Response pattern recognition in paediatric Crohn's disease patients treated with enteral nutrition

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Received 21 January 2008; accepted 18 March 2008

Abstract

Aim: To describe the response pattern to enteral nutrition (EN) in paediatric patients with moderately to severely active Crohn's disease (CD).

Material and methods: A previously described method for assessment of response pattern to various treatments for CD was used. Patients who received EN during the 10-year period 1995–2005 were prospectively registered. Patient data, clinical outcome, time to relapse and subsequent need for treatment were extracted from the files. Four weeks treatment with polymeric ready-to-use liquid formula was given. The clinical outcome was assessed by pattern recognition of the disease course 30 days (immediate response) and 90 days (long-term response) after start of EN.

Results: Thirty-one patients (17/14 M/F), median age 14 years (range 7.5–19.8 years), received 46 courses of EN. Thirty-seven courses (80%) were completed. Immediate response: twenty-five courses (67%) led to complete response (CR), 8 (22%) to partial response (PR) and in 4 courses (11%) no response (NR) was achieved. Long-term response: 21 courses (64%) led to prolonged response (PRO), defined as either maintenance of complete response (CR) or partial response (PR), while 12 courses (36%) were followed by loss of response (LR). The median time to relapse was 8.3 months (range 0.5–39 months).

Conclusion: We found our model of response pattern to be a useful instrument for the description of results obtained during EN in children with CD.

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KEYWORDS
IBD; Crohn's disease; Paediatric; Enteral; Nutrition; Treatment

1. Background

Crohn's disease (CD) is a chronic inflammatory bowel disease (IBD) involving varying parts of the intestine. At time of diagnosis most patients are young adults, but a substantial number of patients are diagnosed before the age of 16 years. The severity of the symptoms may vary, but the nature of the disorder is often severely debilitating to
children and adolescents due to delayed growth and puberty, social limitations, lowering self-esteem and adverse events caused by potent medication such as corticosteroids.

Since the 1970s it has been known that exclusive feeding with formulated liquid nutrition products induce remission in active CD. Among adult CD patients 50–60% achieved remission when treated with enteral nutrition (EN) compared to approximately 70% after treatment with corticosteroids. This has lead to reluctance against the use of EN among adult gastroenterologists even though the remission rate of EN is higher than obtained using many other treatments used for CD (e.g. antibiotics, 5-ASA). In children with CD EN is as effective in inducing remission as corticosteroids.

During EN inflammatory parameters (erythrocyte sedimentation rate, CRP) and cytokine levels in blood and affected mucosa are normalised and mucosal healing is achieved. No differences in efficacy have been demonstrated between different formulas. Thus EN is an attractive alternative to corticosteroids in the treatment of CD and especially in children where the well-known side effects of corticosteroids on growth, bone mineralization and BMI are matters of severe concern. EN is not associated with any side effects, the accumulated use of steroids is reduced and EN has the potential to influence the self-esteem of the young patient in a more favourable direction than corticosteroids. There is, however, a need for more knowledge on the response pattern, the duration of response, and influence on subsequent choices of treatment following a course of EN. In this study the aim was to describe EN with respect to the response pattern and duration of response.

2. Materials and methods

The use of EN therapy has been prospectively registered at the Paediatric Department at Hvidovre Hospital since 1995. Hvidovre Hospital is a referral centre for all IBD patients in the Eastern part of Denmark, which includes approximately 430,000 children below 15 years of age (mean for the study period). The study was, therefore population based and the patients non-selected. Patients with acute CD, who received EN from 1.March 1995 to 28.February 2005, were included in the study. The diagnoses of CD were ensured according to diagnostic criteria of Lennard-Jones. Data concerning gender, age, number of diets, choice of EN, duration of disease, disease localisation and supplementary medical treatment were extracted from the files. Data regarding height, weight, clinical symptoms and blood tests before treatment and in the fourth week of the diet were registered as well. The patients received a 4-week treatment with a polymeric ready-to-use liquid formula to induce remission of disease. No other oral intake was permitted except for water and sugar free chewing gum. The caloric recommendations were calculated according to the patient’s ideal weight. At the start of EN the children were admitted to the hospital for 1–3 days. They were cared for and followed-up by a multidisciplinary team consisting of a paediatric gastroenterologist, a dietician and specialised nurses. The 4-week EN was followed by another 2 weeks scheduled return to normal feeding in a gradual fashion. The time to relapse was assessed for those completing the diet. Relapse was defined as a demand for another course of EN, corticosteroids, infliximab or bowel resection. At relapse the next choice of treatment was registered.

Response pattern was assessed by a modified model (Table 1), first described and published by Munkholm et al. Twenty-eight days after start of EN the patients were classified according to clinical response as having complete remission (CR), partial remission (PR) or no response (NR). Three months after start of EN the patients obtaining CR or PR were further classified as having prolonged response (PRO) or loss of response (LR).

