LIVER DISEASE IN PATIENTS QUALIFIED FOR HOME PARENTERAL NUTRITION – A CONSEQUENCE OF A FAILURE TO ADJUST RTU BAGS IN THE PRIMARY CENTRE?

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If planned improperly, parenteral nutrition may result in a number of severe metabolic complications caused by insufficient or excessive delivery of individual nutrients. One of the most common and the most dangerous complication is parenteral nutrition-associated liver disease (PNALD). Such a complication may also result from using RTU (ready-to-use) bags that are not adjusted adequately to individual patients.

The aim of the study was the analysis of prevalence and determining the cause of liver disease in patients who had been receiving parenteral nutrition in primary centres prior to the implementation of home parenteral nutrition in the specialist centre.

Material and methods. The study enrolled 146 patients who were referred to the Clinic in the period of 2006–2012 in order to be qualified for home parenteral nutrition. Interview and medical documentation revealed that 100 patients had been receiving parenteral nutrition by means of ready-to-use (RTU) bags in their primary centres. In the remaining 46 patients, such feeding had not been implemented. Upon admission, the following parameters were evaluated: bilirubin, aspartate aminotransferase (AspAT), alanine aminotransferase (AIAT), lactate dehydrogenase (LDH), gamma-glutamyltranspeptidase (GGTP), alkaline phosphatase (AP), triglycerides (TG), cholesterol, protein, albumins, amylase, urea, creatinine and C-reactive protein (CRP). The analysis of the results was conducted with the use of the Student’s T-test.

Results. The patients who had been receiving parenteral nutrition manifested significantly increased (p < 0.05) levels of total bilirubin, TG, AIAT, LDH, GGTP, AP and CRP. 23% of patients were diagnosed with jaundice, in 70%, GGTP > 100 i.u. and a half manifested biochemical features of cholestasis. No correlation was observed between the CRP level and results of liver function tests.

Conclusions. It was found that there is a correlation between parenteral nutrition with RTU bags and liver disease. The probable cause of liver disease associated with parenteral nutrition received prior to the transfer to the Clinic is excessive administration of lipids. It can be accompanied by excessive administration of glucose. Modification of parenteral nutrition helped to compensate for liver disorders in all patients.

Key words: TPN, PNALD, RTU

An improper procedure of parenteral nutrition may be associated with a number of metabolic complications. They are connected with insufficient or excessive administration of nutrients or incorrect proportions of individual ingredients in feeding formulas. Metabolic consequences resulting from parenteral nutrition can be divided into deficiency and excess as well as into acute and chronic metabolic complications (1). Table 1 presents selected acute and chronic metabolic complications.
Parenteral nutrition-associated liver disease (PNALD) is one of the most severe metabolic complications (1).

Its diagnosis is based on ruling out alcohol-related, viral, mechanical and parenchymal causes of the disease. The presence or absence of characteristic clinical signs as well as elevated hepatic metabolism parameters, which occur during parenteral nutrition, should be assessed (2).

Moreover, concurrent factors, such as absence of oral or enteral nutrition, receiving parenteral nutrition, recurring catheter-related blood infections and insufficient or excessive administration of nutrients, play a significant role in the pathogenesis of PNALD. In the recent years, it has been demonstrated that using standard soybean oil-based lipid emulsions may increase the risk of parenteral nutrition-associated liver disease (3).

Actions that aim at prevention of PNALD encompass:

– Gradual increase in the energy content of the feeding formula;
– Biochemical monitoring of clinical nutrition;
– Administering proper lipid emulsions based on soybean or fish oils;
– Conducting trophic enteral nutrition.

In parenterally fed patients, the effectiveness of the therapy and appropriate patient care depends on accurate estimation of energy requirement and preparation of a feeding formula with the composition that strictly corresponds to individual patient needs. All errors connected with incorrect selection of nutrients and inadequate energy supply in formulas may become a cause of serious complications, such as PNALD, that hinder further treatment.

The aim of the study was the analysis of prevalence and determining the cause of liver disease in patients who had been receiving parenteral nutrition in primary centres prior to the implementation of home parenteral nutrition (HPN) in the specialist centre.

MATERIAL AND METHODS

The study enrolled 146 patients (86 men and 60 women) who were referred to the Clinic in the period of 2006–2012 in order to be qualified for home parenteral nutrition and, at the same time, to the therapy of the underlying disease. The mean patients’ age was 69.8 years. In the majority of patients, parenteral nutrition was indicated due to: short bowel syndrome (n=109, 75%), malabsorption syndromes (n=12; 8%), paralytic ileus (n=7%) and malignant bowel obstruction (n=18; 10%). Of 146 subjects, 100 patients had been receiving parenteral nutrition by means of RTU bags in their primary centres prior to admission to the Clinic. The remaining 46 patients had not been receiving such nutrition before and these patients constituted a control group. Within the first day of admission, the following biochemical parameters were evaluated in each patient: bilirubin, aspartate aminotransferase (AspAT), alanine aminotransferase (AlAT), lactate dehydrogenase (LDH), gamma-glutamyltranspeptidase (GGTP), alkaline phosphatase (AP), triglycerides (TG), cholesterol, protein, albumins, amylase, urea, creatinine and C-reactive protein (CRP). The analysis of the results was conducted with the use of the Student’s T-test.

