Use of small bowel MRI enteroclysis in the management of paediatric IBD

S. Sanka, A. Gomez, P. Set, N. Rimareva, R.J. Davies, P. Rolfe, G. Noble-Jamieson, F. Torrente, R. Heuschkel, M. Zilbauer

Department of Paediatric Gastroenterology, Hepatology & Nutrition, Addenbrooke's Hospital, Cambridge University, Cambridge, UK
Department of Paediatric Radiology, Addenbrooke's Hospital, Cambridge, UK
Addenbrooke's Hospital, Cambridge, UK
Department of Anaesthetics, Addenbrooke's Hospital, Cambridge, UK

Received 10 August 2011; received in revised form 25 October 2011; accepted 30 October 2011

Abstract

Introduction: Children with inflammatory bowel disease (IBD) frequently present with small bowel involvement at some stage of their disease. Hence, reliable assessment of the entire small bowel is required in order to adjust treatment accordingly. Recently, magnetic resonance imaging (MRI) of the small bowel in combination with luminal contrast agent delivered via a naso-jejunal tube (MR enteroclysis) is an emerging technique demonstrating good results in adult patients. However, data on its use and benefits in children is limited.

Aims: In this study we report our experience on performing small bowel MR enteroclysis (MRE) in children with IBD. Specifically, we reviewed indications, MR findings, advantages and disadvantages of the technique in a tertiary unit.

Methods: A total of 34 MRE studies (29 paediatric IBD patients) were retrospectively analysed. All patients underwent upper and lower endoscopy under general anaesthetic (GA) the day before MR imaging was performed. Nasojejunal (NJ)-tube was placed during endoscopy.

Results: Frequently detected findings included small and large bowel wall thickening, small bowel strictures and intestinal lymph node enlargement. Importantly, in all our clinical cases, MRE results were key to making a clinical decision in the given scenario regardless of whether MRE findings were positive or negative.
1. Introduction

Chronic inflammatory bowel diseases (IBD) are a group of conditions causing recurrent inflammation of the gastrointestinal tract. The two main entities are ulcerative colitis (UC) and Crohn's Disease (CD). While in UC inflammation is restricted to the large bowel, CD can affect any part of the digestive tract. In recent years the incidence of IBD has been increasing and approximately 25% of affected individuals are under 18 years of age. Management of the disease is particularly challenging in the paediatric age group, as growth and development, psychological aspects and disruption of education are all consequences of chronic gut inflammation early in life. As treatment algorithms for UC and CD differ substantially, a reliable diagnosis is essential. However, this can be particularly challenging in children, with first line investigations frequently proving insufficient to clearly distinguish between UC and CD. Current ESPGHAN guidelines recommend all children with suspected IBD undergo upper endoscopy (oesophago-gastro-duodenoscopy; OGD) as well as colonoscopy with intubation of the terminal ileum. While this allows visualisation of the entire large bowel and upper GI tract, only the most proximal and distal part of the small bowel (i.e. duodenum and terminal ileum) can be assessed. In addition, these criteria currently recommend that all children with suspected CD have the extent of their small bowel disease assessed at diagnosis, as about 15% of children with CD will present with exclusive small bowel disease.

Until relatively recently, small bowel imaging in children has relied entirely on conventional barium small bowel follow through and enteroclysis studies. However, several new imaging modalities are now available that offer significant advantages over this more traditional approach. Newer techniques include trans abdominal ultrasound (with Doppler and intestinal contrast), wireless capsule endoscopy (WCE), computed tomography (CT) and magnetic resonance imaging (MRI). Trans abdominal ultrasound is relatively non invasive and may reveal intestinal or colonic wall thickening, but has low sensitivity in showing subtle inflammatory changes and defining disease location. It also remains a very operator-dependant skill. WCE only provides valuable information on the macroscopic appearance of the small bowel mucosa. However this method carries significant additional risk in this patient group given the potential risk of acute obstruction from capsule impaction in stricturing disease. Although an abdominal CT scan provides valuable cross-sectional images, particularly within the pelvis, its routine use in the paediatric setting is precluded by the high radiation burden.

