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Energy expenditure of critically ill neonatal foals

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Summary

Reasons for performing study: Nutritional support in critically ill neonatal foals is of great importance given their high metabolic rate and minimal stores of energy and protein. Nutrient requirements of healthy growing foals have been estimated based on daily milk intake; however, little is known about the resting energy expenditure (REE) of sick foals.
Objectives: To determine REE in critically ill neonatal foals (sepsis and/or hypoxic-ischaemic encephalopathy [HIE] and compare this with REE in control foals.
Methods: Critically ill newborn foals admitted to the Fundació Hospital Clínic Veterinari, Universitat Autònoma de Barcelona, Spain from March 2009 to February 2011 were included in this study. Healthy neonatal foals and foals with nonsystemic conditions were used as controls. Oxygen consumption and CO_2 production were measured with a respiratory monitor connected to a tight fitting facemask and REE (kcal/kg bwt/day) was calculated with the abbreviated Weir formula. Measurements were performed within 24 h of admission and repeatedly during hospitalisation.
Results: Twenty-seven foals were included (16 critically ill foals and 11 controls) and a total of 47 measurements were performed. In the critically ill, REE was reduced (mean ± s.e. 49.5 ± 2.1 kcal/kg bwt/day) on admission relative to the controls. In surviving foals (n = 5), REE before hospital discharge was not different (68.4 ± 7.0 kcal/kg bwt/day) from control foals (64.8 ± 2.7 kcal/kg bwt/day).
Conclusions: REE was lower in critically ill foals upon admission (40–50 kcal/kg bwt/day) and normalised before hospital discharge (60–80 kcal/kg bwt/day).
Potential relevance: Critically ill neonatal foals tolerating enteral feeding would receive approximately their REE when given 10% of their bodyweight in mare's milk daily. For sick neonates unable to tolerate enteral nutrition, provision of 50 kcal/kg bwt/day would be a reasonable goal for parenteral nutrition.

Keywords: horse; energy requirements; critical care; sepsis; nutritional support; indirect calorimetry

Introduction

Nutritional support in critically ill neonatal foals is of great importance because, compared with mature horses, they have minimal reserves in the form of glycogen and fat and a high metabolic rate relative to body mass (Ousey 2003; McKenzie and Geor 2009). To maintain a high metabolic rate and a rapid rate of growth (1–1.3 kg/day) healthy foals consume daily 23–28% of their bodyweight as milk (120–150 kcal/kg bwt/day) during the first 2–3 weeks *post partum* (Oftedal *et al*. 1983; Martin *et al*. 1992). The energy requirements of sick neonatal foals are not clearly understood given the combination of lower physical activity and the possible increase in the rates of energy metabolism following illness or injury (McKenzie and Geor 2009). Sepsis, trauma and severe burns are known to increase metabolic rates in adult human patients (Chiolero *et al*. 1997; Moriyama *et al*. 1999). However, in critically ill children a hypermetabolic state has been reported in some (Coss-Bu *et al*. 2001) but not all studies (Framson *et al*. 2007). In addition, optimal nutrition of critically ill human patients individually tailored by measurement of energy expenditure has been shown to decrease the risk of complications and mortality (Scheinkestel *et al*. 2003; Strack van Schijndel *et al*. 2009). Therefore, a better understanding of the energy expenditure (i.e. metabolic rate) of critically ill neonatal foals is required to provide an optimal nutritional support regime and ensure that the foal has adequate energy provision for basal metabolism, immune function and to maintain bodyweight.

Indirect calorimetry is the method of choice for measuring resting energy expenditure (REE) in hospitalised human patients (Mann *et al*. 1985; McClave and Snider 1992). It is accomplished by performing respiratory gas exchange measurements (rates of oxygen consumption and carbon dioxide production) determined from analysis of expired gas. Rates of oxygen consumption and carbon dioxide production are then used to estimate the REE with the abbreviated Weir formula (Ferrannini 1988).

To the author's knowledge, only 2 studies have previously reported the energy expenditure of a small number of critically ill foals by indirect calorimetry. In one study, only 4 foals with prematurity or neonatal maladjustment syndrome were examined (Ousey *et al*. 1996). In another study, 3 healthy and 6 sick neonatal foals with various disorders were studied under sedation (Paradis 2001). The present study was conducted to determine resting energy expenditure in critically ill neonatal foals at the time of hospital admission and throughout hospitalisation.

