Clinical Nutrition xxx (2016) 1–4

Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

Original article

Resting energy expenditure in adult patients with Crohn's disease

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ARTICLE INFO

Article history:
Received 11 August 2015
Accepted 9 January 2016

Keywords:
Crohn's disease
REE
Body composition
Serum inflammation parameters

SUMMARY

Background & aims: Crohn's disease (CD) is a chronic intestinal disorder of unknown etiology involving any section of the gastrointestinal tract often associated with protein-energy malnutrition (PEM). Increased resting energy expenditure (REE) unmatched by adequate dietary intake is amongst the pathogenetic mechanisms proposed for PEM. Aim of this study was to evaluate REE in CD patients receiving or not immuno-suppressive therapy as compared to controls.

Methods: 36 CD patients (22 M and 14 F, age range 18–55 years) clinically stable and without complications since at least 6 month were studied. REE was evaluated by indirect calorimetry and body composition by BIA. Full biochemistry was performed. Patients were divided into two groups: Group 1 (G1 = 12 patients) without and Group 2 (G2 = 24 patients) with immuno-suppressive therapy.

Results: The two groups were similar for age, height and BMI whereas significantly differed for weight (G1 vs G2: 56.9 ± 7.44 vs 62.3 ± 8.34 kg), fat free mass (FFM: 40.4 ± 5.73 vs 48.2 ± 7.06 kg), fat mass (FM: 17.0 ± 3.55 vs 13.9 ± 5.54 kg) and phase angle (PA: 5.6 ± 1.4 vs 6.5 ± 1.0°). Serum inflammation parameters were significantly higher in G1 than in G2: hs-PCR: 7.76 ± 14.2 vs 7.16 ± 13.4 mg/dl; alfa 2-protein: 11.7 ± 3.69 vs 9.74 ± 2.08 mg/dl; fibrinogen: 424 ± 174 vs 334 ± 118 mg/dl ($p < 0.05$). REE was higher in G2 vs G1: 1383 ± 267 vs 1582 ± 253 kcal/die ($p < 0.05$) both in men: 1579 ± 314 vs 1640 ± 203 and women: 1267 ± 140 vs 1380 ± 132. Nevertheless, when corrected for FFM, REE resulted higher in G1 than G2 (34.8 ± 4.89 vs 33.0 ± 4.35 kcal/kg, $p < 0.05$) group, also higher compared to our, age and sex matched, control population (REE/FFM: 30.9 ± 4.5 kcal/kg).

Conclusions: Our preliminary results show that REE when adjusted for FFM is increased in clinically stable CD patients and mildly reduced by immunosuppressive therapy possibly through a direct action on inflammation and on body composition characteristics.

1. Introduction

Crohn's disease (CD) is a chronic inflammatory bowel disease (IBD) of unknown etiology, which may involve any section of the gastrointestinal tract. Malnutrition is frequently observed in patients with CD due to reduced nutrients absorption for the inflammatory involvement of intestinal mucosa, mechanical obstruction or wide intestinal resections. These factors may act alone or combined, impairing gut ability to maintain protein-energy, fluid, electrolyte or micronutrient balance. Moreover anorexia and catabolic effects of systemic inflammation could contribute to cause weight loss and nutritional deficiencies [1,2].

As far as energy expenditure, several studies [3–6] evaluated the accuracy of REE predictive equations also in CD pediatric patients with conflicting results. Azcue M et al. [7] studied the effect of prednisolone on REE in children with Crohn's disease and found that when REE is corrected for FFM, it does not differ as compared with control group. More recently Wiskin AE et al. [8] studied in sixty children the effect of disease activity, evaluated clinically and by systemic and stool inflammatory markers, and reported that REE/FFM corrected for physiologically relevant confounders was not associated with disease activity.

At our knowledge there is only one study in adult CD patients on the relation between REE and disease activity: Vaisman N et al. [9]

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http://dx.doi.org/10.1016/j.clnu.2016.01.005

studied sixteen CD patients in disease remission and found that in the presence of similar energy intake, REE does not seem to contribute to lower BMI; therefore malabsorption should be indirectly considered the main pathogenetic mechanism of malnutrition in CD.

