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Percutaneous endoscopic gastrostomy placement in paediatric Crohn’s disease patients contributes to both improved nutrition and growth

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Short title: Percutaneous endoscopic gastrostomy placement in Crohn’s disease

ABSTRACT

Aim: This paper describes the outcomes of gastrostomy feeding in patients with Crohn’s disease (CD).

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**Methods:** Patients with CD who attended the Royal Hospital for Children, Glasgow, and received gastrostomy feeding for at least two years between 2003-2010, were identified from the clinical database. The data recorded included the anthropometric data, CD phenotype, the surgical technique that was used, complications, medication, feed type, median feed, calories, volume and clinical outcomes.

**Results:** The study identified 16 patients (14 male) who had a gastrostomy inserted using a pull technique at a median age of 12.6 years at. Of these two required laparoscopic placement. Short-term complications lasting less than one month were experienced by nine (56%) patients and one (6%) experienced long-term complications. Anthropometry significantly improved at follow up compared to baseline: at 12 months the body mass index z-score was 1.11 (p=0.005) and the weight z-score was 0.19 (p<0.05). At 24 months the height z-score was -1.03 (p=0.04). The daily median volume and calories from feeds increased significantly from baseline to post PEG insertion, from 400-738ml and 705 to 860kcal/day (p=0.01).

**Conclusion:** Gastrostomy feeding for paediatric patients with CD was associated with improved nutrition, weight gain and growth outcomes.

**Keywords:** Anthropometry. Children, Crohn’s disease, Gastrostomy, Nutrition.
Key Notes

We studied 16 patients who had gastrostomy insertion for Crohn’s disease at a median age of 12.6 years and followed them for 24 months.

Our findings showed that this method of feeding for paediatric patients with CD was associated with improved nutrition, weight gain and growth outcomes.

Long-term complications only occurred in one of the 16 patients and nine reported short-term complications that lasted less than one month. Patients reported short term complications lasting < one month.

INTRODUCTION

Crohn’s disease (CD) is a lifelong relapsing and remitting inflammatory condition, which can affect any part of the gastrointestinal tract from the mouth to the anus (1). CD is characterised by areas of patchy, transmural inflammation, often leading to granuloma formation. Although it is a life-long condition, it has periods of remission and relapse. The incidence of CD within the paediatric population in Scotland is rising, with a median age at CD diagnosis of 9.7 years and inter quartile range (IQR) of 7.6-11.3) (2). Clinical presentation in the paediatric population can be variable. Abdominal pain is usually a prominent feature, alongside persistent or recurrent diarrhoea with or without blood. Other symptoms may include nocturnal stooling, tenesmus, lethargy, anorexia and nausea. Symptoms such as malabsorption, early
satiety and poor oral intake, lead to problems with growth delay, delayed puberty and malnutrition (3). Growth failure is one of the most significant long-term complications of active CD in the paediatric population (4). Diagnosis can be delayed due to the wide variety of presenting symptoms and this, combined with the diagnosis often being made peri-pubertally, can lead to the development of significant growth issues in some patients.

Once diagnosed, commonly used treatment options for the induction of remission are either corticosteroids or exclusive enteral nutrition (EEN) (5). Corticosteroids can have a negative impact on growth by interrupting normal pubertal growth patterns, leading to pubertal delay and reduced height velocity (5,6). EEN is now recognised as the first-line treatment for active CD and has been shown to induce remission, improve nutritional complications at diagnosis such as weight loss, improve inflammatory markers and promote growth and mucosal healing (5,7,8). Evidence to date suggests that the use of supplementary enteral nutrition, once remission has been induced, may be an effective method of maintaining remission in some patients (9-11).

Using enteral nutrition to induce and maintain remission has clear benefits, but the low palatability of feeds means that up to up to half of patients on EEN require an alternative route of feeding during the primary treatment course (12). The long-term use of a nasogastric tube (NGT) can lead to issues around food aversion and body image (13,14). NGT can also be difficult and uncomfortable to pass. When they are in-situ long-term NGT can lead to problems such as oral aversion and localised trauma with frequent passing of NGT. As a result, gastrostomy tubes are frequently used to deliver long-term enteral nutrition to patients with CD as well as other chronic diseases (15).
There is limited evidence to date on the efficacy and safety of delivering long-term enteral nutrition in paediatric CD via a gastrostomy tube (14,16,17).

