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Which equation should be used to measure energy expenditure in HIV-infected patients?[1]

Qual equação utilizar para avaliar gasto energético de portadores do HIV?

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ABSTRACT

Objective

In view of the practical need to use equations for the evaluation of energy expenditure in HIV-infected patients, the objective of the present study was to determine the concordance between the energy expenditure values obtained by indirect calorimetry as the gold standard and those obtained by predictive equations elaborated from data for the healthy population: Harris-Benedict, Schofield and Cunningham, and by equations elaborated from data for HIV-infected patients: Melchior (1991-1993).

Methods

The study was conducted at the *Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto* on 32 HIV-infected men under treatment with highly active antiretroviral therapy. Resting energy expenditure was measured by indirect calorimetry and estimated on the basis of measurement of O_2 consumption and CO_2 production.

[1] Article elaborated from the thesis of HS VASSIMON, entitled "Oxidative stress and substrate oxidation in HIV-infected men with lipodystrophy syndrome". Universidade de São Paulo; 2011.

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Results

Statistical analysis revealed weak concordance for the Harris-Benedict (0.38) and Cunningham (0.34) equations and satisfactory concordance for the Schofield equation (0.47). Only the two Melchior equations (1991 and 1993) showed strong concordance with the values obtained by indirect calorimetry (0.63 and 0.66, respectively) and could be used in practice.

Conclusion

The best equations seem to be population-specific, such as the Melchior equations elaborated for HIV-infected patients.

Indexing terms: Calorimetry, indirect. Energy metabolism. HIV.

RESUMO

Objetivo

Frente à necessidade prática da utilização de equações para avaliar gasto energético em portadores do HIV, o presente estudo avaliou a concordância dos valores de gasto energético obtidos pelo padrão ouro de calorimetria indireta com equações preditivas desenvolvidas a partir de população saudável: Harris-Benedict, Schofield e Cunningham e equações desenvolvidas a partir de portadores do HIV: Melchior (1991 a 1993).

Métodos

O estudo foi realizado no Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto, com 32 homens portadores do HIV em terapia antirretroviral de alta potência. O gasto energético de repouso foi medido por calometria indireta e estimado a partir de medida de consumo de O_2 e produção de CO_2.

Resultados

De acordo com análise estatística, a concordância foi fraca para equações de Harris-Benedict (0,38) e Cunningham (0,34) e satisfatória para Schofield (0,47). Apenas as duas equações de Melchior apresentaram forte concordância com valores obtidos por calometria indireta (respectivamente 0,63 e 0,66) e poderiam ser utilizadas na prática.

Conclusão

As melhores equações parecem ser população específica, como as de Melchior, desenvolvidas para portadores do HIV.

Termos de indexação: *Calorimetria indireta. Metabolismo energético. HIV.*

INTRODUCTION

In clinical practice, due to the increased life expectancy of Human Immunodeficiency Virus (HIV) infected patients, it is increasingly common to provide care for asymptomatic HIV-infected individuals who are generally of normal weight with preservation of muscle mass and with possible changes in adipose mass occurring in the presence of lipodystrophy[1]. Changes in body composition occur in the lipodystrophy syndrome, including lipoatrophy (loss of subcutaneous fat in certain parts of the body) and lipohypertrophy (accumulation of visceral fat in certain parts of the body) and metabolic changes such as dyslipidemia and insulin resistance, involving an increased risk for cardiovascular diseases[2]. On this basis, the need for nutritional monitoring becomes essential for this group, and a definition of the energy supply necessary for the maintenance of ideal weight is part of this process. Thus, it is necessary to develop practical tools in order to estimate the energy expenditure of this group of individuals.

Indirect Calorimetry (IC) is one of the most precise methods for the estimate of Resting Energy Expenditure (REE). However, the cost of the equipment needed for these determinations is high, its use requires trained personnel and the procedure is cumbersome, so that IC is more appropriate for scientific research[3]. In clinical practice it is possible to use predictive equations developed by means of validation studies which evaluate the variables that influence REE and its relationship with the quantitative measurement of this expenditure when evaluated by a more precise method[3]. Predictive equations are useful for a practical and low-cost estimate of REE. These equations are elaborated for specific populations taking into consideration factors such as body composition, age and gender[4].

Many literature reports have compared predictive equations for specific populations to IC in order to determine the best equation for a given group[5-7]. Lopes *et al.*[5] compared the Food and Agriculture Organization/World Health Organization/United Nations University, Harris and Benedict, Henry and Rees and Schofield equations in 30 subjects of both sexes with grade one obesity residing in the city of *Porto Alegre* (RS). According to the results compared to IC values, none of these equations guaranteed application to this population. With the same objective, Fet *et al.*[6] evaluated women ranging from normal weight to obesity and supported the notion that equations for the prediction of REE can induce to errors and seem to be population-specific. In the cited study, better concordance was observed with the equation elaborated from anthropometric measurements than with existing equations in the literature.