In contrast, imaging the small bowel with MRI is a radiation free technique that has great potential. The effective use of luminal contrast (i.e. small bowel enterography) allows a multi-planar visualisation of luminal, mural and extramural abnormalities with a particularly high contrast resolution of soft tissues. In addition, the use of intravenous contrast (Gadolinium) allows for sensitive detection of areas of tissue inflammation, the complete study thereby providing both inflammatory and obstructive details.

However, a fundamental requirement to detect subtle luminal changes is the ability to distend the small bowel in a controlled and predictable manner during data acquisition. This can be achieved by contrast administration either orally (i.e. fast swallowing) or via nasogastric tube (NGT). This technique is termed MR enterography, as opposed to where contrast is instilled directly into the small bowel via a naso-jejunal tube (NJT), which is known as MR enteroclysis (MRE). The latter method has been reported to provide superior imaging quality and hence greater sensitivity in adults with CD. However data in children on the application of MRE, its diagnostic value and potential role in management of children with IBD remains limited, with only a handful of small cohort studies being reported in the literature.

In this study we report our experience as a regional paediatric gastroenterology centre on performing small bowel MRI enteroclysis, utilising diagnostic endoscopy for the placement of most naso-jejunal tubes. In 29 children we report the indications, findings, advantages and disadvantages of a technique that is becoming a fundamental part of the effective diagnosis and management of children with IBD.

2. Materials and methods

2.1. Patient cohort

Since September 2008 the Department of Paediatric Gastroenterology at Addenbrooke's, in conjunction with the Department of Radiology, has offered SB MRE by standard protocol to children for diagnosis and investigation of IBD. We reviewed all MRE studies carried out with this protocol between September 2008 and November 2010. A total of 29 patients (13 male, 16 female) had 34 MRE studies at an average age of 15.3 years (10.3 to 17.9 years). Prior to the investigation, 19 patients had a confirmed diagnosis of CD, one a previous diagnosis of UC with recurrent small bowel symptoms following colectomy, one IBD-unclassified (IBDU) and the remaining 8 patients were being investigated for suspected CD without obvious colitic symptoms (features suggesting colonic inflammation included loose stools mixed with mucus and fresh blood, urgency, tenesmus and nocturnal diarrhoea).

All patients underwent upper endoscopy the day prior to the MRE. All endoscopies were performed by an experienced paediatric gastroenterologist. The vast majority were also having a colonoscopy for diagnostic purposes...
for disease reassessment, so had undergone low volume, stimulant bowel prep in the previous 24 h (local Senna-Picolax protocol). During upper endoscopy with an Olympus GIF260 under general anaesthesia, a trans-endoscopic NJT was placed under direct vision following completion of luminal biopsies. The oral jejunal tube was transferred nasally by means of a nasal prong, retrieved from the oropharynx by a helpful anaesthetist with a pair of Magill forceps. The NJT was then measured and safely secured to the face with around 20 cms of additional length. The intravenous cannula inserted during anaesthesia was flushed and secured overnight to allow for the administration of intravenous gadolinium during the MRE the following morning. Where distances of travel allowed, children returned home with their family overnight. Children continued the soft/liquid diet they had been on in the 48 h prior to colonoscopy until after the MRE.

2.2. MRI enteroclysis

A total of thirty-four MRI studies were carried out on a 1.5 T scanner (GE Medical Systems). Coronal and axial localiser sequences followed by coronal and axial fast imaging employing steady state acquisition (FIESTA) sequences were initially performed. A Coronal SSFSE sequence was performed out while steadily infusing between 1000–1500 ml of 450 0.5% methylcellulose (Mandeville Medicines) into the nasojejunal tube in situ using a customised manually driven infusion device. Sufficient intraluminal contrast medium was given to achieve adequate filling and distension of the small bowel loops to the ileocaecal junction.

Post methylcellulose infusion, 0.02 ml/kg of intravenous magnevist (dimeglumine gadopentetate, Bayer Schering Pharma) was administered via the intravenous cannula in situ and the following sequences were obtained: coronal and axial 3D T1W sequences and coronal and axial fast FIESTA sequences.