This study aims to describe and evaluate the outcomes of gastrostomy insertion and feeding in patients with CD, including growth outcomes.

PATIENTS AND METHODS

This study was carried out in The Royal Hospital for Children, Glasgow; all patients had been diagnosed with CD using standard diagnostic procedures (18). A prospectively maintained clinical database was used to identify all children with CD who had had gastrostomy tubes placed between 2003-2010 with at least two years of data available before and after gastrostomy insertion. A standardised proforma was created to extract relevant data from medical, dietetic and nursing notes and this is available from the authors on request. All data was recorded for each patient at defined treatment intervals: diagnosis, 24, 12 and six months before, at the time of the gastrostomy tube insertion and six, 12, 24 and more than 24 months after insertion.

The data collected included anthropometric data, such as weight, height and body mass index (BMI). Disease activity was assessed using the physician’s global assessment (12,18). The Montreal classification, which was an appropriate scoring method at the time of the data collection, was used to classify the location and behaviour of CD at the time of fitting the gastrostomy (19). Information was collected regarding any macroscopic or microscopic gastric manifestations of CD at the time of gastrostomy insertion. The surgical
technique used at insertion was recorded along with any associated complications, which were defined as short-term if they resolved within one month of insertion or long-term if they lasted after this period. Information was collected regarding concurrent medication at each time period, along with the type of feed and the median volume of feed and calories received. Pubertal status was assessed using Tanner staging (20). Where available, information was collected regarding inflammatory and haematological values at each time point. This included haemoglobin, platelets, erythrocyte sedimentation rate, C-reactive protein and albumin levels. Previous surgery was also documented.

Statistical analysis was conducted using Minitab software version 15 (Minitab Ltd, Coventry, UK). Body weight, height and BMI were first converted to z-scores according to 1990 UK reference data (21). Analysis of variance (ANOVA) of repeated measurements and Bonferroni’s post-hoc corrections were performed for body weight, BMI, height z-scores and inflammatory markers with the comparison point set as the time of gastrostomy insertion (T+0). The Mann-Whitney test was used for the comparison of non-parametric data. Fisher’s exact test, where needed, was performed using Graph Prism version 15 (GraphPad software Inc, California, USA).

A previous audit of clinical practice identified that no formal ethical approval was needed for this type of study.

RESULTS

Patient demographics and disease classification
Over the course of the study period, 19 patients had gastrostomy insertion. Three of these were excluded from further analysis as the gastrostomy was inserted primarily for an existing significant co-morbid condition not primarily CD. These related to one renal condition, one case of cystic fibrosis and one patient with a pre-existing feeding condition. Of the remaining 16 patients, 14 were male (87.5%). The disease phenotypes are shown in Table 1. The median age at CD diagnosis was 9.7 years (IQR 7.6-11.3) and the median age for gastrostomy insertion was 12.6 years (IQR 9.5-14.0). The patients were followed up for a median of 2.3 years (IQR 0.3-6.5) following gastrostomy insertion.

Gastrostomy insertion, disease and complications

At the time of gastrostomy insertion, two patients had both macroscopic and microscopic gastric CD, two patients just had histological evidence of gastric CD, 10 patients (62.5%) had non-specific chronic inflammation on gastric biopsy at the time of insertion and one patient had normal gastric mucosa. No macroscopic assessment or biopsies were obtained for one patient.

Of the 16 patients, 14 (87.5%) had the gastrostomy insertion endoscopically with the remaining two patients having it placed laparoscopically. A 15fr Freka percutaneous endoscopic gastrostomy (PEG) tube (Fresenius-Kabi, Cheshire, UK), was used in 12 (75%) of the 16 patients, two (12.5%) had 9fr Freka (Fresenius-Kabi) and two (12.5%) had 16fr Corflo PEG (Halyard, Surrey, UK). Six patients (37.5%) received peri-procedural antibiotics. We also noted that 12 (75%) of the patients had their PEG tube changed to a
lower profile button gastrostomy device at a median of 16 (6-20) months after PEG insertion.