Materials and methods

Animals: inclusion and exclusion criteria

All equine foals aged <22 days admitted to the Fundació Hospital Clínic Veterinari, Universitat Autònoma de Barcelona, Spain between March 2009 to February 2011 were eligible for inclusion in the study. Foals were classified into one of two groups: critically ill and control foals (not critically ill). Foals in the critically ill group were recumbent, required intensive care and had a clinical diagnosis of sepsis and/or hypoxic ischaemic encephalopathy (HIE). Diagnosis of sepsis was reached by either positive blood culture or sepsis score ≥12 (Brewer and Koterba 1988). Clinical diagnosis of HIE was reached by compatible history (premature placental separation, dystocia, caesarean section) and clinical signs (loss of suck reflex, unable to nurse from the mare, hyperexcitability, disorientation, seizures) not justified by other diagnoses (Vaala 1994; Furr 1996). Foals in the control group were healthy neonatal foals admitted with their dam and foals with uncomplicated nonsystemic conditions (i.e. meconium impaction, patent urachus, failure of transfer of passive immunity). Foals in the control group were able to stand and nurse with minimal or no assistance. Foals were not included in the study if euthanasia was performed or death occurred prior to complete cardiovascular stabilisation by intensive i.v. fluid resuscitation (isotonic polyionic balanced electrolyte fluids alone or combined with colloids and/or vasopressors) in the initial 12–24 h of hospitalisation. Informed client consent was obtained before enrolment in this study.

Respiratory gas exchange measurements

Determinations of tidal volume, respiratory frequency, minute ventilation, and oxygen and carbon dioxide concentrations in respiratory gases were performed using a respiratory monitor (Ohmeda 5250 RGM respiratory monitor)[a] and tight fitting facemask (Polycarbonate mask and silicone rubber fitting)[b]. Measurements were performed once foals had been stabilised by fluid resuscitation and other supportive treatments within 24 h from admission to the hospital, and subsequently every 48–72 h if possible. Foals had respiratory gas exchange measurements performed while being gently restrained lying down quietly on sternal or lateral recumbency, without administration of sedatives. Intranasal oxygen supply was interrupted 10 min before these measurements. A tight-fitting mask was placed to the level of the bridge of the nose. After an accommodation period of 5 min, measurements were recorded every minute for 20–30 min. Whenever possible, these measurements were performed between feedings and at the same time of the day, generally between 12.00 and 14.00h. To ensure accuracy of the ventilatory gas exchange measurements the respiratory monitor was calibrated repeatedly throughout the study period. Flow measurements and gas composition were calibrated using a calibrating syringe (1-l precision syringe)[c] and gas mixtures[d] with oxygen and carbon dioxide concentrations that spanned the measurement range.

Calculations of energy expenditure

Standard equations were used to calculate oxygen consumption ($\dot{V}_{O_2}$) and carbon dioxide production ($\dot{V}_{CO_2}$), and REE was calculated as follows (Ferrannini 1988):

$$\text{REE (kcal/min)} = 3.9 \cdot \dot{V}_{O_2} + 1.1 \cdot \dot{V}_{CO_2}$$

where $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ are in l/min.

Statistical analysis

Data are presented as mean ± s.e., unless otherwise stated. Resting energy expenditure data were analysed using a one-way ANOVA with group (critically ill vs. control) as independent factor, and one-way ANOVA with repeated measures to compare REE data in critically ill foals over time. The assumptions of equal variance among groups and normal distribution were tested with the Levene Median and Kolmogorov-Smirnov tests, respectively; and the data satisfied both. *Post hoc* comparisons over time were performed using the SNK method. The Sigmastat 3.0 software package[e] was used for statistical computations.

Results

Thirty-nine equine neonates were admitted to the hospital during the study period. Eight were not included in the study because of marked clinical deterioration that lead to death (n = 2) or euthanasia (n = 6) during the initial 12 h of hospitalisation. Of the remaining 31 foals, 4 were excluded from the study: energy expenditure measurements were not acquired in one case; one foal had a severe congenital cardiac malformation; and 2 foals had spuriously low measurements of tidal volume, which was attributed to ill fit between the mask and bridge of the nose. Therefore, 27 foals were included in this study (sepsis n = 8, sepsis and HIE n = 6, HIE = 2 and controls = 11; Table 1)