MRI studies were retrospectively reviewed by two paediatric radiologists who were blinded to the findings on previous imaging. The different sequences of each MRI study were assessed by considering the following parameters; the position of the nasojejunal feeding tube, effect of bowel distension, bowel wall observation (normal and pathological), complications, extra-intestinal manifestations and artefacts which degraded the images.

The bowel was divided into three segments — proximal small bowel (jejunum and proximal ileum), ileocaecal region (30 cm distant to the ileum, ileocaecal junction and caecum) and ascending colon to the anorectal region.

The images were assessed for the presence, location and extent of bowel wall involvement. The number of diseased segments was recorded. To determine the wall thickness (normal <4 mm with adequate distension, regardless of the patient’s age) and the degree of enhancement, each segment was also compared with the other bowel wall segments. The presence, site, length and number of strictures were noted. Complications including sinus tracts/fistulas and collections and extra-intestinal manifestations for example fibro-fatty mesenteric change, increased mesenteric vascularity and abnormal lymphadenopathy were assessed.

3. Results

3.1. Indications

There are several specific scenarios in the management of children with IBD where information about small bowel disease extent and severity is required in order to decide on the appropriate treatment plan (Fig. 1). In our practice these include the following; initial diagnosis (1), treatment escalation with either Azathioprine (2) or anti TNF-alpha (3) — as opposed to possible localised surgical resection, and investigation for potential small bowel strictures in any child with confirmed CD (4).

According to these four scenarios, we assessed the indication of performing each individual MRE study in our patient cohort. Of the total 34 studies, the majority (47%) were
performed as an assessment prior to commencing treatment with anti-TNF-alpha agents (Infliximab = 14), as diagnostic studies in 24% and to identify disease complications (18%). Other less common indications included assessment prior to commencing a second-line immunosuppressant (e.g., anti-TNF agent (Adalimumab) or Methotrexate) (Table 1).

3.2. Radiological findings

We analysed our data to highlight and summarise the most important radiological findings in all MRE studies we performed. In addition to small bowel changes, we also analysed changes in the large bowel, documented lymph node enlargement, vascular engorgement and fibro-fatty proliferation.

The most frequently observed finding in the small bowel was abnormal enhancement, which was observed in 17 studies. Twelve of these studies also showed small bowel thickening, two of which had involvement of two separate sites. Terminal ileum thickening alone was noted in eight studies. Strictures were identified in two patients.

Large bowel abnormalities were found in 12 studies (41.3%). Similar to findings in the small bowel, the most common large bowel abnormality was wall thickening (83.3%, 10/12). Three patients had associated "fatty stranding" at different locations within the large bowel mesentery. Abnormal enhancement in the large bowel was noted in only two patients. Enlarged lymph nodes were noted in seven studies, with mesenteric lymph nodes most commonly involved. Vascular engorgement was noted in five, and fibro fatty proliferation in eight patients.

MRE findings are summarised in Table 2 and a selection of representative images illustrated in Fig. 2.

3.3. Benefits and changes in management according to MRE findings

It is important for an invasive, time consuming and expensive procedure to provide the clinician with high quality information, which positively influences the future management of a patient. We therefore analysed MRE findings as to how these investigation impacted on our patient management, i.e. efficacy confirming a diagnosis, or leading to changes in management/treatment.

In all our clinical cases, the results of MRE studies were key to making a clinical decision in the given scenario.

<table>
<thead>
<tr>
<th>Indication</th>
<th>No. of studies</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) Diagnosis</td>
<td>8</td>
<td>23</td>
</tr>
<tr>
<td>(2) Pre-Azathioprine</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>(3) Pre-anti TNF</td>
<td>16</td>
<td>47</td>
</tr>
<tr>
<td>a) Infliximab</td>
<td>13</td>
<td>38</td>
</tr>
<tr>
<td>b) Adalimumab</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>(4) Identify complications</td>
<td>6</td>
<td>18</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Total:</td>
<td>34</td>
<td>100</td>
</tr>
</tbody>
</table>

Importantly, this was regardless of whether MRE findings were positive or negative. Specifically, out of the eight studies performed with an aim to making a diagnosis, seven normal studies allowed exclusion of IBD and children could be discharged. One patient presenting with IBDU was found to have extensive small bowel involvement and hence could be diagnosed with CD.