Short-term complications were reported in nine patients, with seven (77%) of these experiencing more than one complication. The complications reported include pain at the insertion site (57%), six (66%) reported over granulation, six (66%) reported a wound infection around the site that required treatment using oral and topical antibiotics and three (33%) patients reported problems with leakage. Only one patient reported long-term complications. This patient had multiple complications, including over-granulation, leakage, pain and infection. We found that six (37%) patients had no complications recorded following gastrostomy insertion.

The majority of patients (10/16, 62%) of patients had not undergone any surgery prior to gastrostomy placement. Of those that underwent surgery, 2/16 (12%) underwent a right hemicolectomy at the time of gastrostomy insertion and the remaining 4/16 (26%) had surgery prior to gastrostomy insertion. The type of surgery prior to gastrostomy insertion included right hemicolecotomy, ileostomy formation and division of adhesions in one patient. The remaining three patients underwent incision and drainage, with packing for perianal wound sepsis.

**Anthropometric data and pubertal status**

Table 2 displays the anthropometric data of the study patients pre and post PEG insertion. ANOVA with Bonferroni post-hoc correction demonstrated a significant increase in BMI z-scores (p=0.005) at six months post insertion and both body weight z-scores (p=0.03) and BMI z-scores (p=0.04) at one year.
post insertion. The height z-score improved significantly compared to baseline at two years post insertion (p=0.04) and at greater than two years post insertion maximal follow up (p=0.03). No statistical significant differences were observed at any other time points. Figure 1 highlights body weight, BMI and height of the 16 patients at the specific time points in the study.

Detailed pubertal information was available for 11/16 patients. All patients were pre pubertal at the time of the gastrostomy insertion. The majority of patients (8/11, 73%) remained pre pubertal with no further significant pubertal progression noted two years after insertion.

Inflammatory markers

Inflammatory markers were available for 15/16 patients at the specified time points in the study. Platelets were found to decrease significantly by 12 months after the PEG placement (p=0.02) with no statistical significance observed for any other blood markers at specified time points after appropriate corrections for multiple testing.

Enteral nutrition

All patients had received at least one course of exclusive enteral nutrition (EEN) prior to PEG placement. EEN was received by 9/16 (56%) of patients following insertion of the gastrostomy tube. Supplementary feeds were received by 10/16 patients prior to PEG placement and five of these were via an NGT and five orally. Following insertion of the gastrostomy tube, all patients received supplemental feeds.
Feeds given were either polymeric or elemental formulas. The specific feed choice was at the discretion of the dietetic/medical team. Polymeric feeds given included Modulen IBD (Nestle Health Sciences, Yorkshire, UK), Nutrison Energy (SHS Nutricia, Wiltshire, UK), Nutrison Standard (SHS Nutricia) and Nutrison Fibre (SHS Nutricia). Liquid supplements included Calogen (SHS Nutricia) and Fortijuice (SHS Nutricia). Elemental feeds used were Elemental E028 Extra (SHS Nutricia). Prior to PEG insertion 6/16 (37.5%), patients were on elemental feeds, one on polymeric and the remaining patients received Modulen IBD (Nestle Health Sciences) via NGT for EEN. After the gastrostomy insertion, 3/16 patients were on elemental feeds, 3/16 received Modulen IBD with the remaining 9/16 patients on other polymeric feeds.

The median volume of enteral nutrition delivered per day prior to PEG insertion (10/16 pts) was 400ml (range 0-550ml), which increased to 738ml (392-1300ml) following gastrostomy insertion (p=0.009). The median daily calorie intake prior to gastrostomy insertion was 705kcal (410-1080kcal), compared with 860kcal per day post gastrostomy insertion (642-1392kcal) (p=0.01).