Clinical management and progression of critically ill neonatal foals

All critically ill foals (n = 16) were initially treated with aggressive i.v. fluid therapy, broad spectrum i.v. antibiotics (penicillin and amikacin, or ceftiofur), and received supplemental intranasal oxygen. If failure of transfer of passive immunity was confirmed foals received one litre of plasma and plasma immunoglobulin G concentration was measured again. Nutritional support by enteral feeding of mare's milk or parenteral nutrition was decided by the attending clinician depending on the foal's condition. Foals on enteral feeding received hourly administration of 1–8 ml/kg bwt of mare's milk or milk replacer by nasogastric feeding tube (2.5–20% of their bodyweight in milk daily). None of the foals included in this study required total parenteral nutrition and only 6 of 16 critically ill foals had glucose added to i.v. fluids to treat hypoglycaemia. Of 16 critically ill neonatal foals included in this study, 11 were discharged from the hospital 6–22 days after admission (median 13 days) and 5 were subjected to euthanasia due to deterioration of their clinical condition despite intensive supportive care.

Energy expenditure

Resting energy expenditure was approximately 25% lower in critically ill foals (mean ± s.e. 49.5 ± 2.1 kcal/kg bwt/day, n = 16) compared with control foals (64.8 ± 2.7 kcal/kg bwt/day, n = 11, P<0.001) during the initial 24 h of hospitalisation (Table 1). A significant change in REE was detected over time in critically ill foals (P = 0.031). Energy expenditure in critically ill foals was not different in the third or fourth days compared with the initial 24 h of hospitalisation. Before hospital discharge, energy expenditure in surviving critically ill foals (n = 5) was higher (68.4 ± 7.0 kcal/kg bwt/day) relative to energy expenditure measured during the initial 24 h of hospitalisation (42.8 ± 3.6 kcal/kg bwt/day), whereas REE remained unchanged in nonsurviving critically ill foals over time (Fig 1). The difference in REE in surviving critically ill foals over time was significantly different (P = 0.058).

Discussion

The main findings of this study were: 1) energy expenditure in critically ill neonatal foals was lower than that in control foals (healthy or without life-threatening conditions); and 2) in surviving critically ill neonatal foals, energy expenditure increased over time to values similar to those measured in controls.

In critically ill patients, nutritional support is an essential part of management. In man, it has long been recognised that determination of individual energy expenditure by indirect calorimetry and optimal nutritional support decreases the risk of complications and mortality (Barton 1994; Giner *et al*. 1996; Schoeller 2007). Depending upon the disorder (i.e. trauma, sepsis, severe burns), the energy requirements of critically ill paediatric human patients have been reported to range from lower to higher than healthy subjects (Coss-Bu *et al*. 2001; Bauer *et al*. 2002; Framson *et al*. 2007). In sick neonatal foals the energy requirements were thought to be increased (Bernard 1993). Energy requirements of healthy active and growing neonatal foals have been estimated at 120–150 kcal/kg bwt/day based on daily milk intake by foals and energy density of mare's milk (Martin *et al*. 1992; Ousey *et al*. 1996, 1997). However, this sizeable caloric requirement is not only used for basal metabolic needs but also to maintain a fast rate of growth in the neonatal period (1–1.3 kg/day in a 50 kg foal), given that approximately 50% of the energy intake is utilised for growth and the rest for basal metabolic needs, thermoregulation and activity (Ousey *et al*. 1996, 1997). It is unclear what the energy needs are in critically ill neonatal foals given the combination of: (1) decreased activity and temporary reduction/absence of growth, and (2) a possible hypermetabolic state as a consequence of the systemic inflammatory response and increased tissue energy consumption (McKenzie and Geor 2009). To the best of the authors' knowledge only studies have previously reported the energy expenditure of a small number of critically ill foals determined by indirect calorimetry. In one study, the energy expenditure of 4 foals with prematurity or neonatal maladjustment syndrome was quite variable (45–113 kcal/kg bwt/day) (Ousey *et al*. 1996). In another study, the mean energy expenditure of 6 sick neonatal foals was 44 kcal/kg bwt/day. In the second study, the heterogeneity of the foals, the use of sedatives in some foals, and the lack of calibration of the metabolic cart used for indirect calorimetry measurements might have compromised the validity of the results (Paradis 2001). In the present study, energy expenditure of control foals was 64.8 ± 2.7 kcal/kg bwt/day, which is similar to that reported by Ousey *et al*. (Ousey *et al*. 1996) (73.4 ± 2.7 kcal/kg bwt/day) in healthy foals; and the energy expenditure of critically ill foals was 49.5 ± 2.1 kcal/kg bwt/day in our study, which is also similar to that reported in the aforementioned studies with fewer ill foals (Ousey *et al*. 1996; Paradis 2001). In the present study, surviving critically ill foals had their energy expenditure normalised to values similar to control foals before discharge from the hospital, whereas energy expenditure in nonsurvivors remained stable over time and was approximately 25% lower than controls.

