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Modification of the Harris-Benedict Equation to Predict the Energy Requirements of Critically Ill Patients during Mild Therapeutic Hypothermia

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Abstract. *The aim of the present study was the comparison of calculated and measured values of the energy expenditure of critically ill patients during the different phases of therapeutic mild hypothermia. Patients and Methods: Five patients (mean age 40.6 years, range 23 to 68 years, 2 females) suffering from severe acute cerebral injuries who underwent mild hypothermia were prospectively included into the study. Indirect calorimetry measurements were made at intervals of 3-4 hours and subsequently, during the steady state, at least every 12 hours. The results were compared with the basal metabolic rate calculated by the Harris-Benedict equation. Results: A close linear correlation between body temperature and basal metabolism could be observed across a wide range of temperatures from 30.5˚C to 38.3˚C ($r=0.82$, $p<0.001$). One degree drop in temperature led to a 5.9% reduction in energy. During mild hypothermia, oxygen consumption was reduced by 71 mL/min (95% confidence interval 57 to 86 mL/min; $p<0.001$) as compared to base line. The basal metabolism rate was decreased by 30.3% (95% confidence interval 24.7 to 35.9%, $p<0.001$). The average value recorded was 16.7% below the values calculated in accordance with the Harris-Benedict equation (95% confidence interval 12.8 to 20.6%). Conclusion: The immediate reduction in oxygen requirements achieved by hypothermia is linearly correlated with the reduction in temperature and the hypothermia induced reduction in oxygen requirement recorded by indirect calorimetry is considerably below that calculated in accordance with the Harris-Benedict equation. If indirect calorimetry should not be available and the Harris-Benedict equation is used, a corrective factor is therefore needed to avoid an inaccurate calorie administration.*

Mild hypothermia at a body temperature of 32˚C-34˚C is recommended in the current guidelines of the International Liaison Committee on Resuscitation (ILCOR) as a neuroprotective measure during the acute phase following cardiopulmonary reanimation (1). It is also used in patients suffering from severe cerebral stroke or brain trauma to reduce intracranial pressure (2, 3). The exact pathophysiological mechanisms which enable patients to benefit from mild hypothermia have still to be thoroughly investigated. However, it is known that the calcium flow into the cells is reduced, the blood-brain barrier is stabilized, the initial increase in excitatory amino acids such as glutamate is reduced and nitric oxide synthetase activity is suppressed (3).

Early and appropriate nutritional support also appears to have a positive influence on the course of the disease of critically ill patients (4). The applied calorific dose should be adapted to the resting energy expenditure (REE), to prevent the detrimental effects of hypo- or hyperalimentation. The REE depends upon a number of factors such as age, gender, physique, illnesses and medication. The gold standard for the determination of exact energy requirements is indirect calorimetry (5) which is, however, technically complicated and personnel intensive. Thus, the equation first published by Harris and Benedict on 4th December 1918 is still frequently used to determine the calorific requirements of patients (5). The Harris-Benedict formula has been shown to be precise and unbiased, however an activity factor has to be applied to correctly calculate the calorific needs of mechanically

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ventilated, critically ill patients (6). Whether this approach is also suitable for patients with mild hypothermia has still to be investigated. Thus, the aim of this prospective study was to examine the difference between the measured REE values and values calculated using the Harris-Benedict equation during the phases of mild hypothermia. An additional aim was to adjust the activity factor for patients with mild hypothermia in order to guarantee an adequate implementation of the Harris-Benedict formula in cases where indirect calorimetry is not available.

Patients and Methods

Patients. Five Patients (mean age 40.6 years, range 23 to 68 years, 2 women) suffering from severe acute cerebral injuries were prospectively included into the study. All the patients were in deep, pathological coma when included into the study (Glasgow Coma Scale following the initial phase of stabilization between 4-5 points) and were subject to artificial respiration, analgosedation with fentanyl and midazolam and, when necessary, relaxation. Mild hypothermia was prospectively induced by active cooling using temperature controlled, water-cooled venovenous filters. The study protocol was audited and approved by the local ethics committee. The close relatives of the subjects were briefed on the study and gave written, informed consent.