Aim of our study was to evaluate REE, expressed as total value or corrected for FFM unit, in clinically stable adult Crohn's Disease patients, receiving or not immuno-suppressive therapy and correlate REE with body composition parameters as compared to age and sex matched control group.

2. Materials and methods

36 Crohn disease patients (22 men and 14 women, age range 18–55 years), clinically and nutritionally stable since at least 6 months, consecutively undergoing a routine clinical nutritional counselling at the Clinical Nutrition Outpatient Unit, Department of Clinical Medicine and Surgery Federico II University Hospital in Naples from 2007 to 2013 were included in this study.

Patients with fistulae, ileostomy, or colostomy impairing absorption or with other associated metabolic, endocrine and organ or apparatus complications were excluded.

All measurements were performed in fasting conditions early in the morning.

Weight was measured to the nearest 0.1 kg using a platform beam scale and height to the nearest 0.5 cm using a stadiometer (Seca 709; Seca, Hamburg, Germany). BMI was calculated as weight (kg) divided by squared of height (m). Bioimpedance analysis (BIA) was performed at 50 kHz (Human Im Plus II, DS Medica) at room temperature of 22–25 °C. Measurements were carried out on the non-dominant side of the body in the post-absorptive state, after being in the supine position for 20 min [10]. The measured BIA variables were resistance (Rp) and phase angle (PA) [11]; Fat Free Mass (FFM) and Fat Mass (FM) were estimated using the prediction equations developed by Kushner [12].

This parameter, deriving from arctangent of resistance and reactance ratio, can be considered a prognostic index of the integrity of the cell membrane. It identifies extra/intracellular water distribution: a low phase angle being a common finding in severe malnutrition [13].

Resting Energy Expenditure was measured (REE) by indirect calorimetry using a canopy system (V max29, Sensor Medics, Anaheim, U.S.A.) at an ambient temperature of 23–25 °C. The instrument was checked by burning ethanol while oxygen and carbon dioxide analyzers were calibrated using nitrogen and standardized gases (mixtures of nitrogen, carbon dioxide and oxygen). Subjects were in the post-absorptive condition (12–14 h fasting), lying down on the bed, in a quiet environment. Females of child bearing age were evaluated in the immediate post menstrual phase. After a 15 min adaptation period, oxygen consumption and carbon dioxide production were determined for 45 min. The inter-day coefficient of variation (as determined in six individuals on subsequent days) was less than 3%. Energy expenditure was then calculated employing the abbreviated Weir's formula, neglecting protein oxidation [10].

Blood samples were collected for routine biochemistry and inflammation parameters (C-reactive protein, fibrinogen and alfa 2 protein); all measurements were determined by routine laboratory methods at the Department of Laboratory Medicine of the University Hospital Federico II, Naples.

Patients were divided into two groups:

- G1: Group 1 (12 patients; M = 4, F = 8) without pharmacological treatment
- G2: Group 2 (24 patients; M = 18, F = 6) taking conventional immuno-suppressive treatment with TNFα antagonists alone or in association with amino salicilates.

At the time of measurement and since six months before, no patient was treated with corticosteroids.

2.1. Statistical methods

Results are expressed as mean and standard deviation. Statistical analysis was performed using one-way ANOVA and Mann–Whitney test to compare data between groups. Chi-squared test was used for assessing prevalence. Differences were considered significant when $P < 0.05$.

3. Results

Anthropometric measurements of the two groups did not show significant differences for age (33 ± 8.7 vs 33 ± 13 years), height (168 ± 11 vs 170 ± 8.0 cm), BMI (20.2 ± 2.32 vs 21.5 ± 2.48 kg/m^2); the two groups significantly differed for weight (56.9 ± 7.44 vs 62.3 ± 8.34 kg), fat free mass (40.4 ± 5.73 vs 48.2 ± 7.06 kg), fat mass (17.0 ± 3.55 vs 13.9 ± 5.54 kg) and phase angle (5.6 ± 1.4 vs 6.5 ± 1.0°) (Table 1). 25% of patients in G1 (3/12) and 8% in G2 (2/24) were underweight (BMI< 18.5 kg/m^2). The percent of patients with PA below 5.0° was significantly higher in G1 (4/8 patients −50.0%) compared with G2 (2/24 patients − 8.3%).