Nutritional requirements for growing healthy foals include energy for basal metabolism, rapid body growth, exercise, thermoregulation etc. (McKenzie and Geor 2009). Based on the energy expenditure values determined in the present study, 50 kcal/kg bwt/day can be used as the maintenance energy requirements of sick neonatal foals (i.e. to meet basal energy needs and maintain bodyweight in a thermoneutral environment). Therefore, when enteral nutrition is provided using mare's milk, which has an energy density of approximately 500–570 kcal/l (Martin *et al*. 1992; Ousey 2003) daily administration of 10% of the foal's bodyweight in milk should meet its energy requirements.

TABLE 1: Findings in 3 groups of newborn foals admitted to the hospital: critically ill foals that survived (1–11), critically ill foals that did not survive (12–16) and foals without any systemic condition (17–27)

Foal	Breed Sex	Age (days)	Weight (kg)	Sepsis score	V_T (ml)	RR (breaths/min)	$\dot{V}_{O_2}$ (ml/kg)	$\dot{V}_{CO_2}$ (bwt/min)	REE (kcal/kg bwt/day)	Diagnosis
1	PRE ♀	2	40.0	21	71	50	5.7	6.6	42.5	Sepsis and HIE
2	PRE ♂	2	69.0	14	309	28	7.1	7.2	51.3	Sepsis and HIE
3	PRE ♀	2	40.5	10	190	37	4.9	4.9	35.3	Sepsis, HIE, FTPI, premature (30 days)
4	WB ♂	2	50.5	10	177	64	7.1	6.8	50.6	HIE
5	Arabian ♂	2	34.0	14	162	28	8.6	7.9	60.8	Sepsis, femoral nerve paralysis
6	Arabian ♂	8	56.2	12	234	41	5.9	6.9	44.0	Sepsis
7	WB ♀	3	52.3	6	198	56	6.7	7.1	48.9	HIE
8	PRE ♂	7	25.0	16	148	53	7.4	8.6	56.9	Sepsis, FTPI
9	Arabian ♀	2	40.5	11	170	24	4.6	5.2	34.2	Sepsis, HIE, premature (15 days)
10	Arabian ♂	9	54.0	5	398	34	7.9	9.7	59.5	Sepsis
11	Arabian ♀	8	60.4	3	380	47	6.7	8.5	50.9	Sepsis
12	Falabella ♂	3	11.8	8	88	28	7.9	8.1	57.1	Sepsis, VSD
13	Lusitano ♂	2	50.0	12	249	24	7.1	6.9	51.1	Sepsis and HIE
14	Arabian ♀	2	45.1	15	223	28	7.2	7.4	52.1	Sepsis, DIC
15	PRE ♂	3	53.0	8	155	30	5.6	5.0	39.1	Sepsis and HIE
16	PRE ♂	4	40.3	9	271	29	7.7	9.0	57.4	Sepsis, NMD, FTPI
Mean ± s.e.					*214 ± 23*	*38 ± 3*	*6.8 ± 0.3*	*7.2 ± 0.3*	*49.5 ± 2.1**	
17	PRE ♀	8	45.0	2	276	30	9.5	8.9	67.6	Patent urachus
18	Arabian ♀	19	51.5	0	395	23	8.0	8.3	58.4	Resolved colic, suspected intussusception
19	PRE ♂	5	54.3	8	353	35	10.1	11.4	74.7	Difficulty nursing, suspected mild HIE
20	WB ♂	4	61.1	3	416	33	11.8	12.5	71.4	Patent urachus
21	PRE ♀	2	42.0	7	293	45	10.0	10.9	73.5	Meconium impaction
22	PRE ♀	2	27.0	6	174	23	8.0	8.6	58.8	Born in hospital from mare with lymphoma
23	PRE ♂	4	39.8	5	272	30	8.2	8.5	63.1	FTPI
24	PRE ♂	3	55.0	4	366	41	10.1	10.5	75.7	Difficulty nursing, suspected mild NMD
25	WB ♂	4	57.8	3	317	43	7.2	7.2	53.2	FTPI
26	Paint ♂	21	57.0	2	370	38	9.0	10.3	66	Corneal ulcers
27	WB ♀	3	41.1	4	248	26	6.9	7.2	50.1	Meconium impaction
Mean ± s.e.					*316 ± 22*	*33 ± 2*	*9.0 ± 0.4*	*9.5 ± 0.5*	*64.8 ± 2.7*	