Cooling. A pressure-controlled roller pump was used to perfuse blood into a non-permeable microcapillary using a temperature-controlled water bath as a heat exchanger (Jostra, Hirrlingen, Germany). A dual-lumen 15 French catheter was inserted into one of the femoral veins. The catheter, connecting tubes and heat exchanger were all coated with heparin. No further heparin was applied during the treatment. A bladder thermometer was continuously used to monitor core body temperature. Active cooling was undertaken immediately after admission to the intensive care unit. An extracorporal temperature of 28˚C-30˚C was accepted in order to rapidly achieve an intracerebral target temperature of 32˚C-34˚C, controlled by an intracerebral temperature probe. When the target temperature was achieved, the cooling was correspondingly adjusted and maintained at a constant temperature over a period of 48 hours. Gradual rewarming was subsequently undertaken over a period of 24 hours (1˚C/4.8 hours).

Nutritional support. The aim of the treatment was the administration of the calorie requirement as determined by indirect calorimetry. Enteral tube feeding was begun at an early stage via a nasogastric tube in all patients, however, only small amounts could be administered due to deep sedation and relaxation. Therefore, a commercially available parenteral nutrition was used in all patients (Braun Melsungen, Germany). The rate of flow was adjusted to conform to the values recorded by indirect calorimetry.

Indirect calorimetry. Indirect calorimetry was carried out using a Deltatrac I Metabolic Monitor (Datex Ohmeda Inc., Louisville, USA). Measurements were made by trained technicians at intervals of 3 - 4 hours and subsequently, during the steady state, at least every 12 hours. All the measurements were made under standardized conditions including FiO_2 below 0.45.

Harris-Benedict equation. The basal metabolic rate expressed in kilocalories per day was mathematically calculated using the Harris-Benedict equation (7):

REE=66.5 + 13.75 x W + 5.003 x H - 6.775 x A (for males)
REE=655.1 + 9.563 x W + 1.85 x H - 4.676 x A (for females)
W=Weight in kg, H=Height in cm, A=Age in years

The body weight was measured with a bed-scale, height was specified by manual tape measuring. If needed the result was further multiplied by an activity factor (6).

Statistical methods. The statistical analysis was undertaken using MedCalc for Windows Version 8.0.0.0 (MedCalc Software, Mariakerke, Belgium). Normally distributed data were shown as mean±standard deviation and other data as mean with 95% confidence interval. The factors of statistical significance were calculated using Student's *t*-test, while Pearson correlation coefficients were used for correlation. The correlation between basal metabolism and body temperature was determined *via* linear regression analysis.

Results

The cooling of the patients was started within 408±227 minutes of the initial trauma. The intraparenchymal cerebral target temperature was achieved after 113±81 minutes of cooling. The average fall in temperature compared to the target temperature (32˚C- 34˚C) was 3.5˚C per hour. In total the variation in temperature compared to the reference temperature was 5.1±0.7˚C. During the steady state of hypothermia, core body temperature measured 31.9±0.7˚C. A representative time course of the temperature and the REE is shown in Figure 1. Oxygen consumption compared with the baseline temperature (Oxygen consuption at 37˚C) was reduced by 71 mL/min (95% confidence interval 57 to 86 mL/min; $p<0.001$) and the basal metabolic rate was decreased by 30.3% (95% confidence interval 24.7 to 35.9%, $p<0.001$) during the period of steady state hypothermia. Every drop in temperature by one degree led to a 5.9% reduction in energy. A close linear correlation between body temperature and basal metabolism could be observed across a wide range of temperatures from 30.5˚C to 38.3˚C (r=0.82, $p<0.001$; Figure 2). The average value recorded was 16.7% below the values calculated in accordance with the Harris-Benedict equation (95% confidence interval 12.8 to 20.6%).