With regards to specific treatment decisions in patients with an established diagnosis of CD, MRE findings allowed a clear choice of either surgical resection or further medical management (i.e. commencing of Infliximab, Humira, Azathiaprine, Methotrexate).

Of all patients undergoing MRE, six went on to have bowel surgery after review of the studies together with our adult laparoscopic colorectal surgeon. Four children had uncomplicated ileo-caecal resections, one child had a small bowel stricture resected and one child had extended right hemicolectomy. A summary of changes in patient management according to MRE findings is provided in Table 3.

3.4. Practical set up and tolerability of procedure

In addition to the high quality of MRE data obtained and its value in supporting clinical decisions, the feasibility and tolerability of such a procedure is crucially important if it were to become a regular investigation in paediatric patients. While small bowel MRE is frequently used in adults, little has been reported on the practicalities and the tolerability of this procedure in children.

Although we did not formally assess tolerability, the procedure was well tolerated in almost all children. Two children did not tolerate the complete procedure protocol. In one child the study was abandoned due to discomfort from a critical small bowel stricture (positive finding on MRE), the other child was unable to tolerate the procedure in the MRI scanner due to claustrophobia.

Siting of a NJ tube in an awake child can be traumatic and time consuming. The time required for insertion can be minimised by using X-ray screening, however this clearly has a further cost in radiation burden. In order to avoid these disadvantages, we found that placing the NJT by direct vision during upper endoscopy (under GA) the afternoon before the MRE study ensured a quick, safe and easy placement of the tube without further the requirement for
further imaging to confirm tube position. Macroscopic and histological findings of the intestinal mucosa at the time of the MRE study provide valuable contemporaneous information to obtain maximal information on the entire gut at an important clinical timepoint.

4. Discussion

Accurate assessment of small bowel involvement in children with IBD is difficult but often essential in order to make critical clinical decisions such as when and how to escalate treatment.

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Changes in management according to MRE findings.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis</td>
<td>8 Seven normal studies-patients discharged</td>
</tr>
<tr>
<td></td>
<td>One patient with IBDU had no small bowel findings, no changes were made to his management.</td>
</tr>
<tr>
<td>Pre Azathioprine</td>
<td>2 Both patients were commenced on Azathioprine due to pan-enteric disease</td>
</tr>
<tr>
<td>Pre-anti TNF-alpha (Infliximab = 13, Adalimumab 3)</td>
<td>16 Infliximab commenced in 7 patients, 4 patients had an ileo-caecal resection. Adalimumab commenced in three patients. One patient was referred psychological support and continued on current treatment.</td>
</tr>
<tr>
<td>Identify complications</td>
<td>6 Significant structuring disease noted in one study. Remaining 5 studies were normal and current management was continued.</td>
</tr>
<tr>
<td>Other (pre 2nd-line immunosuppressant; Methotrexate)</td>
<td>2 One patient underwent surgery, one patient commenced on methotrexate.</td>
</tr>
</tbody>
</table>
There are now several means of imaging the small bowel, yet many have significant disadvantages for use in children. Hence, guidance to the appropriate use of individual imaging techniques in children with IBD is required.

Limited data is currently available on the evaluation and validation of the various small bowel imaging techniques used in paediatric IBD. However, a recent study performed by Casciani and colleagues compared MR enterography with capsule endoscopy in children with suspected IBD concluding that both methods are accurate and may be used given appropriate indications.13 Gee et al evaluated MR enterography as a primary imaging technique for the assessment of paediatric Crohn’s Disease.14 Comparison of MR to CT imaging as well as considering histological sampling revealed that MR enterography was superior to CT with a 90% sensitivity and 82.6% specificity in detecting small bowel inflammation. Another recent study assessed the accuracy of MR enterography in diagnosing paediatric IBD. Horsthuis and colleagues demonstrated a moderate to good specificity and sensitivity in diagnosing CD.15 Taken together, these studies highlight the fact that MR based small bowel imaging techniques are useful in evaluating small bowel inflammation in children with IBD.