V_T = tidal volume, RR = respiratory rate, $\dot{V}_{O_2}$ = oxygen consumption, $\dot{V}_{CO_2}$ = oxygen consumption, REE = resting energy expenditure, PRE = Andalusian (Pura Raza Española), WB = warmblood; HIE = hypoxic-ischaemic encephalopathy, FTPI = failure of transfer of passive immunity, VSD = ventricular septal defect, NMD = nutritional myodegeneration (white muscle disease). *Critically ill foals (survivors and nonsurvivors) significantly different from control foals P<0.001.

In this study, intranasal oxygen supplementation was interrupted for up to 45 min in order to determine oxygen consumption accurately. None of these foals were in respiratory distress and no adverse effects were noted during removal of oxygen supplementation, as judged clinically by heart rate and respiratory rate and effort. However, the need to interrupt oxygen supplementation may restrict the utilisation of indirect calorimetry in critically ill foals with compromised cardiorespiratory function.

In man, in order to minimise variability, measurements of REE are usually performed at a standardised time relative to the time of the last meal and time of day (McClave and Snider 1992). In the present study, indirect calorimetry measurements were performed between hourly feedings if the foal was receiving enteral nutrition and every effort was made to standardise the time of the day when REE was measured, but this was not always possible. Additionally, variations in the post absorptive state and degree of excitability of these foals may also have increased data variability.

The results of this study should be interpreted considering the following limitations: 1) the use of hospitalised neonatal foals with nonsystemic conditions as controls in this study with critically ill foals; 2) the possibility of a significant leak and inaccurate collection of respiratory gases when using a tight-fitting mask; 3) the lack of daily energy expenditure measurements performed in all foals throughout their hospital stay; 4) the relatively low number of foals included in each group; and 5) the heterogeneity of disease in critically ill foals inherent to a clinical study (severity of condition, timeframe from onset to referral etc.).

In conclusion, resting energy requirements as estimated by indirect calorimetry in critically ill foals are approximately 50 kcal/kg bwt/day, which is much lower than the energy requirements for growing, active, normal foals. As critically ill neonatal foals recover, their energy requirements increase to ~65–70 kcal/kg bwt/day, which is similar to control foals. Based on these findings, sick neonatal foals that tolerate enteral nutrition and receive at least 10% of bodyweight in mare's milk daily should be expected to meet approximately their REE needs and maintain bodyweight. In foals that require parenteral nutrition, 50 kcal/kg bwt/day is a reasonable goal of energy provision.

Conflicts of interest

The author did not declare any conflict of interest.

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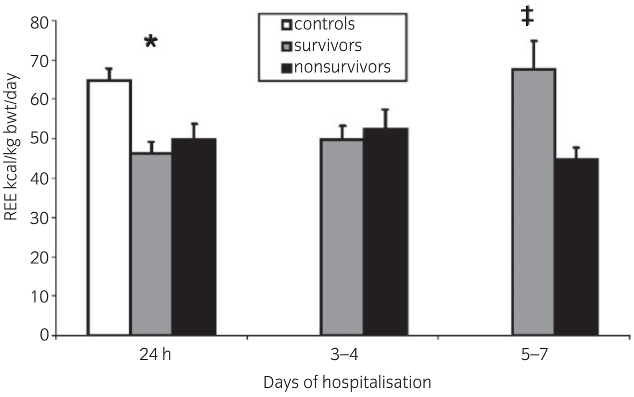

Fig 1: Resting energy expenditure (REE) in newborn foals with critical illness (sepsis and/or hypoxic-ischaemic encephalopathy) and control newborn foals (without any systemic condition) over time (mean ± s.e.). *At admission REE in critically ill foals (critically ill foals that survived and critically ill foals that did not survive) was significantly different than foals without a systemic condition P<0.001; ‡In critically ill foals that survived (n = 5) REE 5–7 days was higher (P = 0.058) than REE at admission.

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Manufacturers' addresses

[a]Ohmeda, Boulder, Colorado, USA.
[b]Galemed Corp, Wu-Jia, I-Lan, Taiwan.
[c]Vitalograph, Maids Moreton, Buckingham, UK.
[d]Scott Medical Products, Plumsteadville, Pennsylvania, USA.
[e]Jandel Scientific, San Rafael, California, USA.

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