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Vermeulen, M.A.R.

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Nutrition and amino acid metabolism in critically ill patients

Abstract

Mechteld A.R. Vermeulen

This thesis approaches amino acid metabolism in critically ill patients from bench to bedside, in which there is a central role for glutamine, citrulline, arginine and enteral nutrition. The relationship between glutamine, citrulline and arginine has been known for decades. Glutamine is converted into citrulline in the gut after which citrulline is converted into arginine in the kidneys: the intestinal-renal-axis. The first step is through glutamate conversion.

Critically ill patients are preferentially enterally fed. However the sufficiency of the gut in critically ill patients is not precisely known, hence it is important to determine the intestinal-renal-axis of glutamine in those patients, as opposed to non critically ill patients, also in relation to clinical parameters.

Attempting to better understand the function and fate of glutamine in this group of patients, firstly glutamine and glutamate were studied in relation to intestinal function *in vivo*. This thesis proves that the glutamine-to-glutamate deamidation is crucial in reversing intestinal hyperpermeability *in vitro*. This illustrates the importance of the enteral –rather than parenteral- approach of glutamine or glutamine enriched nutrition.

However when alanyl-glutamine was added to enteral nutrition in critically ill patients without multiple organ failure or sepsis, this thesis concludes that no higher plasma concentrations of glutamine were observed. Even so, conversion rates to citrulline and arginine were not promoted and protein synthesis was similar in glutamine supplied versus normally fed critically ill patients.

In surgical patients results were different: When alanyl-glutamine (intervention dose of 0.5 g/kg/d) was given preoperatively, renal arginine production doubled as reflected in plasma concentrations.

Although numerous studies were previously performed in order to understand amino acid metabolism in relation to illness and disease, most were postabsorptive studies. Therefore it remained unclear whether plasma amino acid concentrations would alter during enteral nutrition. We studied a group of septic and cardiogenic shock patients that were optimally enterally fed. We noticed a vast amount of amino acid deficiencies at admission. After three to five days, almost all amino acid concentrations increased. In contrast taurine decreased by >50% during ICU stay. This downward slope was associated with longer periods of mechanical ventilation and ICU support.

When the potential benefit of glutamine administration is seen in the light of the intestinal renal axis, the next step to do was studying arginine and the competitive nitric oxide inhibitor asymmetric dimethylarginine (ADMA) in critically ill patients. We observed a relation between disequilibrium of arginine and ADMA and markers of severity of disease and cardiac index.

Finally, this thesis critically approaches newly published trials on glutamine. We conclude that the use of glutamine in specific populations should be carefully chosen.

While in the old days studies focused on single nutrients (such as glutamine and arginine), the context of embedded optimal nutrition is different now. The effect of nutrition on glutamine metabolism is described in this thesis. Different groups of interest could be identified for a similar approach of metabolic investigation. In the future, the use of nutrition, enriched nutrition and specific nutrients will probably be more nuanced and more tailored than we were used to in the pro-glutamine era.