able to measure CO_2 via an infrared sensor and to calculate its production per minute (VCO_2) based on instantaneous flow. Ventilator-derived VCO_2 values provide a continuous measurement and thus a potentially more accurate reflection of the 24 h metabolic status. Since VCO_2 values can be automatically subtracted from the ventilator, this may be a promising alternative for IC.

The aim of our study was to investigate whether ventilator derived VCO_2 values are comparable to IC derived VCO_2 values and to determine if ventilator based assessment of REE is more accurate than predominantly used equations.

2. Materials and methods

2.1. Subjects

Children up to the age of 18 years on mechanical ventilation through the Servo-I® with VCO_2 module (Maquet, Rastatt, Germany) were included in the study when admitted to our PICU. Ventilator settings had to meet the criteria of Deltatrac® Metabolic Monitor usage: inspired oxygen fraction (FiO_2) less than 60%, tube leakage <10% (determined by comparing inspired and expired tidal volumes) and Positive End Expiratory Pressure (PEEP) < 10 cmH_20. Patients on High Frequency Oscillation (HFO), Extra Corporal Membrane Oxygenation (ECMO) and Nitric Oxide (NO) support were excluded. The institutional review board of the Erasmus MC approved the study protocol (MEC-2014-169), and (parental) informed consent was obtained before the study was started. The study has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

2.2. Measurements

VCO_2 values were simultaneously collected over 1 min intervals from IC (Deltatrac II® Datex-Ohmeda, Finland) and ventilator (Servo-I® with the Capnostat-III sensor, Maquet, Rastatt, Germany) over at least a 10-min period during steady state (less than 10% fluctuation in VCO_2 and VO_2 by IC). Before each study, the calorimeter was calibrated with a reference gas mixture (95% O_2, 5% CO_2, Datex Division Instrumentarium Corp.) The properties of the Deltatrac® metabolic monitor have been described before [11]. Per-minute measurements from IC with an RQ < 0.67 or >1.3 or ventilator derived VCO_2 values of 0 were discarded, since these values are physiologically impossible.

REE by IC was calculated using the modified Weir formula (REE (kcal/day) = $[3.941{*}VO_2 + 1.106{*}VCO_2]{*}1440$ [8]). For the Servo-I derived VCO_2 values REE was calculated using the following formula: REE = $5.5{*}VCO_2$ (L/min)*1440 [10].

REE was calculated using the following predictive equations: Schofield-weight, Schofield-weight/height [3] and the WHO (based on weight) [4]. The following clinical data were recorded from the Patient Data Management System (PDMS) for all patients: sex, age, weight and height, diagnosis category, ventilation mode and settings, ICU stay and survival, FiO_2, temperature, PRISM-II score on admission, use of catecholamines/sedatives/muscle relaxants and beta blockers and length of stay at moment of measurement.

2.3. Statistical analysis

Descriptive statistics were expressed as means ± standard deviations (SD) in case of normally distributed data; otherwise data are expressed as medians with interquartile ranges (IQR). Relative differences between IC and other methods were calculated as follows: ((value IC − value other method)/value IC)*100%. Paired samples t-tests were performed to check if there was a difference in mean values between methods. Spearman's correlation coefficient (ρ) was used to describe the association between methods of measurement in case of non-normality. This correlation coefficient was also used to describe the association between patient weight and the absolute value of the relative difference between methods. Linear regression analysis was performed to detect proportional and fixed bias between Servo-I® derived VCO_2 values and IC-derived VCO_2 values. This method was chosen because the predictor (IC derived VCO_2 values) is expected to be free of error (due to steady state measurements). Bland–Altman analysis was used to assess the agreement 1) between Servo-I® and IC derived VCO_2 values and 2) between IC derived REE values and calculated REE values (Servo-I® and predictive equations) [12]. Accuracy was also quantified by the proportion of comparable measurements, defined as a relative difference ≤10% between values derived from the Servo-I® or predictive equations, and those of IC, to be clinically useful. Inaccuracy was quantified by the proportion of measurements with a relative difference >30%, to determine the prevalence of large errors [13]. Differences between the children with and without comparable measurements were analysed using independent samples t-tests, Mann–Whitney tests or chi-square tests, depending on the outcome used.

The statistical analyses were performed using IBM SPSS statistics 21 for Windows (IBM, Chicago IL, USA). All statistical tests were two-sided and statistical significance was defined as a p-value < 0.05.

3. Results

Measurements were performed in 41 children, the median age was 2.3 years (IQR 0.3–8.4) and 56% were male. Seventy-two percent of the children were admitted with a medical diagnosis, mostly due to respiratory insufficiency (39%). Patient characteristics are shown in Table 1a. A controlled ventilation mode was used in 66% of the children; median fractional inspired O_2 concentration was 26% (IQR 21–31). Metabolic measurements, performed on the 2nd day of ICU stay (median), lasted 30 min on average. Ventilator settings and metabolic measurement data are shown in Table 1b.

Correlation between Servo-I® derived VCO_2 values and IC-derived values was excellent [ρ = 0.965 (95% CI 0.935–0.981)]. However, despite being a necessary condition for agreement, high correlation does not automatically imply good agreement. Figure 1a shows the Bland–Altman plot for agreement between the two methods for measuring VCO_2 values. Measurements were not comparable with a mean relative difference of 15.6% ($p = 0.002$, one-sample t-test), due to underestimation of VCO_2 values by the Servo-I®. The 95% limits of agreement were wide (−42.4% and 73.6%). Linear regression of Servo-I derived VCO_2 values on IC derived values showed a regression line with a slope of 1.15 (95% CI:1.07–1.23) and an intercept at −15.66 (95% CI: −23.32; −8.01). The slope of this regression line was significantly different from 1 ($p < 0.001$), and the intercept was significantly different from 0 ($p < 0.001$), reflecting both proportional and fixed bias.

Comparable measurements, defined as a difference ≤10% between Servo-I® derived VCO_2 values from and those of IC to be clinically useful, were seen in 18 children (44%). When comparing these 18 children to the 23 children with a difference >10%, it was shown that children with comparable measurements were significantly older (median 7.4 vs. 0.6 years, $p < 0.001$), and taller (median 121 vs. 65 cm, $p < 0.001$) with higher weight (median 23 vs. 6.3 kg, $p = 0.001$), suggesting that the size of the differences between the methods decreases with age and weight (Table 1a). There was no significant difference in diagnosis, PRISM, heart rate, temperature, use of medication, ventilation mode or supplied