

Nutritional desynchronization in patients with nocturnal parenteral nutrition

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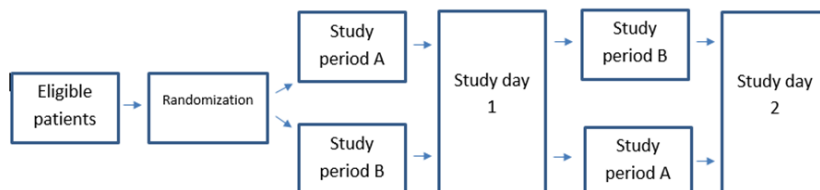
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Description of the initiative

Human physiology is characterized by a circadian rhythm driven by the biological clock. Misalignment with this rhythm is associated with increased risk for chronic diseases such as obesity, cardiovascular disease and type 2 diabetes. Many patients on parenteral nutrition (PN) are on cyclic infusion of nutrition during the nighttime for practical reasons, but this pattern of feeding is not concordant with their biological clock. Circadian rhythms are present in bone and in glucose metabolism as well as in protein synthesis. We hypothesize that nocturnal feeding negatively affects bone turnover, nitrogen balance, sleep/wake rhythms and glucose metabolism. The aim of this study is to determine the effect of nocturnal versus daytime cyclic infusion of PN in adult patients on bone turnover, nitrogen balance, sleep and wake rhythm, peripheral clock genes expression and glucose metabolism.

Planned activities & deliverables



We will conduct a crossover pilot study including 20 adult chronic intestinal failure patients on home parenteral nutrition. Participants will maintain their usual oral (daytime) food intake during the entire study period. During study period A patients will administer their nutrition overnight for 2 weeks. After 2 weeks, they crossover to daytime nutrition infusion. Blood glucose will be monitored continuously using a flash glucose monitoring system to assess glucose variability and patients will wear an actigraph to determine 24h sleep/wake rhythms. Participants will be asked to keep an oral food diary during the entire study period and monitor their sleep quality (VAS scale).

After each 2 weeks, patients will be admitted to the research unit at 8 AM (T=0) for a period of 24 hours. They will be on nil per mouth with the exception of water and their prescribed PN.

Assessments of in-hospital study day;

1. Blood sampling at T=0: triglycerides, Alkaline Phosphatase, sodium, potassium, magnesium, calcium, albumin, phosphate, creatinine, urea, 25OH vitamin D, TSH
2. Blood sampling every 4 hours from T=0 onwards: P1NP, CTX-1, glucose, insulin, glucagon, cortisol, clock gene expression in peripheral leucocytes, PTH
3. Energy expenditure and substrate oxidation every 4 hours using indirect calorimetry
4. 24h faecal excretion for BOMB calorimetry.
5. 24h urinary excretion for calcium, magnesium, sodium, phosphate, potassium, urea, creatinine, nitrogen

This research will lead to important insights in the health effects of nocturnal medical nutrition and might result in revision of nutrition guidelines regarding timing of feeding.

Resources & enablers

- Total budget of this study is €80.000. The MNI grant will be used for laboratory measurements (€20.000) & part of the salary costs (€10.000)
- Other salary costs are covered by NWO doctoral grant for teachers (023.018,051), and by an AGEM innovation grant 2021-II, Amsterdam UMC, Amsterdam, The Netherlands (€50.000)

Results/outcomes & expected impact

The effect of nighttime feeding on bone turnover, nitrogen balance, sleep/wake rhythm, circadian rhythm (clock genes) and glucose metabolism has never been studied in humans. The results of this study could have direct implications for all patients on nocturnal nutrition in and outside a health care setting. After this pilot study, a larger randomized trial will be started in patients on enteral nutrition. This study also provides a unique human model to investigate the effects of nutritional desynchronization.



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