**Medication**

The medications delivered at each time point are summarised in Table 3. Following gastrostomy insertion, the proportion of patients receiving methotrexate therapy, infliximab therapy, adalimumab and growth hormone increased.
DISCUSSION

This case series summarises the experience and safety of gastrostomy insertion for young people with CD. The results from this study indicate there were significant improvements in anthropometry after gastrostomy insertion including height z-score at two years and maximum follow up. The volume and calories of supplemental enteral nutrition delivered following gastrostomy placement significantly increased compared with that before gastrostomy placement. In terms of safety many patients had some form of minor complications in keeping with gastrostomy placements in other disease groups (22).

The results of this current study clarify the findings from other similar studies looking at gastrostomy placement in patients with CD. Cosgrove et al summarised their experience of 10 paediatric patients who had gastrostomies placed with CD in their centre (17). They concluded that gastrostomy placement was safe in this patient group and reported an improvement in height z scores (-1.4 to -1.1, p=0.038) at one year following gastrostomy insertion that was similar to our own study, where we showed the same improvement but after two years. A similar paediatric study by Israel et al showed improvement in linear growth following placement of gastrostomy in 16 patients, although the follow-up time period was not clearly stated (13). In their report, all patients resumed normal growth, with eight patients demonstrating accelerated catch up growth. Of note this group received 50-75% of their estimated average requirements via overnight feeds, which may have had an impact on oral feeding due to satiety. However, in the current study weight gain coincided with an increase in energy intake and feeds...
volume, which suggested minimal or no compensation of oral intake. Both these studies demonstrated an improvement in height velocity following a period of gastrostomy feeding, suggesting increased energy delivery is possible, albeit in different proportions of requirements between the two studies.

Israel et al also reported a low complication rate, with only minor complications reported, and they therefore reported that gastrostomy placement should be considered safe in this patient group (13). Mahajan et al reported on their findings on gastrostomy placement in both paediatric and adult patients with CD. The indications for gastrostomy placement included nutrition and gastric decompression following abdominal surgery (23). They reported a higher complication rate in those that had gastrostomy placed for decompression versus nutritional support (14% versus 3.5%). They did not make any observations regarding growth and did not differentiate between the adult and paediatric populations, thus making specific comparison of their results to our patient group difficult. Anstree et al reported their findings of adult patients with CD and gastrostomy placement, their sample size was small at nine patients and the duration of follow up was not stated (14). They reported an improvement in BMI in 6/9 patients and no major complications.

Gastrostomy tube insertion site infection was reported as a minor complication in our study, with 28% requiring antibiotics for treatment. Ahmad et al reported that 18% of patients developed wound infection, although the study participants had not received any prophylactic antibiotics prior to insertion (24). More recent evidence demonstrates that peri-procedural antibiotics reduce the wound infection rate to around 3%, so we now routinely give peri-

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procedural antibiotics to all patients receiving gastrostomies, including those with CD, which was not consistently the case during this study period (25,26).

A significant increase was reported in volume and calorie intake following gastrostomy insertion in our series – this increase would be higher still in our current patient group as we now predominantly use 1.5kcal/ml feeds in this patient group as opposed to E028 or Modulen IBD. Supplementary feeding has been shown to be beneficial for maintaining remission, but we are unable to clearly determine whether supplemental enteral nutrition played a role in remission rates in this patient group (9,10,27,28). We collected the data retrospectively and several patients had significant changes to their concomitant medication. This meant we could not estimate the effect maintenance feeds were having in isolation.

In the published literature it is well documented that improving nutritional status will have a positive impact on improving growth, but this has not been clearly demonstrated in paediatric CD following a short-term course of EEN (29,30). However, it should be noted that age and changes in pubertal status should be factored into any improvement in nutritional status, as improved nutrition may induce pubertal changes that would result in a growth spurt (13). The exact reasons for the improved growth in this patient cohort may result from optimised nutritional support, but are likely also to have been impacted, at least in part, by other concurrent management changes. Pubertal progression was not documented to be a major factor in the growth improvement. However there were changes in medication, with a documented increase in the number of patients receiving methotrexate, infliximab and adalimumab therapy, as well as a number of patients receiving
growth hormone following gastrostomy insertion. All of these treatments are recognised to have a beneficial impact on linear growth, reflecting that the modern management of paediatric CD patients with growth failure is often multifaceted and that treatment of this difficult problem does not rely on one individual treatment modality but several different approaches in combination (4).