RESULTS

The analysis of medical documentation indicated that levels of total bilirubin, TG, AlAT, LDH, GGTP, AP and CRP were higher in patients (n=100) who had been receiving parenteral nutrition prior to admission to our
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Table 2. Selected biochemical parameters that were not statistically significant in the examined groups of patients

<table>
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<tr>
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<th>Patients not receiving PN</th>
<th>Patients fed with RTU bags</th>
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<tbody>
<tr>
<td></td>
<td>mean</td>
<td>median</td>
</tr>
<tr>
<td>Albumins (mg/dl)</td>
<td>3,20</td>
<td>3,20</td>
</tr>
<tr>
<td>Urea (mg/dl)</td>
<td>37,87</td>
<td>33</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>1,04</td>
<td>0,85</td>
</tr>
<tr>
<td>Cholesterol (mg/dl)</td>
<td>131,66</td>
<td>119,5</td>
</tr>
<tr>
<td>Amylase (i.u.)</td>
<td>59,68</td>
<td>48</td>
</tr>
<tr>
<td>AspAT (i.u.)</td>
<td>36,78</td>
<td>31,5</td>
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</table>

centre than in the control group (n=46) in whom parenteral nutrition had not been implemented. The differences between the groups were statistically significant (p < 0.05).

The results are presented in fig. 1-7. The mean duration of parenteral nutrition with RTU bags prior to admission to our centre was 32 days.

Fig. 1. Total bilirubin concentration (mg/dl) in patients who had and had not been receiving parenteral nutrition

Fig. 2. Triglyceride concentration (mg/dl) in patients who had and had not been receiving parenteral nutrition

Fig. 3. Alanine aminotransferase concentration (i.u.) in patients who had and had not been receiving parenteral nutrition

Fig. 4. Lactate dehydrogenase concentration (i.u.) in patients who had and had not been receiving parenteral nutrition
DISCUSSION

The following aspects are important in selecting an adequate programme of parenteral nutrition: appropriate concentration of nutrients and their proportions, estimating total and resting energy requirement, administering the feeding formula at correct times and a sterile venous line for formula administration since an infected catheter may also cause hepatic complications. The energy value of parenteral nutrition must correspond to patient energy requirement and thus include the following factors: sex, physical activity, underlying disease, concomitant conditions and patient nutritional status. It is crucial not to overfeed the patient chronically since it may result in severe life-threatening metabolic disturbances. Estimating patient’s resting energy expenditure (REE) may facilitate determining proper energy content in the feeding formula (4).

In clinical practice, REE is calculated with the use of mathematical equations that include sex, age, weight and height, e.g. equations of Harris–Benedict, Owen, Ireton–Jones and Mifflin (5). The method of indirect calorimetry is believed to be the most reliable in REE measurement. By measuring oxygen uptake and/or carbon dioxide production, it enables an accurate calculation of individual REE (6). Unfortunately, this method is not commonly available and still, mathematical equations are used. The medical documentation of patients (n=100), who were receiving parenteral nutrition with RTU bags as they were awaiting admission to the specialist centre, indicates that patients were most likely given formulas incorrectly adjusted to their clinical condition. It appears that energy requirement was considerably overestimated. In our retrospective study, it is not possible to unequivocally state what caused such overestimation; perhaps the mathematical equation to calculate resting energy requirement was incorrect or energy was delivered based on a subjective opinion of the medical team. Currently, numerous discussions are held regarding the question of which REE equation is the most appropriate for individual patients (7). In the case of excessive parenteral nutrition, first changes are relatively easy to compensate for due to great regeneration capacity of the liver. Removal of the factor, i.e. excessive energy delivery, causes remission of biochemical hepatic damage (el-
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elevated transaminase, bilirubin and alkaline phosphatase plasma levels).

A chronic administration of too large energy doses in parenteral nutrition exacerbates changes detected in radiological, laboratory and histopathological examinations of the liver. As in individuals with competent alimentary tract, steatosis of the liver (fatty liver) may occur, characterised by hepatomegaly. In initial stages, fatty liver is reversible. Therefore, following modification of nutrition, e.g. by temporary discontinuation of parenteral nutrition or reducing energy content in the feeding formula, it is possible to minimise or eliminate this complication. Patients who chronically receive excessive amounts of nutrients may develop irreversible lesions, such as hepatic fibrosis and, in extreme cases, even cirrhosis. Numerous studies reveal a correlation between hepatic function disorders and administration of proper lipid emulsions in the formula for parenteral feeding.

Based on long clinical experience and being one of the first Polish centres for chronic home parenteral nutrition, we recommend the following strategy of managing PNALD:

- temporary discontinuation of parenteral nutrition and only hydrating patients;
- reducing the amount of lipid emulsions or their removal from the feeding formula until hepatic parameters return to normal (9);
- qualitative change in the composition of lipid emulsions, i.e. reduction of lipid emulsions obtained from soybean oil and replacing them with olive oil-based emulsions or using omega 3-polyunsaturated fatty acids (9).
- using amino acids particularly intended for patients with hepatic insufficiency (10);
- reducing carbohydrate energy.

The aforementioned strategy of nutritional management in patients with PNALD should be conducted until hepatic parameters (AspAT, AlAT, Bilirubin and GGTP) return to normal. If energy requirement is difficult to calculate in a patient who awaits admission to a specialised centre for implementation of home parenteral nutrition, the safest management consists in administering lower energy doses than indicated by mathematical calculations.

CONCLUSIONS

1. The probable cause of liver disease associated with parenteral nutrition by means of RTU bags received prior to the transfer to the Clinic was excessive administration of lipids and concurrent excessive administration of glucose.
2. Modification of parenteral nutrition helped to compensate for liver disorders in all patients.
3. High CRP levels in patients who received ready-to-use bags resulted from a concomitant infection of the central catheter through which feeding formulas were administered. It also contributed to additional septic liver damage.

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