

poor growth, specific facial features, asymmetry of the lower and upper limbs for length and width. Detailed physical examination revealed a small triangular face with prominent forehead, micrognathia, lips with downturned corners, and fifth finger clinodactyly on both hands. On admission into our hospital, the examination measured a weight of 9.0 kg (-4.9SD) and a length of 88.4 cm (-5.2SD). Anthropometrically she was classified as second grade malnutrition according to World Health Organization (WHO) charts. By contrast, her twin sister was physically and anthropometrically normal.

Intrauterine growth retardation, postnatal growth retardation, normal head circumference and asymmetry of the body were the major criteria that made the clinical diagnosis of Russell-Silver syndrome. Confirmation of Russell-Silver syndrome was made based on clinical findings, birth history and results of molecular genetic testing showed hypomethylation of the paternal imprinting center 1 (IC1) of chromosome 11p15.5.

Recombinant human growth hormone (rhGH) was administered by subcutaneous injection once daily, in the evening, at a dose of 0.05 mg/kg/day. The check-up visits in the outpatient were held every three months, and the following issues were evaluated: response to treatment, tolerability, and laboratory test results, with particular emphasis on carbohydrate metabolism and bone age progression. Currently, after 28 months of rhGH treatment, the girl has grown 18 cm, reaching a body height of 106.5 cm (-3.2SD, Δ Ht SDS: 2SD). Her current weight is 14.1 kg (-2.9SD, Δ Wt SDS: 2SD). So far, no serious adverse events have been observed.

Conclusion: This is the first case of monozygotic twin with Russell Silver syndrome reported in east Asian population. The possibility of rhGH treatment can be considered in cases of documented GH deficiency in patients with Russell Silver syndrome, under close endocrinologic supervision.

Diabetes Mellitus and Glucose Metabolism

IMPACTS OF METABOLISM ON CLINICAL CHALLENGES

The Effect on Ketogenesis of Withholding Early Parenteral Nutrition in Critically Ill Children, as a Potential Mediator of the Improved Acute Outcome.

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Introduction: In adults and children, withholding parenteral nutrition (PN) for 1 week in ICU (late PN), hereby accepting macronutrient deficit early during critical illness, as compared with supplementing insufficient enteral nutrition with PN (early PN), accelerates weaning from mechanical ventilation, reduces infections, and shortens ICU stay^{1,2}. We hypothesized that these benefits are in part mediated by fasting-induced ketogenesis.

Methods: This is a secondary analysis of the Early versus Late Parenteral Nutrition in the Pediatric ICU (PEPaNIC) RCT (N=1440)². First, for a matched subset of 96 patients with a PICU stay of ≥ 5 days, daily plasma 3-hydroxybutyrate (3HB) concentrations were determined to identify the time point of maximal effect of late PN versus early PN, if any, on 3HB. Thereafter, for all patients with a plasma sample available on that “maximal effect day” (or last day for shorter stayers), plasma 3HB and insulin concentrations were quantified (N=1142). The independent association between plasma 3HB on that day and outcome was assessed by multivariable Cox proportional hazard analysis for time to live weaning from mechanical ventilation and for time to live PICU discharge and by multivariable logistic regression for incidence of new infection and PICU mortality, adjusted for randomization to late PN versus early PN and baseline risk factors (demographics, diagnosis, illness severity). In a sensitivity analysis, models were further adjusted for key regulators of ketogenesis (plasma insulin, blood glucose, corticosteroids and catecholamines) to assess whether any effect was direct or indirect.

Results: In the matched cohort, late PN increased plasma 3HB as compared with early PN (P<0.0001 for PICU-days 1 to 5), with maximal effect observed on PICU day 2. In the 1142 patients, plasma 3HB concentration on that “maximal effect day” was (mean \pm SEM) 0.19 \pm 0.05 mM in early PN patients and 1.17 \pm 0.02 mM in late-PN patients (P<0.0001). Adding these plasma 3HB concentrations to the multivariable models, adjusted for baseline risk factors and randomization, showed that higher plasma 3HB concentrations were independently associated with a higher likelihood of early live weaning from mechanical ventilatory support (P=0.0002) and of early live PICU discharge (P=0.004). As the 3HB concentrations replaced the effect of the randomization, this suggested that the 3HB effect statistically explained these effects of the randomization. Further adjustment for key regulators of ketogenesis did not alter these findings. The effect of late PN versus early PN on plasma 3HB did not explain its impact on infections and was not related to mortality.

Conclusion: Withholding early PN increased plasma 3HB concentrations in critically ill children, a direct effect that mediated an important part of its beneficial impact on recovery.

¹Casaer M. et al, N Engl J Med 2011²Fivez T. et al, N Engl J Med 2016

Reproductive Endocrinology

BASIC MECHANISMS IN REPRODUCTION: FROM BEGINNING TO END

AMH Preserves Fertility in Chemotherapy-Treated Mice Through a Mechanism Involving Autophagy

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Chemotherapy-induced ovarian failure and infertility is an important concern in female cancer patients. The follicular ovarian reserve is established early in life then keeps declining regularly along reproductive life. This reserve is constituted