**Conclusion**

In conclusion, this study demonstrated that gastrostomy insertion in paediatric patients was safe and well tolerated. Gastrostomy insertion could be a useful strategy to promote growth, as well as deliver supplemental enteral nutrition to keep patients in remission for as long as possible. Further research should explore the effectiveness of gastrostomy insertion on other aspects of nutritional status and growth and the impact on health expenditure using multicentre intervention controlled trials.

**Funding:**

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**List of Abbreviations:**

CD – Crohn Disease
IQR - inter quartile range
EEN – exclusive enteral nutrition
NGT – nasogastric tube
BMI – body mass index
PEG – Percutaneous endoscopic gastrostomy

Conflict of Interest

RKR has received support from MSD Immunology, Abbott, Dr Falk, Nestle and Ferring Pharmaceuticals. PM has received support from Nestle, Dr Falk and MSD. EB has received speaker’s fees from Nestle. HD has received speaker’s fees from Ferring. KG has received support from Nutricia and Nestle. GW has received support from MSD Immunology and Dr Falk.

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CD in the first year following diagnosis after induction of remission with EEN: supplemental enteral nutrition is better than nothing!.. *BMC Gastroenterology* 2014;14:1.


Table 1: Phenotypic classification and disease behaviour in paediatric patients with CD undertaking enteral feeding via PEG

<table>
<thead>
<tr>
<th>Disease location</th>
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<th>Disease behaviour</th>
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<td>Terminal ileum (L1)</td>
<td>2</td>
<td>Non-stricturing, non-penetrating (B1)</td>
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<tr>
<td>Colon (L2)</td>
<td>4</td>
<td>Non-stricturing, non-penetrating and perianal (B1p)</td>
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<tr>
<td>Ileocolonic (L3)</td>
<td>1</td>
<td>Stricturing (B2)</td>
</tr>
<tr>
<td>Upper GI (L4)</td>
<td>1</td>
<td>Penetrating (B3)</td>
</tr>
<tr>
<td>TI and Upper GI (L1+L4)</td>
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<td>Non-stricturing, non-penetrating and perianal (B1p)</td>
</tr>
<tr>
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<td>Stricturing and perianal (B2p)</td>
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<td>Penetrating and Perianal (B3p)</td>
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<td></td>
<td>T-24</td>
<td>T-12</td>
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**Anthropometry**

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<th>T+24</th>
<th>T-12 VS T+0 p value</th>
<th>T-6 VS T+0 p value</th>
<th>T-0 VS T+0 p value</th>
<th>T-0 VS T+12 p value</th>
<th>T-0 VS T+24 p value</th>
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<td>Weight SDS</td>
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<td>-1.42</td>
<td>-1.47</td>
<td>-2.00</td>
<td>-0.86</td>
<td>-1.11</td>
<td>-0.96</td>
<td>-1.17</td>
<td>1.00</td>
<td>0.73</td>
<td>1.00</td>
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<td>BMI SDS</td>
<td>-0.68</td>
<td>-0.89</td>
<td>-1.42</td>
<td>-0.92</td>
<td>-0.12</td>
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<td>Height SDS</td>
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Table 3: Concomitant medical treatment in children receiving enteral feeding via PEG

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<td>Prior to PEG placement</td>
<td>At PEG placement</td>
<td>Post PEG placement</td>
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<tr>
<td>Exclusive enteral nutrition (EEN)</td>
<td>16</td>
<td>1</td>
<td>9</td>
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<td>Azathioprine/6MP</td>
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<td>4</td>
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<td>Infliximab therapy</td>
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<td>Adalimumab therapy</td>
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<tr>
<td>Growth hormone</td>
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<td>0</td>
<td>5</td>
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Figure 1: Changes in height, weight and BMI SDS 24 months prior to, and 24 months after, gastrostomy insertion.