Energy intake and basal metabolic rate during maintenance chemotherapy

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Abstract

Energy intakes and basal metabolic rates were determined in 26 children receiving chemotherapy in remission from acute lymphoblastic leukaemia or solid tumours and 26 healthy controls matched for age and sex. Body weight and height on the two groups were comparable, although one patient was stunted (height for age) and three others wasted (weight for height). Energy intake in the patients at 7705 kJ/day (1842 kcal) and controls at 7773 kJ/day (1866 kcal) and basal metabolic rate (BMR) in the patients at 4873 kJ/day (1172 kcal) and controls 4987 kJ/day (1196 kcal) for the two groups were not significantly different. Although the energy intake:BMR ratio for both groups was 1.59, the range of values for the patient group was large (0.96–2.73) and appeared to be greater than that observed in the control group (1.23–2.46). These results demonstrated that during this period of chemotherapy there was no evidence of raised energy expenditure at rest or reduced energy intake in the patient group. No indication of undernutrition in the patients as a group was evident, although some individuals might require further clinical nutritional assessment.

Malnutrition is one of the major problems for children with cancer.¹ Previous studies have shown that at diagnosis these patients are adequately nourished, suggesting that the cause of the malnutrition is predominantly iatrogenic.² Though the link between nutritional status and clinical outcome remains incompletely defined, impaired immune function associated with the therapeutic management in combination with malnutrition, either additively or synergistically, may increase the susceptibility of the child to infection.³ This in turn may influence clinical outcome.

In the long term poor nutrition will also limit growth and development. Growth deficits have been recorded in a large group with a diagnosis of acute lymphoblastic leukaemia but it was unclear whether the deficit was attributable to the disease process itself, infection, or the therapeutic management of the patient.⁴

Attention has been principally directed towards studying the changes in energy intake and expenditure during the initial period of intensive treatment after diagnosis.^{5–7} Energy requirements may be raised as a result of cachectic side effects of treatment or infection. The limited number of published studies in children with recently diagnosed cancer have suggested that energy expenditure at rest may

indeed be greater than predicted.^{5–7} However, in two studies this appeared to be normalised within seven days of initial treatment.^{5, 6} In the study conducted by Merritt and colleagues basal metabolic rate (BMR) was raised over a period of 30 days.⁷ Although all these studies appear to indicate some degree of raised metabolism at diagnosis of cancer and during the first month of treatment, energy requirements during the longer period of maintenance chemotherapy that follows remain unknown.

The purpose of this study was to examine the effect of maintenance chemotherapy alone on the energy intake and BMR of patients without active disease. Measurements of energy intake and BMR were carried out in a group of patients receiving continuous chemotherapy, after the attainment of remission from acute lymphoblastic leukaemia or solid tumours. Their results were compared with those from normal healthy children matched for age and gender.

Subjects and methods

PATIENTS

Twenty six children (aged 5 to 16 years) receiving chemotherapy took part in the study. Sixteen patients with a diagnosis of acute lymphoblastic leukaemia were on Medical Research Council UK acute lymphoblastic leukaemia (UKALL) trials (three girls, 13 boys). Their diagnosis was made a minimum of six months before this study. Measurements of energy intake and BMR were made in the week before their monthly vincristine and prednisolone block.

The remaining 10 patients (seven girls, three boys) included one with chronic granulocytic leukaemia and nine with various solid tumours. They were all on UK Children Cancer Study Group (UKCCSG) trials or related studies. Before participating in this study each patient had received a minimum of three courses of chemotherapy, in addition to initial diagnostic or therapeutic surgery. Energy balance was assessed in the week before a block of chemotherapy. All patients were clinically well and afebrile throughout the study period.

CONTROLS

Local schools were approached for control subjects. Both parents and head teachers gave their consent for the children who volunteered to participate in this study. They were all free from illness at the time the energy balance measurements were made. Ethical approval for the study was granted by the Southampton and South West Hampshire Health Authority.

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Accepted 4 November 1991

METHODS

Weighed dietary intake was recorded for a period of seven days in the standard manner described by Marr, using digital electronic scales (Hanson).⁸ The children and their families were instructed in the use of the scales and how to record their food and drink consumption in a notebook provided. The dietary record was checked during a follow up interview with the dietitian (SAB). These were then coded according to the McCance and Widdowson food tables,⁹ with additional data from the supplements to the food tables¹⁰⁻¹² and manufacturers' information. Using a computerised database (Microdiet), analysis was carried out to determine the estimated metabolisable energy intake over the seven day period. Energy intakes were expressed in absolute units, corrected for differences in fat free mass, and in relation to that recommended by the Department of Health and Social Security.¹³

In this study, energy expenditure at rest or BMR was defined as the minimum energy expenditure for maintaining essential bodily functions under standardised resting conditions, 12-18 hours' postprandial, in a neutral thermal environment.¹⁴ All measurements were performed between 0730 and 1030 after an overnight fast. BMR was determined by indirect calorimetry using an open circuit ventilated hood system. Oxygen consumption and respiratory exchange ratio were measured to calculate BMR.¹⁵ During the measurement the subjects lay supine on a bed listening to selected music or story tapes. Room temperature was maintained at 22-24°C. The measurements were conducted for a minimum period of 30 minutes after a stable energy expenditure was achieved.