Regarding the HIV-infected population, only one article comparing equations and IC was detected in the literature. In a study of 70 HIV-infected men and 16 healthy men, Batterham *et al.*[8] did not detect concordance between predictive equations and values obtained by IC and stated that the changes in body composition may be responsible, at least in part, for this observation.

In view of the practical necessity of using equations, the objective of the preset study was to evaluate the concordance between the resting energy expenditure values obtained by IC, the method considered to be the gold standard, and the estimates obtained using predictive equations.

METHODS

This was an analytical study conducted at the University Hospital, Faculty of Medicine of *Ribeirão Preto* (HC/FMRP). The study was approved by the Research Ethics Committee of the Institution (HCRP nº 1991/2007) and all subjects gave written informed consent to participate. The participants were 32 HIV-infected men on Highly Active Antiretroviral Therapy (HAART) selected at the Acquired Immunodeficiency Syndrome Outpatient Clinic of the Unit Specializing in Infectious-Contagious Diseases (UETDI) of HC/FMRP. Inclusion criteria were age between 18 and 60 years, male gender, stable weight (tolerated variation of 10% in one year), a previous diagnosis of HIV infection, use of HAART for at least 6 months, and T CD4 cell count of more than 200cells/mm^3. Exclusion criteria were severe thyroid or renal, cardiac pulmonary and hepatic changes, signs of opportunistic infections at the time of the study, use of glucocorticoids during the last year, age of less than 18 years or more than 60 years, female gender, patients not on HAART, and T CD4 cell count of less than 200cells/mm^3.

The mean age of the participants was 44±6 years, the time since the diagnosis of HIV infection was 8.5±4 years, and the time of HAART use was 7±4 years. All subjects had undetectable viral load and a T CD4 cell count of 482±224 cells/mm^3. Mean body mass index was 24±3kg/m^2.

IC and REE predictive equations

Resting energy expenditure was estimated using an IC apparatus (Sensor Medics Corporation, Yorba, Linda, CA, USA) by the analysis of consumed Oxygen Volume (VO_2) and produced Carbonic Gas Volume (VCO_2) measured in expired air. The participants were asked to breathe normally while lying down, with a transparent canopy covering their head and chest for 30 minutes. The temperature of the examination room was controlled and constant (23-25°C) and, if a participant entered equilibrium, i.e, if he presented a <10% fluctuation in minutes of ventilation and oxygen consumption and a <5% fluctuation of the respiratory quotient, the procedure could be stopped after 15 minutes. VO_2 and VCO_2 values permitted the determination of the production of energy which is equal to energy expenditure in a situation of equilibrium, i.e., with no loss or gain in the form of heat or of chemistry. The value was expressed as calories, providing the REE in the fasting situation. The formula of Weir[9] was used to express the results as calories/day: REE (kcal/day)=$5.5VO_2$+$1.76VCO_2$.

The resting energy expenditure values obtained by IC were compared to those of the predictive values listed in Table 1[10-14]. Depending on the equations available in the literature, the results can be reported in different energy units, i.e., calories, kilo joules or mega joules. After the results were obtained, various units were converted to kcal, considering that 1kcal is equivalent to 4.18 joules and 1 mega joule is equivalent to a 1,000 kilo joules.

Dual-energy X-ray Absorptiometry (DXA) was applied to all patients by a trained technician for the determination of the muscle mass values to be included in the equations, using a Hologic apparatus model QDR 4500W®. One of the authors (H. S. Vassimon) determined weight and height. The individuals were fasting, wearing light clothing and no shoes and were asked to remove jackets and coats, if present. Weight was measured with a Filizola® electronic scale of the platform type with a maximum capacity of 300.0kg and precision of 0.1kg. Height was measured with a stadiometer with 0.1cm precision, with the subjects standing with their heels touching, with their arms along the body, their back touching the vertical rod, and positioned in the center of the equipment. Body Mass Index (BMI) (weight in kg divided by height squared) was calculated in order to classify the nutritional status of the participants according to the World Health Organization.

Data were analyzed statistically with the aid of the SAS software, version 9.1. Continuous variables are reported as mean, standard desviation. To achieve the main objective of the study the St. Laurent[15] coefficient was applied to test concordance between values (continuous variables), considering IC as the reference method for comparison. The results of concordance were analyzed according to the classification proposed by Landis & Koch[16], whereby a coefficient of 0.81 to 1.00 indicates almost perfect concordance, a coefficient of 0.61-0.89 indicates strong concordance, a coefficient of 0.41 to 0.60 satisfactory concordance, a coefficient of 0.21 to 0.40 weak concordance, and a coefficient below 0.20 poor concordance. Bland & Altman[17] graphs were obtained as another parameter for the evaluation of concordance of the data.