Discussion

The immediate reduction in oxygen requirements achieved by hypothermia was in direct proportion to the reduction in temperature. Our recorded values corresponded to the results achieved by Bruder *et al.* (8), Tokutomi *et al.* (9) and Bardutzky *et al.* (10), demonstrating that the values recorded by indirect calorimetry are considerably below those calculated in accordance with the Harris-Benedict equation. Especially the findings of Bruder *et al.* suggested that the body temperature was the main determinant of energy

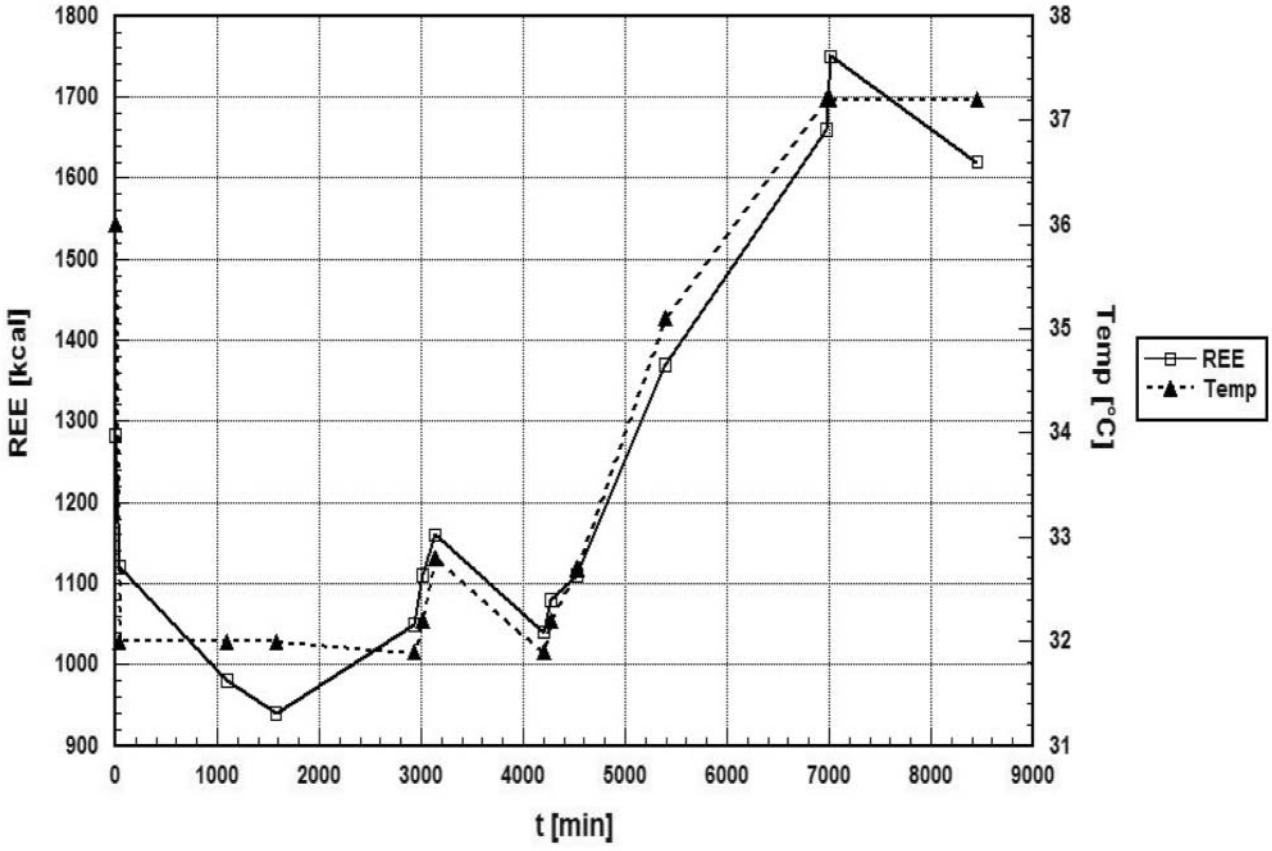

Figure 1. *Representative time course of temperature and resting energy expenditure (REE).*

expenditure while the anesthetic agents had only a little influence (8). Thus, it seems necessary to reduce caloric intake during the hypothermia phase to levels below those which would normally be calculated, in order to minimize the negative effects resulting from parenteral overfeeding such as steatosis hepatis and hepatocellular injury (4). Should indirect calorimetry be unavailable, the Harris-Benedict equation may be used, however, the activity factor needs to be adjusted to the specific situation of mild hypothermia. On the basis of our data which demonstrate a linear correlation between a reduction in temperature and a reduction in calorie consumption of 5.9% per degree Celsius, the actual caloric requirement can be calculated as:

$$\textit{Actual Caloric Requirement} = REE \times (1 + 0.059 \times (T_{actual} - 37))$$

By this approach calorie administration can be adjusted to meet the real requirements during each phase of mild hypothermia. However, since the induction and re-warming phases are relatively short as compared to the steady state phase and the defined target temperature for mild hypothermia is 32˚C-34˚C, a simplified corrective factor of 0.75 might be employed for clinical routine.

