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BASAL METABOLIC RATE IN METABOLIC DISORDERS

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Basal metabolic rate (BMR) is the energy used for preserving body functions of a living body in awake state. BMR is a feature of metabolic function and could reveal metabolic adaptation to diseases or nutritional interventions. Determined by indirect calorimetry or with predictive equations, BMR is used in initial and subsequent assessment of medical nutrition therapy. Measured BMR is more accurate in comparison with predicted BMR in special in concurrent co morbidities. Obesity, diabetes and other metabolic disorders, could modify BMR by various mechanism with consequently implications on medical decisions. Frequently associated, obesity and diabetes could act in opposite directions but did not restore normal BMR. A related metabolic parameter is a respiratory quotient (RQ), which indicate the proportions of macronutrients (carbohydrate, lipid and protein) metabolized by the investigated individual.

Keywords: basal metabolic rate, respiratory quotient, indirect calorimetry, diabetes, obesity.

INTRODUCTION

The term "metabolism" means "changes" and is used for all chemical and energy transformations that occur in the human body[1]. All biochemical changes in a biological system conform to the general laws of thermodynamics. Accordingly to the first thermodynamic law, inside all biological system: "*energy is neither lost nor gained, all is transformed*".

In a living system, chemical energy (from foods), may be transformed into heat, electrical energy and mechanical energy. Suitable fuel (food) is required to produce energy necessary for maintaining the normal daily activity. Death from starvation occurs when the available energy reserves are depleted. Conversely, excess storage of oversupply energy results in overweight and various degrees of obesity.

Metabolic disorders includes, among others, diabetes mellitus, the metabolic syndrome, dyslipidemia, hyperuricemia and gout and a large number of inborn errors of metabolism.

The energy expended by an individual depends on the four main factors: (1) the basal metabolic rate (BMR); (2) the thermogenic effect of food; (3) physical activity and (4) increased or decreased environmental temperature. These components could be evaluated by specific methods, all related to the production and utilization of the energy in the human body.

DIRECT CALORIMETRY

Using a direct calorimeter (in a bomb calorimeter – a metal vessel surrounded by a water insulated container), the energy of foodstuffs ignited by an electric spark, will be assessed by the increase of the temperature of the water.

The caloric values of carbohydrate, fat and protein determined by calorimeter bomb are: 4.1 kcal/g, 9.3 kcal/g and respectively 5.3 kcal/g. The same values are obtained in the human body for carbohydrate and fat. Because the oxidation of proteins is incomplete (the end product of the protein catabolism consisting in urea and other nitrogenous compounds), the caloric value of protein in the body is only 4.1 kcal/g[1].

INDIRECT CALORIMETRY

Indirect calorimetry is the standard actual method for measuring BMR. The methods determined the oxygen used and carbon dioxide

production in expired air and computed the resulted calories.

Indirect calorimetry measurements should be done in thermo neutrality, standard atmospheric pressure, standardized fasting state, no influence of other factors as smoking, medication, active drugs, active substances, normal thyroid function, mental and physical rest. An initial steady – state when the patient is maximum relaxed but awake is obtained and initial 15 minutes of recorded data are discarded in this attempt.

BMR is determined by measuring O_2 consumption and CO_2 production using an oxygen filled spirometer and a CO_2 absorbing system (Fig. 1).