In contrast to MR enterography, MR enteroclysis relies on luminal contrast agent being delivered directly into the duodenum through a NJ tube. Although there are currently no studies documenting the sensitivity and specificity of MR enteroclysis over MR enterography in children, adult studies have confirmed the advantages of the former and its higher sensitivity in detection of small bowel lesions of Crohn’s disease.16 Hence it seems reasonable to be able to apply this technique to children where small bowel involvement occurs frequently.17

Here we report on the application and our experience of MR enteroclysis in paediatric clinical practice of a large tertiary IBD centre. The siting of a trans-endoscopic NJ tube while under general anaesthesia for upper endoscopy and colonoscopy, following bowel prep for colonoscopy, provides maximum detail on pan-enteric disease activity at a single time point. Furthermore, the insertion of both NJ tube and intravenous cannula during an afternoon endoscopy list, with subsequent MR enteroclysis on the following morning, was a system that was well tolerated by children and their families. All children living within an hour of the tertiary IBD centre. The siting of a trans-endoscopic NJ tube while under general anaesthesia for upper endoscopy and colonoscopy, following bowel prep for colonoscopy, provides maximum detail on pan-enteric disease activity at a single time point. Furthermore, the insertion of both NJ tube and intravenous cannula during an afternoon endoscopy list, with subsequent MR enteroclysis on the following morning, was a system that was well tolerated by children and their families. All children living within an hour of the hospital were able to return home after the endoscopy list and return for the MRE the following day. Moreover, placement of NJ tube under direct vision during endoscopy allowed us to avoid any further x-ray studies to confirm correct position.

As stated above, an essential aspect of all small bowel imaging modalities currently available, it to use imaging to answer appropriate questions in a given clinical scenario. By making use of MR enteroclysis at specific time points in our clinical management algorithm, we have been able to maximise the clinical return. At times where treatment escalation may require the longer-term use of potent immunosuppressants, accurate localisation of disease is crucial to appropriate and effective surgical intervention. Well-timed, localised, small bowel or ileo-caecal resection with primary anastomosis can provide many years of relapse-free remission (and catch up growth), without the need for such early exposure to the risks of immunosuppressant use.18

As a retrospective review of our practice, we found that 31/34 studies were carried out in four specific clinical scenarios, not surprisingly at times when it was important to know whether small bowel disease was localised enough to allow surgery. Each study, whether it was positive or negative, therefore impacted directly on the subsequent clinical decision, with surgical intervention in each of our 6 cases leading to a prolonged, immunosuppressant-free period of remission.

In summary, we report the simple, well-tolerated and successful use of MR enteroclysis in children with IBD. By defining specific clinical scenarios at which such detailed information is most useful, we were able to perform MR enteroclysis within 24 h of full endoscopic evaluation. Not only did this allow the siting of an NJ tube under direct vision at endoscopy, but also provided the best possible pan-enteric assessment of disease at a crucial clinical decision point. Such accurate information then allows critical clinical decisions to be made with the greatest of confidence.

Conflict of interest

On behalf of all authors I state that this manuscript has not been published previously and is currently not under consideration elsewhere for publication. The authors declare there is no conflict of interest and all authors have contributed to this study in either of the following aspects: (1) the conception and design of the study, or acquisition of data, or analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, and (3) final approval of the version to be submitted.

Acknowledgements

Authors have contributed to this study in either of the following aspects:

1) Conception and design of the study, or acquisition of data, or analysis and interpretation of data: Sanka, S; Gomez, A; Set, P; Rimareva, N; Davies, J; Rolfe, P; Noble-Jamieson, G; Torrente, F; Heuschkel, R; and Zilbauer, M.
2) Drafting the article or revising it critically for important intellectual content, (3) final approval of the version to be submitted: Sanka, S; Gomez, A; Heuschkel, R; and Zilbauer, M.

References

5. Bremner AR, Pidgeon J, Fairhurst J, Beattie RM. Ultrasound scanning may reduce the need for barium radiology in the