RESULTS

Table 2 shows the REE results estimated by IC and those obtained mathematically by means of equations. Analysis of the percent value obtained from the predictive equations compared to the total IC value revealed that only the Melchior equations of both 1991 and 1993 approached the real value. Greater discrepancies

Table 1. Predictive equations of resting energy expenditure for HIV-infected individuals.

Author	Formula	Unit
Harris Benedict[11]	66.5 + (13.8 x weight) + (5.0 x height) - 6.8 x age)	kcal/day
Schofield[14]	(0.048 x weight) + 3.653	MJ/day
Cunnigham[10]	(370 + 21.6 x lean mass) x 4.18	kJ/day
Melchior *et al.*[13]	1366 +126 x lean mass	kJ/day
Melchior *et al.*[12]	1379 + 123 x lean mass	kJ/day

Note: Weight in kg; height in cm; age in years; lean mass in kg. KJ: Kilo Joule; MJ: Mega Joule.

Table 2. Energy expenditure measured by indirect calorimetry and estimated with predictive formulas. *Ribeirão Preto* (SP), Brazil, 2008.

	Resting energy expenditure (kcal/day)
Indirect calorimetry	1880 ± 286
Harris-Benedict[11]	1603 ± 179
Schofield[14]	1695 ± 131
Cunningham[10]	1544 ± 149
Melchior *et al.*[13]	1965 ± 208
Melchior *et al.*[12]	1929 ± 203

Note: Data are reported as mean ± standard deviation.

Table 3. Concordance of the energy expenditure values obtained with predictive equations and by indirect calorimetry. *Ribeirão Preto* (SP), Brazil, 2008.

Method	St Laurent coefficient	95%CI	
Harris-Benedict[11]	0.38	0.23	0.52
Schofield[14]	0.47	0.35	0.60
Cunningham[10]	0.34	0.23	0.50
Melchior *et al.*[13]	0.63	0.53	0.71
Melchior *et al.*[12]	0.66	0.57	0.74

Note: Statistical analysis: St. Laurent concordance test. CI: Confidence Inteval de 95%.

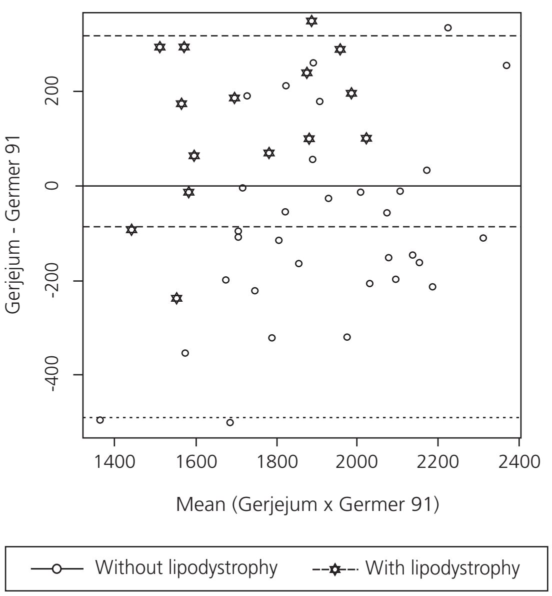

Figure 1. Comparison of the Melchior (1991) equation and of resting energy expenditure values obtained by indirect calorimetry. *Ribeirão Preto* (SP), Brazil, 2008.

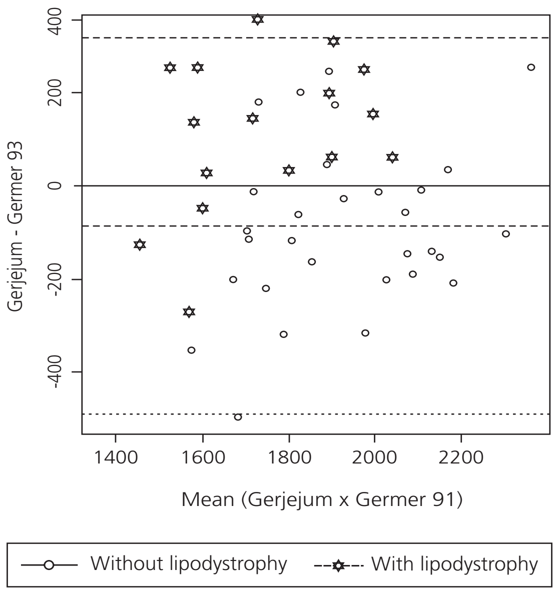

Figure 2. Comparison of the Melchior (1993) equation and of resting energy expenditure values obtained by indirect calorimetry. *Ribeirão Preto* (SP), Brazil, 2008.

were observed between IC and the Cunningham[10] and Harris & Benedict[11] equations.