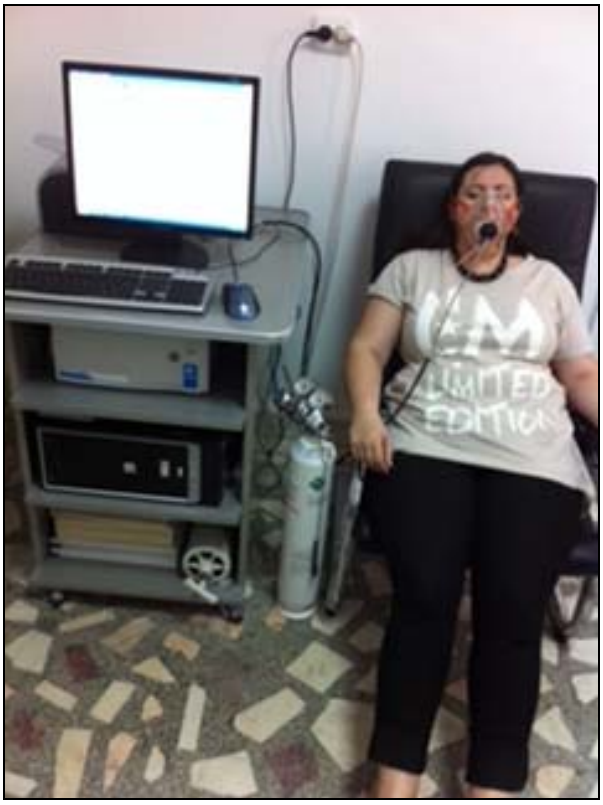

Fig. 1. The device (COSMED, Italy) used in the determination of BMR.

From these values can be calculated the Respiratory Quotient (RQ), which is the ratio, in the steady state of the value of CO_2, produced into the body, to the volume of O_2 consumed per unit of time. The RQ of carbohydrates is 1:00, and that of fat is ~ 0,70. This difference results from the fact that hydrogen and oxygen are present in carbohydrate in the same proportion as in water. In facts extra oxygen is necessary for the formation of H_2O (Table 1). Any value between these corresponds to a specific carbohydrate/fat ratio, indicating the primary oxidative substrate. For example, an RQ equal to 0.88 indicate that the percentage of oxidizing substrates is 60% for carbohydrate and 40% for lipids.

Table 1

Respiratory Quotient for Carbohydrate and fat*

Carbohydrate	$C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O$
Exemple-Glucose	RQ = 6/6 = 1.00
Fat	$2C_{51}H_{98}O_6 + 145O_2 \rightarrow 102CO_2 + + 98\ H_2O$
Exempe-tripalmitate	RQ = 102/145 = 0.703

* RQ for protein in the body is a complex process. A mean value of 0.82 has been calculated

The amount of carbohydrate, protein and fat used in metabolic processes can be calculated on the base of determined non protein RQ and the urinary nitrogen excretion. Processing of fat necessitates more oxygen and produce less carbon dioxide then carbohydrate metabolism. During lipogenesis from glucose, endogenous oxygen is released.

Carbohydrates are a chemical compound richer in oxygen than the fat newly formed. The non-protein RQ is obtained from initial RQ after quantification of oxygen consumed and carbon dioxide resulted from ingested protein metabolism. The protein amount is calculated from nitrogen excretion. When nitrogen excretion is not determined, a situation possible in clinical practice, non-protein RQ is approximated. In a normal protein intake of 12% of caloric amount this approximation is only 1%[2]. RQ for protein is 0.81, so, if carbohydrate and fat are in normal proportion, is not necessary a correction for protein.

If RQ is more than 1, it is considered that carbohydrate are used for lipid synthesis. Formation of lipid from glucose, either in liver or in adipose tissue, is metabolically important in storage energy. A RQ >1 is not a feature of natural nutrition but is found in parenteral nutrition. Parenteral nutrition with carbohydrate increased carbon dioxide production and inconstantly oxygen consumption.

The RQ can be obtained also from an organ. RQ of an organ can be calculated at equilibrium by multiplying its blood flow per unit of time with the arterial-venous differences for O_2 and CO_2 across the organ.

For research or even for clinical information, the determination of energy consumption parameters from individual organ are of great importance in drawing inferences about the metabolic changes occurring inside them. The RQ for the brain, for instance, is regularly 0.97–0.99 indicating that the main fuel is carbohydrate. In some instances, ketone bodies could cover a small proportion of energy for this organ, but only in the presence of glucose, even in small quantities.