REE was significantly different between the two groups (G1: 1383 ± 267 vs G2:1582 ± 253 kcal/die) both in men: 1579 ± 314 vs 1640 ± 203 kcal/die and women: 1267 ± 140 vs 1380 ± 132 kcal/die. When corrected for FFM, REE was higher in G1 than in G2 (34.8 ± 4.89 vs 33.0 ± 4.35 kcal/kg; $p < 0.05$) (Table 1). In both groups of patients REE/FFM was higher than our sex and age matched reference control group, represented by hospital staff (120 M: age 30.6 ± 11.5 years, BMI: 22.4 ± 1.3 kg/m^2, REE/FFM 30.9 ± 4.5; 110 F: age 29.8 ± 4.5 years, BMI: 21.7 ± 2.4 kg/m^2, REE/FFM 30.2 ± 4.3).

In Table 2 some hematological parameters are reported: basic inflammatory blood parameters were significantly higher in G1 than in G2 (hs-RCP (7.76 ± 14.2 vs 7.16 ± 13.4 mg/dl); alfa 2-globulin (11.7 ± 3.69 vs 9.74 ± 2.08 mg/dl); fibrinogen (424 ± 174 vs 334 ± 118 mg/dl) whereas serum albumin values, although within the normal range, were significantly higher in G2 than in G1 (4.2 ± 0.5 vs 3.7 ± 1.1 g/dl).

Prevalence of fibrinogen and alfa 2 globulin above normal limit was higher in G1 than G2 (G1:50.0% vs G2: 41.7%; 33.3%vs 12.5% respectively); furthermore prevalence of blood hemoglobin, total

Table 1
Anthropometric measurements, body composition and REE of untreated (group 1) and treated (group 2) clinically stable CD patients.

		Group 1		Group 2	
		n.12		n.24	
		Mean	SD	Mean	SD
Age	*years*	33.3	8.8	33.2	13.1
Weight	*kg*	56.9*	7.4	62.3	8.3
Height	*cm*	168	11	170	8
BMI	*kg/m^2*	20.3	2.3	21.5	2.5
FFM	*kg*	40.4*	5.73	48.2	7.06
FAT	*kg*	17.0*	3.55	13.9	5.54
PA	*degrees*	5.6*	1.4	6.5	1.0
REE	*kcal/die*	1383*	266	1583	253
REE/FFM	*kcal/kg*	34.8	4.9	33.0	4.3

*$p < 0.05$ group 1 vs group 2.

Please cite this article in press as: Sammarco R, et al., Resting energy expenditure in adult patients with Crohn's disease, Clinical Nutrition (2016), http://dx.doi.org/10.1016/j.clnu.2016.01.005

Table 2
Biochemistry of some routine and inflammatory parameters in untreated (group 1) and treated (group 2) CD patients.