3. Results

EN therapy was initiated 46 times in 31 patients. 17 males and 14 females (median age 14 years; range 91–238 months) were treated. Twenty patients received 1 course, eight 2 courses, two 3 courses and one 4 courses. The median duration of CD was 24 months (range 0–71 months). Six patients (13%) had involvement of the small intestine, 19 (41%) of the colon only and 21 (46%) of both the small intestine and the colon, corresponding to 46 courses. The polymeric nutrition product consisted of Isosource in 21 courses, of other formulas (Nutrison, Fortini, Elemental 028) in 18 courses and of a combination of these products in 7 courses. The majority of courses were given orally, but in 3 courses (2 patients) a nasogastric tube and in 2 courses (1 patient) a percutaneous endoscopic gastrostomy tube was used. At the time of starting EN 16 patients (35%) received corticosteroids, 21 patients (45%) 5-ASA and 14 patients (30%) azathioprine.

Thirty-seven (80%) 4-week courses of EN were completed. In 25 (67%) of these the patients achieved CR, 8 (22%) PR and 4 (11%) NR (Fig. 1). Three months after start of treatment the 33 initially responding courses (CR or PR) were further evaluated. Twenty-one (64%) were associated with PRO and 12 (36%) with

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Model of response pattern</th>
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<td>Immediate response</td>
<td>Long-term response</td>
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<tr>
<td>30 days after start of EN</td>
<td>90 days after start of EN</td>
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<td>CR = Complete remission: ≤2 stools/day; no blood, pus, mucus, abdominal pain or weight loss</td>
<td>PRO = Prolonged response: Maintenance of CR or PR</td>
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<tr>
<td>PR = Partial Remission: ≤4 stools/day; blood, pus, mucus, abdominal pain less than daily; or weight loss</td>
<td>LR = Loss of response</td>
</tr>
<tr>
<td>NR = No Response: No regression of clinical symptoms or need of bowel resection</td>
<td>Symptoms requiring another course of treatment</td>
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LR (Fig. 2). Fifteen of the 25 courses initially leading to CR and 6 of the 8 leading to PR were associated with PRO 3 months after treatment. Courses associated with NR or followed by LR led to other choices of treatment. Following NR 3 infliximab treatments were given and one intestinal resection was performed. After LR, 2 further courses of EN, 2 treatments of infliximab, and 8 corticosteroid courses were given.

The median time to relapse was 8.3 months (range 0.5–39). Looking separately at the CR-group the median time to relapse was 9.6 months (range 0.5–39), compared with 4.6 months in the PR-group (range 1–9 months). Twelve patients (36%) among those responding to treatment (CR + PR) received corticosteroids as a supplementary treatment to the EN (75% tapering during EN), with a median dosage of 0.4 mg/kg entering EN and a median dosage of 0.14 mg/kg at the end of EN. In the same group 11 patients (33%) were treated with azathioprine.

4. Discussion

This is the first study to describe in a systematic way the response pattern of EN in paediatric population-based non-selected CD patients. This method was adapted for the evaluation of response pattern from Munkholm et al.,9 Faubion et al.,10 and Tung et al.11 who used it for assessment of response to corticosteroid treatment in adult and paediatric IBD patients. We recently used the same method to evaluate response of infliximab in paediatric CD patients.12 In these four studies special attention has been drawn to describe the phenomenon of dependency, defined as the need for another course of the treatment in question within a 30-day period in order to maintain the response. In the present study we did not evaluate EN dependency, because none of our patients received another course of EN within the first 30 days following completion of the first course. Therefore evaluation of response pattern was modified as shown in Table 1.
The CR rate in this study (67%) was similar to rates reported in former paediatric studies evaluating EN\(^4\) and comparable to results obtained during treatment with corticosteroids.\(^3\) Twenty-two percent achieved PR, the majority being without clinical symptoms, but not registered as achieving CR because of a minor weight loss. These patients drank the EN formula without using a tube and many of them found it difficult to consume the calculated optimal volume, this leading to a minor weight loss.

Relapse may occur after EN as well as after any other treatment for CD. One third of our patients lost response within 3 months after starting treatment. The median time to relapse was 8.3 months. Even when experiencing a relapse about one third of the patients preferred another course of EN. Half of the patients received corticosteroids at next relapse, but their previous experience of EN may result in future choices of EN and thus lead to a reduced exposure to corticosteroids in the long run when compared to patients not familiar with EN.

This study covers a 10-year period. It is possible that the response pattern may have changed over the time due to more frequent use of azathioprine and infliximab. Many new treatment regimens require a systematic model for evaluation. We have found our model of response pattern to be useful for the assessment of various treatments for CD. We recommend it as a tool for evaluation of future CD treatments.

Acknowledgements

This study received financial support from the Danish Crohn Colitis Foundation. AP and VW designed the study, LS and NKN collected the data, AP, VW, LS and NKN carried out the data analysis, NKN drafted the manuscript and AP carried out the final revisions of the manuscript. All authors read and approved the final manuscript.

References