PREDICTIVE EQUATIONS

Estimation of caloric value of BMR and the proportion of oxidized substrate is useful in nutritional and metabolic state assessment and food intake recommendation. It is also useful for estimation of nutrients storage and allowance.

The first prediction equation was computed in 1919 by Harris and Benedict from Carnegie Institution in Washington and still remain the standard BMR estimation[3]. This equation used gender, age, height and weight as variables. Afterwards other variables were used in an attempt to obtain accuracy for general situation or particular circumstances.

Estimation of BMR from the sum of individual internal organs basal metabolic rate has been determined in normal weight persons[4]. Metabolic rate of specific tissue were determined and then multiplied with their mass for computing BMR. Initial calculated for normal weight persons, they were verified for obese, in which these rates overestimated with 2% energy requirement[5]. This decrease was explained by infiltration of metabolic active tissues with adipose tissue which had a lower energy consumption.

As resources for indirect calorimetry are insufficient and the method is time consuming necessitating special conditions for patients, predictive equations for BMR estimation were developed. These predictive equations started from analyzing data obtained from healthy normal subjects and established the best available correlations between BMR and variables as gender, age, height, weight. Some equations used body surface and even metabolic parameters as blood glucose level[6]. In an effort to obtain more accurate results, the resulted equations had been compared in groups with different ethnicity, pathology or other different conditions. The precision of an equation for a special clinical situation should be judged individually[7]. The most important independent predictor variables for BMR are weight, height, age, gender and free fat mass.

Table 2

Predictive equations

Predictive equations in male	
Harris-Benedict [9]	66 + (13,8 × weight (W) + (5 × height (H) – (6.8 × age (A)
Owen[8]	879 + (10.2 × W)
Mifflin StJeor[10]	(9.99 × W) + (6.25 × H) – (4.92 × A) + 5
Berstein [14]	(11 × W) + (10.2 × H) – (5.8 × A) – 1032
FAO/WHO/ONU [15] 18–30 years	15.4 × W + 27 × H + 717
FAO/WHO/ONU [15] 30–60 years	11.3 × W + 16 × H + 901
FAO/WHO/ONU) [15] > 61 years	8.8 × W + 11.128 × H + 1071
Predictive equation in female	
Harris-Benedict[9]	655 + (9.5 × W) + (1.9 × H) – (4.7 × A)
Owen[8]	795 + (7.18 × W)
Mifflin[10]	(9.99 × W) + (6.25 × H) – (4.92 × A) – 161
Bernstein[14]	(7.48 × W) – (0.42 × H) – (3 × A) + 844
FAO/WHO/ONU [15] 18–30 years	13.3 × W + 334 × H + 35
FAO/WHO/ONU[15] 30–60 years	8.7 × W + 25. × H + 865
FAO/WHO/ON [15] > 61 years	9.2 × W + 637 × H +302

W – weight; H – height; A – age.

In clinical practice or research, the most frequently used equations were Harris Benedict, Mifflin St Jeor, WHO/FAO/UNU and Bernstein (Table 2). The equations mentioned in Table 2 were intensively used in studies as benchmark for further evaluation. In most studies data obtained with predictive equation overestimated the measured BMR[8,9]. The initial equation of Harris–Benedict was considered that overestimate with 5% in Mifflin study[10] and 6% for male and 13% for female in Owen study[8,11]. Benedict himself considered that his own equation had an accuracy of ±10% [12]. Schofield equations[12] which was adopted by WHO/FAO/UNU overestimate BMR in obese people. These results were considered a consequence of slower increase rate of BMR in heavier persons, even the measurements were made in Schofield study lots comprising only 14.6% overweight and 4.5% obese[13].