		Group 1			Group 2		
		Values out of the normal range			Values out of the normal range		
		Mean ± SD	Below minimum (prevalence)	Above maximum (prevalence)	Mean ± SD	Below minimum (prevalence)	Above maximum (prevalence)
Hemoglobin	*g/dL*	12.8 ± 1.6	4/12 (33.3%)	0/12 (0%)	13.5 ± 1.3	3/24 (12.5%)	0/24 (0%)
White cells	*μL*	6496 ± 1694	2/12 (16.7%)	0/12 (0%)	7148 ± 2159	4/24 (16.7%)	2/24 (8.3%)
Lymphocytes	*μL*	1762 ± 656	1/12 (8.3%)	0/12 (0%)	1767 ± 877	3/24 (12.5%)	1/24 (4.2%)
Total Proteins	*g/dL*	6.7 ± 0.9	5/12 (41.7%)	1/12 (8.3%)	7.1 ± 0.7	5/24 (20.8%)	1/24 (4.2%)
Albumin	*g/dL*	3.7 ± 1.1	5/12 (41.7%)	1/12 (8.3%)	4.2 ± 0.5	0/24 (0%)	0/24 (0%)
Hs-CRP	*mg/dl*	7.8 ± 14.2*	6/12 (50.0%)	0/12 (0%)	7.0 ± 13.4	10/24 (41.7%)	0/24 (0%)
Fibrinogen	*mg/dl*	423 ± 174*	0/12 (0%)	6/12 (50.0%)	323 ± 118	1/24 (4.2%)	10/24 (41.7%)
Alfa-2 protein	*mg/dl*	11.7 ± 3.7*	1/12 (8 3%)	4/12 (33.3%)	9.5 ± 2.1	0/24 (0%)	3/24 (12.5%)

*$p < 0.05$ group 1 vs group 2.

proteins and albumin below normal values was higher in G1 than G2 (33.3% vs 12.5%; 41.7% vs 20.8% and 41.7% vs 0% respectively).

4. Discussion

These preliminary results show that REE, when expressed as absolute value, appears to be higher in CD patients receiving immuno-suppressive therapy, and characterized by higher total FFM and phase angle, as compared to pharmacologically untreated patients. On the other hand, when expressing energy expenditure as REE/kg FFM we found higher values in untreated patients.

A reasonable explanation for these findings could be related to the positive effects of immuno-suppressive therapy that positively affects, by reducing inflammation, total FFM with a proper body composition. Also FFM characteristics appear to be positively affected by chronic anti-inflammatory therapy as suggested by higher phase angle recorded in group 2 treated patients. On the opposite G1 pharmacologically untreated patients tend to show a “sarcopenic” type of body composition with reduced FFM, also characterized by a lower phase angle, and increased FAT when compared to G2 patients.

The effect of immunosuppressive therapy appears therefore beneficial as far as nutritional status evaluated through energy expenditure (correctly expressed as REE/kg FFM) and body composition. Nevertheless we observe that these beneficial effects due to pharmacological intervention do not completely normalize Energy Expenditure since patients still show a REE/kg body weight higher than our age/sex matched control group.

Several studies that have examined the effect of disease activity in children with Crohn disease have shown either no change [14–17] or increased REE during active disease [18]; however these studies have not corrected REE results for body size and composition. Only Wiskin AE et al [8] found that when expressing energy expenditure as REE/kg FFM it resulted in higher values for those with the lowest FFM, therefore this does not seem to represent hypermetabolism as it has been suggested previously [19–22].

We know that FFM contains both internal organs and skeletal muscle, organ mass being more metabolically active than skeletal muscle [23]. In individuals with lower FFM, the relative organ mass contribution to REE increases thus partially explaining the higher values of REE while expressed per kg FFM. Nevertheless the contribution of pro-inflammatory factors to this finding is highly suspicious as suggested by the reduction of REE/kg FFM in pharmacologically treated CD patients.

This study has some limitations due to the small number of subjects examined and the absence of adequate dietary recall. On the other hand the two groups of patients appear rather homogenous having been selected among outpatients attending our Clinical Nutrition Unit in stable clinical and nutritional conditions. From these preliminary findings we suggest that the correction of REE related to kg FFM is a more accurate way for the interpretation of energy expenditure data in CD patients. Chronic immunosuppressive treatment appears to be beneficial in the long term for the nutritional status of Crohn disease patients. Careful nutritional monitoring should be recommended in Crohn disease patients.

Conflict of interest

The authors declare that they have no competing interests.

Statement of authorship

M.M., F.P., F.C. designed research; M.C.P., L.A., R.S, I.C. conducted research; M.M., analyzed data; L.S., R.S., F.C. wrote the paper. M.M. had primary responsibility for final content. All authors read and approved the final manuscript.

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