As a limitation, the present pilot study included only a small number of patients leading to a variation of measurement results between the patients. To precisely calculate the activity factor needed for adjustment, a larger trial should therefore be performed.

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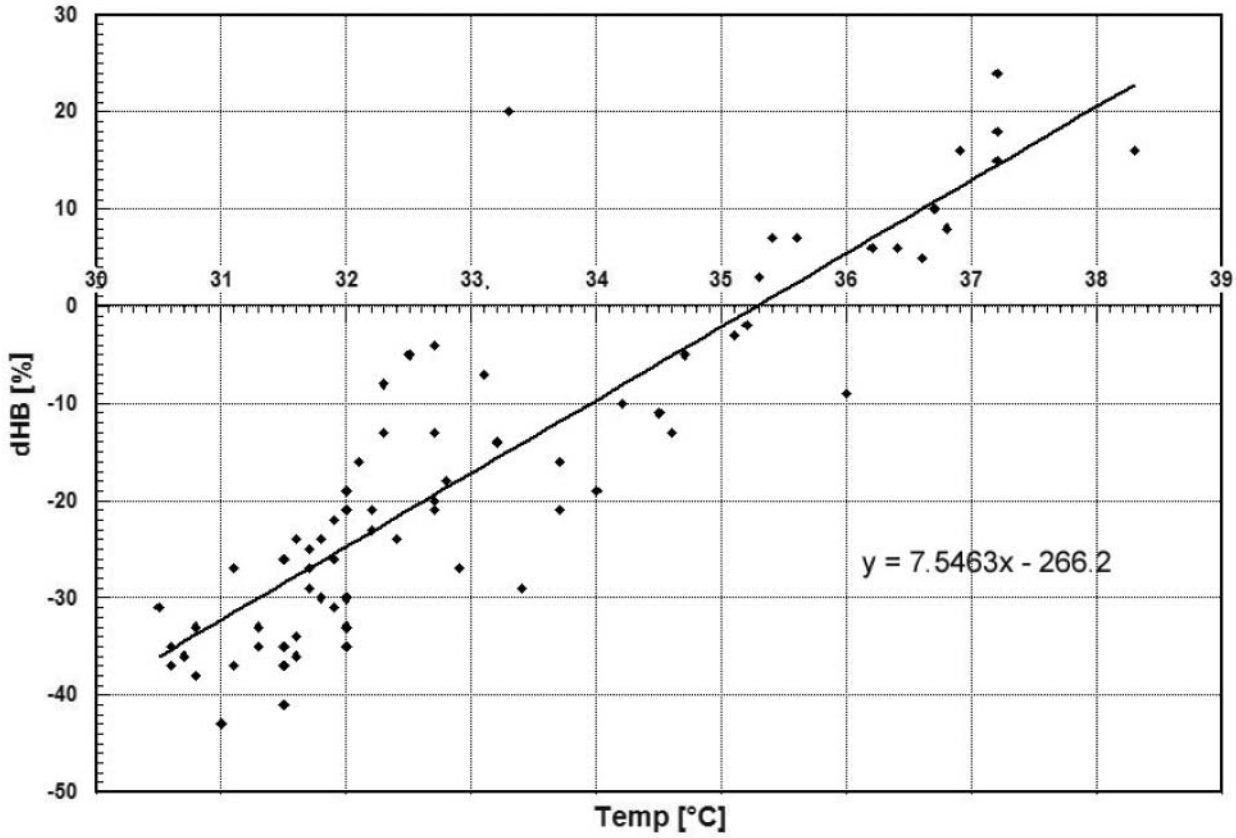

Figure 2. *Correlation between time course and the difference of calculated and measured energy expenditure (dHB %).*

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