THE SIGNIFICATION OF BMR

Basal metabolic rate (BMR) or basal energy expenditure (BEE) represents the amount of energy utilized by a body in physical and psychological resting state, after a night sleep, awake, without any previous physical activity, in postabsorbative state (more than 10 hours after last meal) and neutral environment. *Resting energy expenditure* (REE) is defined as basal metabolic rate, in which one of the conditions excepting the resting state is not fulfilled: less than 10 hours after meal intake, after a low intensity physical activity; other small modification from basal conditions. It is very similar with resting metabolic rate (RMR) which necessitate only 2–4 hours of fasting and is 10% higher than BMR.

BMR it is not the lowest level of energy required for maintaining life. Lower levels of energy could be found during sleep, coma, hypothermia, under nutrition. Total energy expenditure includes BMR (which represent 35–70% of total energy expenditure), dietary-induced thermogenesis (which represent about 10% of BMR)[15] and energy used in volitional or non-volitional physical activity.

Regularly the BMR is measured by indirect calorimetry, but can be also computed using some predictive equations.

Predictive equations are a necessity in clinical practice secondary to difficulties and scarce resources in calorimetry devices. For their computation, different variables as individual organ BMR, free fat mass (FFM) BMR[4], fat body mass, body surface, age, gender, height, weight, various biomarkers are used (Table 3). Predictive equations diversity is the result of the attempt of obtaining accurate data in different physiological and pathological conditions.

Table 3

Factors affecting the metabolic rates[1]

Muscular exertion during or just before measurement
Recent ingestion of food*
High or low environmental temperature
Height, weight and surface area
Sex
Age
Growth
Reproduction
Lactation
Emotional state
Body temperature
Circulating levels of thyroid hormones
Circulating epinephrine and nor epinephrine levels

*Soon after ingested foods an increase of the metabolic rate is due to their "specific dynamic action" (SDA)

The internal organs (liver, heart, brain, kidney), which have 7% on body weight, are responsible for 60% of BMR[16] in comparison with muscle mass, which has 40% of body weight and is responsible for 18% of BMR. Energy processes involved are mitochondrial proton leak[17], protein synthesis and degradation, ion pumps as Na K ATPase, biochemical reaction. BMR is increased in young age, males[18,19], with increasing of body weight and free fat mass. BMR is modified by genetic factors, ethnicity, normal physiological state or co morbidities, nutritional factor, sympathetic activity and stress.

BMR increases with the development of body mass from early childhood to maturity, remains almost stable between 20 an 40 years of age and than decreases with age. BMR decreases with 2–3% per decade after 50 years of age[20,21]. The mechanisms incriminated for decreasing of BMR with age were reduction in mass and function of internal organs and muscle mass. Decreasing of organ mass is between 10–20% at 80 years in comparison with 20 years, excepting for heart. Heart mass increases with age in a similar proportion[22]. Because BMR is mainly composed by internal organ metabolic rate, an organ reduced activity as in brain neural degenerative disorders, significantly decreases the BMR[8,23]. Reduction of muscle skeletal mass is also an aging feature. But

even corrected for free fat mass, BMR remained different for older people in comparison with young people[24]. Renal failure and malnutrition are associated with decrease BMR. Chronic brohopneumopathy, diabetes and lung cancer are associated with increased BMR.

In humans, BMR declines with age, especially after 30 years, with ~0,69Mj/day/decade for man and with 0.43 Mj/day/decade for woman[26]. The decline in BMR with age has been related to the progressive lost of the fat free mass (sarcopenia), heat producing tissues and the decrease in fitness level[27].The BMR increase with higher level of plasma norephrinefrine concentration found in highly fit, physically active adult subjects but not in sedentary elderly persons[28].

The relation of BMR with gender even after free fat mass correction is not very well sustained by latest data. The difference between male and female using Harris Benedict initial calculation was 8% [9]. Though some authors considered that the regression equation could be similar regardless of gender when free-fat mass is used as variable[9,25]. For other authors, gender is important in predicting BMR in children and teenagers but not in adults[16].