BMR was expressed in kJ/day, corrected for difference in fat free mass, and as a percentage of that predicted on the basis of age, gender, weight, and height.¹⁶

Height was determined using a Holtain stadiometer. Weight was determined by standing balance scales. Standard deviation (SD) scores were determined for height. Nutritional

status was described by determining weight for height as a percentage, and height for age as a percentage, using Tanner and Whitehouse centile charts.¹⁷

Fat free mass was determined from skinfold thickness (biceps, triceps, subscapular, and suprailiac) measured by Holtain calipers. Both the equations of Brook¹⁸ and Durnin and Rahaman¹⁹ were used to estimate body density because of the wide range of ages within the groups. Siri's equation was used to estimate fat mass.²⁰ The significance of differences between groups was assessed from the unpaired Student's *t* test.

Results

The characteristics of patients and controls are shown in table 1. The healthy controls had a mean height for age of 101% (range 94-111%) and a mean weight for height of 102% (range 82-132%). Their mean SD score for height was -0.09 with a range of -1.6 to 1.67. Thus all the controls were within +2 SD scores of the median for height. These values would suggest that the control group were representative of the normal healthy population of children.

The mean values for body size and composition of the patients were similar to those of their controls. However, when the range of values for the patients' height for age (52-166%) and weight for height (66-125%) were considered, four patients appeared to be in the poorly nourished range according to the classification of Waterlow *et al.*^{21 22} One patient (with acute lymphoblastic leukaemia) was less than 90% of height for age, or stunted, and three patients (with solid tumours) were less than 80% of weight for height, or wasted. The group with acute lymphoblastic leukaemia tended to be relatively shorter but exhibited a greater weight for their height than the group with solid tumours.

The mean BMR of the two groups whether expressed as kJ/day, or in kJ/kg of fat free mass/day, were very similar (see table 2). When

Table 1 Age and anthropometric variables of healthy controls and patients receiving chemotherapy. Values are mean (SEM)

	Controls	Acute lymphoblastic leukaemia and solid tumour	Acute lymphoblastic leukaemia	Solid tumour
Age (years)	10.0 (0.6)	10.1 (0.6)	10.1 (1.0)	10.0 (1.0)
Weight (kg)	33.1 (2.4)	32.4 (2.3)	31.6 (2.4)	33.7 (4.5)
Height (cm)	136.4 (3.4)	138.3 (3.7)	135.5 (4.3)	142.9 (6.7)
SD score	-0.09 (0.16)	0.14 (0.27)	-0.39 (0.33)	0.99 (0.35)
Weight for height (%)	102 (2)	94 (3)	100 (3)*	85 (3)*
Height for age (%)	101 (1)	101 (1)	100 (6)	104 (2)
Fat free mass	27.2 (1.9)	26.3 (1.7)	25.4 (1.9)	27.6 (3.4)

*Solid tumour significantly different from acute lymphoblastic leukaemia at p<0.01.

Table 2 Energy intake and BMR of healthy controls and patients receiving chemotherapy. Values are mean (SEM)

	Controls	Acute lymphoblastic leukaemia and solid tumour	Acute lymphoblastic leukaemia	Solid tumour
BMR (kJ/day)	4987 (183)	4873 (207)	4852 (254)	4907 (372)
BMR (kcal/day)	1193 (44)	1166 (50)	1161 (61)	1174 (89)
BMR/kg fat free mass (kJ/kg/day)	197 (9)	194 (7)	198 (7)	189 (13)
% Predicted as % of predicted BMR	101 (3)	98 (2)	97 (2)	100 (3)
Energy intake (kJ/day)	7773 (261)	7705 (459)	7617 (584)	7846 (782)
Energy intake (kcal/day)	1860 (62)	1843 (110)	1822 (140)	1877 (187)
Energy intake/kg fat free mass (kJ/kg/day)	308 (14)	304 (14)	310 (19)	296 (21)
Energy intake as % of RDA ¹³	87 (10)	85 (4)	83 (6)	89 (7)

RDA=recommended daily amount.

Individual energy intake: BMR ratio for 26 healthy controls and 26 patients receiving chemotherapy (both acute lymphoblastic leukaemia and solid tumours). Bar indicates mean value for group.

the measured BMR was expressed as a percentage of the BMR predicted for age, gender, height, and weight,¹⁶ there was no significant difference between the two groups. There were no apparent differences in BMR between the two treatment groups.

The range of values for energy intake was larger in the patient group: 4.4–13.2 MJ/day (1053 kcal–3158 kcal) than the control group: 5.5–10.9 MJ/day (1316–2608 kcal). However, the mean energy intake values were very similar whether expressed as kJ/day or kJ/kg of fat free mass/day (see table 2). When the mean energy intake of the two groups were compared as a percentage of the recommended daily amount for energy,¹³ the chemotherapy group value (85%) was not significantly different from that of the control group (87%). There were no apparent differences in energy intake between the two treatment groups.