Table 3 presents the St. Laurent[15] coefficient obtained by comparing the values of the predictive equations to the values obtained by IC. It can be seen that only the REE values calculated with the Melchior equations showed strong concordance with those obtained by IC. Figures 1 and 2 contain graphs comparing the values obtained by the Melchior *et al.*[12,13] equation to those obtained by IC.

DISCUSSION

The Harris & Benedict[11] equation is still one of the main instruments used to evaluate REE in the general population, but the original validated study involved 136 men, 103 women and 94 children of North American origin considered to be healthy. Equations were developed for each gender, including only body weight, height and age as independent variables[11]. Schofield[14] considered jointly the data of 114 studies considered to be scientifically adequate, corresponding to a final sample of 7,173 healthy individuals (4,809 men and 2,364 women) mostly of European or North American origin. Equations were developed for each gender, including age and body weight as independent variables, without considering height. Cunningham[10] proposed an equation based on a review of studies published since 1980 evaluating REE and total energy expenditure in healthy populations of both genders and pointed out the influence of lean mass as a determinant variable of these values, including only lean mass in the equation.

The central point of the present study was the observation that most of the predictive equations developed for the general population were not sensitive for the estimate of REE in HIV-infected individuals. In this case, the equations underestimate REE compared to the values obtained by IC. Some factors that might explain the lack of concordance of the equations are: a) equations developed based on a healthy population not infected with HIV, b) clinical condition of hypermetabolism presented by the group evaluated, and c) the lack of inclusion of muscle mass as a variable of the equation. An equation is more precise for the specific population for which it was developed and in the case of the present study only two equations used HIV-infected subjects. In contrast, regarding hypermetabolism, this situation was observed both before and after the use of HAART[18,19]. Increased REE in HIV-infected individuals has been described since the onset of the disease but its causes have not been fully clarified. Some of the factors reported in the literature as being involved in this situation of hypermetabolism are: the action of HIV itself, the presence of opportunistic infections, the action of antiretroviral agents, and/or the presence of lipodystrophy syndrome[18,20-22]. A previous study suggested that muscle tissue may be the site responsible for the increased energy expenditure in HIV-infected individuals with lipodystrophy syndrome[23]. With the objective of discriminating the participation of the various sites in REE in HIV-infected patients with lipodystrophy syndrome, Kosmiski *et al.*[23] obtained a metabolic map of adipose tissue, skeletal muscle, brain, bone and residual mass (including intestine, lungs, liver, heart and kidneys) based on DXA values combined with specific metabolic rates for each site described in the literature. Multivariate regression analysis revealed that the estimated metabolic rate was elevated only in the skeletal muscle of HIV-infected patients with lipodystrophy syndrome and not in HIV-infected patients without the syndrome or in healthy controls. Thus, lean mass, which is considered to be the main determinant of REE for the general population, becomes a stronger variable for HIV-infected persons with lipodystrophy syndrome and therefore an important variable to be included in equations for REE estimates.

Within this context, the equations of Melchior *et al.*[12,13] were the only ones showing strong concordance with IC values, having been developed for HIV-infected individuals and considering muscle mass as the variable. The equation published in 1991[13] was based on 50 HIV-infected individuals with a diagnosis of AIDS, with the presence of opportunistic infections or Kaposi sarcoma, with the presence of cachexia and the absence of antiretroviral use. In contrast, the equation published in 1993[12] was elaborated based on 129 malnourished HIV-infected patients with no secondary infections. Only the quantity of lean mass was included in these equations as the independent variable, supporting the importance of this variable for predictive REE equations in HIV-infected individuals. The limiting factor of the Melchior equation would be the question of malnutrition, a situation no longer currently present in most HIV-infected patients on HAART.

CONCLUSION

Of the five equations evaluated, the two equations of Melchior, developed from HIV-infected individuals, were those closest to IC values and could be applied in clinical practice for the estimate of the energy requirements of this group.

The Schofield equation would be an alternative in cases in which the Melchior equation cannot be calculated. Most of the predictive equations of REE in the literature were inadequate for HIV-infected individuals. The best equations seem to be population-specific, such as those of Melchior, developed for HIV-infected individuals.

ACKNOWLEDGMENT

Research supported by *Fundação de Amparo à Pesquisa do Estado de São Paulo* (Grant 2009/12449-7).

COLLABORATORS

HS VASSIMON conceived the study and participated in writing the manuscript; JP MONTEIRO participated in the definition and execution of the project. FJA PAULA and AA MACHADO cooperated with data collection, providing equipment and patient selection. AA JORDÃO participated in orientation and in revision of the text. A KUTSCHENKO was responsible for the statistical analysis.

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Received on: 24/2/2012
Final version on: 17/10/2012
Approved on: 12/11/2012