No influence on BMR from fat distribution and consequently abdominal/hip circumference ratio was found[8]. The most significant hormonal influence is supported by thyroid hormones which increase oxygen consume, heat production and BMR of all internal organs excepting the brain.

BMR depends of body structure, metabolic alteration and psychological disturbances. So, what are the modifications induced by obesity and diabetes on BMR?

BMR IN OBESITY

Obesity is a state defined by a BMI over 30 and consists of accumulation of fat in subcutaneous and visceral region. The accumulation of fat in internal organ is a feature which reduces their caloric consumption of internal organs decreasing the number of metabolic active cells.

The adipose tissue has a lower energetic expenditure than lean mass: 4.5kcal/kg/day in adipose tissue in comparison with 13 kcal/kg/day in skeletal muscle. Secondary to fat accumulation BMR augments in absolute value, but energy consumption per kilogram of body weight is reduced compared with energy consumption per free fat mass kilogram which is normal. However, BMR adjusted per weight is not similar to all obese patients. In morbid obesity, lower level of BMR/kg total weight were found in higher BMI and heavier subgroup. These patients are more energetically efficient and accumulate more adipose tissue. In nutritional intervention with low caloric diets or in fasting, BMR is reduced, the patients did not lose the expected weight and are frequently suspected of non compliance. BMR reduction in fasting state is about 15% and explain weight preserving in these conditions. Leptin level modulates BMR, increases BMR in obesity and decrease it in fasting condition. Obese patients with higher BMR adjusted to weight are considered hyper-metabolizer patients. These patients are considered to support metabolic adaptation for reduction of further gain weight. This category was often associated with more diabetes, but it could be also associated with different increassed blod glucose levels, but below the values diagnostic for diabetes[29]. The leptin resistant state with dysfunctional satiety and BMR reduction could be a cause of obesity. Leptin resistant state is produced by a defective regulator expression of leptin receptor gene[30].

BMR IN METABOLIC SYNDROME

Metabolic syndrome with obesity has a lower energetic requirement in comparison with diabetes with associated obesity. BMR adjusted for free mass is decreased in metabolic syndrome[31]. That induces the idea that more efficient energetically, metabolic syndrome is a particular state prone to accumulation of fat tissue. Some of the mechanisms considered involved are genetic modification for uncoupling proteins (UCP) with decreased mitochondrial function and lipotoxic mechanism.

BMR IN DIABETES MELLITUS

BMR in diabetes is increased and correlate with the level of glycemic imbalance. It is considered that BMR is increased in Caucasian diabetic patient with 6%[32,33]. There are many mechanism implicated in increasing BMR in diabetes, such the increased oxidation's level for carbohydrates, augmentation of neoglucogenesis and hepatic glucose output, increased sympathetic activity and decreased capacity of glycogen synthesis.

Thermogenetic effect of food is also modified, with reduction of heat loss[34]. Increasing blod glucose levels and metabolic imbalance increased BMR with 8% over a glycemic level of 180mg/dl[6,35].

Neoglucogenesis augments energy consumption with secondary BMR increase. Glucose oxidation increase RQ in post absorptive phase in diabetes versus normoglycemic or dysglycemia (Impaired Fasting Glucose – IFG or Impaired Glucose Tolerance-IGT), by increasing the quantity of glucose which is oxidized[31]. High level of fatty acids representative for diabetes decrease insulin effect, uptake of glucose in muscle, defects of uncoupling proteins with consequently BMR modification.

There are studies that raise assumption that insulin resistant state and higher blod glucose levels during OGTT are associated with lower weight gain[36,37]. Increasing of glycemia augments BMR and equations that introduced glycemia as a variable are developed[6]. Their practical evaluation is still on debate.

CONCLUSIONS

Indirect calorimetry is the election method for BMR estimation. BMR is modified in pathologic circumstances as diabetes and obesity. BMR estimation using predictive equations is a current practice but the result should be analyzed with caution. In special subgroups of glycemic imbalance and BMI, the presence of already elaborated specific equation could be considered.

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