Commentary

Development of liver dysfunction under artificial nutrition: a reason to modify nutrition therapy in the intensive care unit?

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See related research by Grau *et al*., http://ccforum.com/content/11/1/R10

Abstract

Actual research suggests that artificial nutrition in critically ill patients can be associated with alterations in liver dysfunction biomarkers such as enzymes and serum bilirubin. In addition to known patient-dependent and nutrient-dependent factors, the time of initiation of nutrition therapy seems to influence the risk of altered biomarkers, whereas age and gender, weight, range of clinical scores, type of primary diagnosis, necessity for mechanical ventilation, and the composition of the lipid emulsion used within total parenteral nutrition had no significant effects. This commentary analyzes these new results in the light of known relationships between illness and artificial nutrition therapy.

In this issue Grau and colleagues [1] report the results of a multicentre study performed in 40 Spanish intensive care units (ICUs) dealing with the development of hepatobiliary disorders under artificial nutrition. This problem is not new: in 1971 Peden and colleagues first described total parenteral nutrition (TPN) as a cause of hepatic dysfunction [2]. Today, three types of hepatic disorder can be related to parenteral nutrition (PN) and, to a smaller extent, to enteral nutrition (EN): steatosis, cholestasis, and gallstones [3]. Prevalence rates published in recent review papers varied from 25% to 100% in adults and from 7.4% to 84% in pediatric patients [3,4]. Diagnosis of PN-associated hepatobiliary disease is mostly based on the analysis of liver enzymes and serum bilirubin as biomarkers. The definition of cutoff values can vary between medical units, which may partly explain the broad range of the prevalence rates.

The etiology and pathogenesis of PN-induced liver dysfunction are not fully known or understood. It is assumed that both patient-derived and nutrition-derived factors are involved. Obviously, most patients who need PN and/or EN are critically ill or have a primary gastrointestinal disorder such as Crohn's disease or short bowel syndrome. These clinical conditions are often associated with disease-specific metabolic alterations which are seen in themselves as risk factors for the development of liver dysfunction during the course of illness: systemic inflammation due to the release of proinflammatory cytokines, altered membrane function, limited capability of successful antioxidative defense, or bacterial overgrowth [4]. Development of liver dysfunction may then be further promoted by the intravenous supply of a probably unbalanced or inadequate nutrient solution.

Several nutritional factors have been claimed to increase the risk for hepatobiliary complications [3]. The strongest evidence is available for energetic overfeeding: if the caloric intake is considerably higher than the need of the patient, increased hepatic fat deposition will occur, stimulated by high release of insulin. As nicely shown in a current review [5], the prevalence of PN-associated liver dysfunction in newborn infants decreased with diminished energy intake. The composition of energy-providing macronutrients seems to be of minor importance if the delivery of carbohydrates, fats, and amino acids remains in a 'physiological' range [4]. Single micronutrients may also be involved in the etiology of liver dysfunctions [3,4]. There is some evidence that deficiencies in glutamine, taurine, choline, and carnitine may negatively influence liver metabolism, resulting in non-physiologically high biomarker concentrations. In addition, fatty acid composition [6] and the phytosterol content [7] of the lipid emulsion used may influence liver metabolism and the risk for liver dysfunction.

The study by Grau and colleagues [1] adds further information on potential factors influencing the risk for development of liver dysfunction. On the basis of a multivariate analysis, an early use of artificial nutrition (within 24 hours of admission to the ICU) can delay or even avoid the

EN = enteral nutrition; ICU = intensive care unit; PN = parenteral nutrition; TPN = total parenteral nutrition.

appearance any type of liver dysfunction in their mixed patient population. It can be speculated that a delayed nutritional support of (already malnourished) ICU patients may impair liver metabolism. Interestingly, age and gender, weight, range of clinical scores, type of primary diagnosis, necessity for mechanical ventilation, and the composition of the lipid emulsion used within TPN had no significant effects on the prevalence of increased biomarker concentrations. Earlier data strongly suggest that enteral stimulation providing even small amounts of liquid can considerably decrease the risk for hepatic complications by avoiding bacterial overgrowth, endotoxemia, and abnormal bile acid metabolism [4]. It is therefore surprising that Grau and colleagues [1] still observed, in 18% of their patients receiving EN, high levels of biomarkers. The authors comment that most patients on EN were medical, needed more mechanical ventilation, and had a longer ICU stay; they were therefore more seriously ill, which might explain the unexpectedly high prevalence rate. However, the possibility cannot be excluded that the enteral solutions used might not have the correct composition with regard to key nutrients (see above).

As confirmed in the study [1], there is a potential risk for the development of liver dysfunction associated with PN or EN, diagnosed with the use of biomarker analysis. Which consequences have to be drawn in clinical practice? Should we retard or even skip artificial support in adult ICU patients? On the basis of present knowledge the answer is no. Early nutritional support providing energy and a balanced mixture of all indispensable and conditionally indispensable nutrients is a live-saving treatment and must therefore be an integral component of modern medical therapy. In many cases the primary disease is the decisive cause of the development of liver dysfunction; intravenous or even enteral nutritional support may be an aggravating factor. By modifying present PN and EN nutrition concepts this latter risk can be minimized. Sufficient endogenous availability of nutrients and metabolites such as glutamine, taurine, choline, and probably carnitine can help to maintain hepatic functions. Because it is known that ICU patients have a higher need for nutrients such as glutamine [8], an adequate exogenous supply within the frame of pharmaconutrition [9] can prevent intracellular and extracellular deficiencies. Furthermore, it is worth mentioning that increased concentrations of biochemical markers such as liver enzymes can occur within 2 to 4 weeks of PN/EN therapy and in most cases these return to normal even when PN is continued; a chronic liver dysfunction is generally not to be expected.

Competing interests

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