Human Splanchnic Amino Acid Metabolism

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1. BACKGROUND AND AIM
Amino acid metabolism is a key component of the body’s ability to grow, adapt, and perform in an ever-changing environment [1]. Amino acids are essential for life as the building blocks for proteins providing structure, for enzymes that regulate all body processes, and as precursors for hormones, neurotransmitters, and e.g. nucleic acids. This diversity and essential nature of amino acids make them critical to any understanding of metabolic regulation. It has been known for years that the various body compartments play specialized roles in amino acid homeostasis, through either uptake or release [2]. However, the separate roles of specific organs in amino acid metabolism in humans remain unclear, particularly with respect to the splanchnic organs. This is because these organs and their efferent vessels are relatively inaccessible. As a result, most available data concern overall splanchnic balances, including contributions from all organs in the splanchnic bed [3]. In the past, the relative contributions of the gut and liver to net splanchnic amino acid balances have been evaluated in humans by our group [4]. In these studies, the role of other splanchnic organs was not explored. The sampling of blood from the portal vein only in these studies implied while it was assumed that this represents gut metabolism, other organs also deceiving blood into the portal vein might have played a role. Here, we wanted to explore the relative contribution of the small and large bowel, the spleen and the kidneys. This was also stimulated by our recently growing interest in the human microbiome. In fact, the human distal gut microbiome contains a variety of clusters of orthologous groups of genes involved in essential amino acid biosynthesis [5]. In this study, we aimed to evaluate interorgan amino acid exchange among the intestine, liver, spleen, and kidneys in patients undergoing upper abdominal surgery. Insight into the interorgan handling of amino acids in humans is needed to clarify normal human physiology. Importantly, this human model gave us the unique opportunity to distinguish between the small intestine and colon in amino acid handling. This knowledge may in future be applied to optimize dietary supplementation of certain amino acids [6-8] and may be used for theoretical modelling of amino acids in humans.

2. METHODS
20 patients planned to undergo a pylorus preserving pancreaticoduodenectomy (PPPD) as treatment of benign or malignant tumors were included in this study at the surgical outpatient clinic of Maastricht University Medical Center (MUMC*). Under general anesthesia, blood from these patients was sampled during surgery from the portal vein, hepatic vein, superior mesenteric vein, inferior mesenteric vein, splenic vein, renal vein, and the radial artery. Subsequently, the difference between arterial and venous concentrations of 20 amino acids was determined by HPLC as a semi-quantitative measure of amino acid metabolism across a given organ. A p-value below 0.05 was considered statistically significant.
3. RESULTS

Our data showed a net release of 32.7±7.3 µmol/L serine by the kidneys into the systemic circulation. Besides, we found a significant uptake of glutamine by the small intestine (124.8±21.0 µmol/L), accompanied by a net release of 36.4±5.8 µmol/L citrulline. This, however, was not seen for the colon. Interestingly, a trend of net hepatic uptake of citrulline (9.7±1.6 µmol/L) was observed, next to a remarkable alanine, arginine, and methionine uptake (117.1±19.0 µmol/L; 26.1±4.2 µmol/L; 6.6±1.1 µmol/L). Glutamate, on the other hand, was significantly released by the liver into the circulation (67.9±11.0 µmol/L).

4. CONCLUSION

This design provided us with unique qualitative and quantitative information on integrative amino acid physiology. The well-known intestinal glutamine-citrulline pathway appears to be present in the small intestine but not in the colon in vivo. In the future, this knowledge may be applied to optimize dietary supplementation of certain amino acids in critically ill patients.

Keywords: amino acids, human interorgan metabolism

References