When the energy intake is expressed as a ratio of the BMR the mean values for the two groups were exactly the same, 1.59. The range of values does vary considerably, especially for the patient group: patients, 0.96–2.73 and controls, 1.23–2.46 (see figure). There were no apparent differences in energy intake:BMR ratio between the two treatment groups.

Discussion

Parents of children receiving cytotoxic drugs often express concern that their child may not be eating adequately to satisfy their body's requirements for energy and nutrients. Anorexia and weight loss are prevalent in cancer patients, and those children who have been receiving treatment for long periods of time are more likely to be malnourished.²³ Furthermore several studies which followed up children in long term remission from cancer demonstrated a tendency toward poor growth.^{4 24–26} A limitation in growth has to relate to an imbalance between energy intake and energy expenditure

and must include consideration of three factors: poor dietary intake, increased faecal losses, and the nature and magnitude of metabolic demand. Deficiencies of specific micronutrients that may also limit growth once energy needs are satisfied should not be overlooked.

Two studies have measured energy expenditure at rest in children with cancer. Kien and Camitta report a limited series of observations in eight children with newly diagnosed acute lymphocytic leukaemia.⁵ BMR was measured by indirect calorimetry for a five minute period during which time some of the children slept. The results were expressed as a percentage of published values for normal children and revealed that the mean increase in BMR was 50% (range 16–166%) above normal. This study is frequently cited as evidence of a raised metabolic demand in children with cancer. It should be noted that apart from potential errors associated with such a brief period of measurement, no attempts were made to compare these results with the BMR determined in a control group. It is also not possible to determine whether these measurements were made before or after treatment was initiated.

In a subsequent study by Stallings *et al* greater attention was paid to technical detail and measurements of BMR were made in nine children with newly diagnosed acute lymphoblastic leukaemia before and during the first two weeks of chemotherapy.⁶ Energy expenditure at rest was determined in the patients who were subdivided into two groups with differing tumour burden. They found that only the three patients with a high white cell count at diagnosis exhibited a BMR that was 13–45% greater than that predicted from age, sex, and size. The remaining six patients with low tumour burden exhibited BMR values comparable with that predicted from age, sex, and size. The raised BMR of the high tumour burden group rapidly returned to normal with treatment. While chemotherapy treatment *per se* did not appear to raise BMR, changes in substrate utilisation were observed that appeared to be more persistent. They noted that as most chemotherapy programmes for children with acute lymphoblastic leukaemia last up to three years, longitudinal follow up of intermediary metabolism is important to determine whether there is a profound and permanent effect on metabolism, growth, and development.

In this present study energy intakes and BMRs were determined in children receiving ongoing chemotherapy while otherwise well and having no evidence of active disease. Both patients and healthy controls appeared to consume equivalent amounts of energy with their mean values between 13–15% less than their recommended daily amount for energy. Both groups exhibited values for BMR that were comparable, whether expressed in standard units, per kg of fat free mass, or as a percentage of that predicted from age, sex, height, and weight.

The mean ratio of energy intake to BMR (BMR factor) was the same for both groups, 1.59. There is very little published information on energy intake:BMR ratios in children of this

age group against which our results may be compared. This value is slightly lower than the desirable energy allowance for populations expressed as a ratio of BMR estimated from patterns of physical activity for this age group (boys 1.76, girls 1.65).²⁷ The range of BMR factors of the patients was large (0.96–2.73) and appeared to be greater than that reported for the control group (1.23–2.46; see figure).

Seven of the children receiving chemotherapy reported energy intakes that were less than or only slightly greater than their BMR values. These patients were not the ones who fell into the category of being stunted or wasted. Those patients already showing signs of poor growth may have experienced energy deprivation in the past and their metabolism adapted to the reduced intake. There would be no method of measuring whether this was during early childhood, at the time of the initial disease, or during previous treatment.

Though this may be interpreted as evidence that the food intake of these children was insufficient, it is important to recognise that this may also reflect the under-reporting of food intake.²⁸ Considerable efforts were taken in this study to limit the possibility of inaccurate reporting of food intake. In addition the problem of under-eating during the period of measurement should not be ruled out.²⁹ There was no evidence of energy imbalance, as indicated by measurements of weight, between the start and end of the diary recording. It was not possible to make measurements of habitual physical activity during this study.

This study represents the first occasion in which energy intakes and basal metabolic rates have been determined beyond induction chemotherapy. We found that in the week before chemotherapy the dietary intake of energy and the expenditure of energy at rest of a group of patients receiving chemotherapy gave little evidence to suggest that undernutrition was a problem for these patients. However, the sample size was relatively small, the group fairly heterogeneous and possibly not representative of their respective patient populations. For example the patients with acute lymphoblastic leukaemia were older than a typical patient population. If there is a long term energy deficit leading to poor growth in some children with acute lymphoblastic leukaemia, further studies need to investigate these components of energy balance during other stages of the cycle of treatment and with a younger homogeneous patient group.

We thank the children and their parents whose cooperation was essential for the completion of this study. JAK is supported by the Leukaemia Research Fund. The support of the Wessex Medical Trust is gratefully acknowledged.

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