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Infliximab in the Home – Does it Affect the Health-Related Quality of Life of Pediatric Patients with Inflammatory Bowel Disease?

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Objectives

Inflammatory bowel disease is characterized by an unpredictable course of relapsing and remitting symptoms often treated with infliximab. Historically infliximab was administered in the hospital setting or infusion centers. However, recently some providers have prescribed infliximab via home infusions. The goal of this study was to compare health-related quality of life in pediatric patients receiving infliximab in the home compared to those receiving infliximab in our hospital infusion center.

Methods

Inclusion criteria included English-speaking patients ages 9-17 years with a confirmed diagnosis of inflammatory bowel disease who were adherent with infliximab infusions. At subsequent visits, subjects (home infusions) and controls (hospital infusions) completed the IMPACT III, a self-administered health-related quality of life questionnaire.

Results

38 patients (18 subjects, 20 controls) were included. Of the participants, 33 had Crohn's, 3 had ulcerative colitis and 2 had indeterminate colitis. The mean age at diagnosis was 11.5 years. Across the 6 domains assessed by the IMPACT III, there were no significant differences in health-related quality of life between subjects and controls.

Conclusions

While home infusions allow patients to receive therapy in comfortable settings at convenient times, location of infusions did not affect health-related quality of life scores. Despite this, home infusions are a convenient alternative to hospital-based infusions that should be considered in the patient requiring long-term therapy with infliximab. Measuring health-related quality of life in pediatric patients with inflammatory bowel disease may allow clinicians to identify additional needs and provide supplementary resources to improve their overall well-being.

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INTRODUCTION

Inflammatory bowel disease (IBD) is a constellation of chronic, inflammatory diseases of the gastrointestinal (GI) tract that is characterized for many individuals by an unpredictable course of relapsing and remitting symptoms.[1] Given that IBD in children is commonly more aggressive than in adults, pediatric patients often require therapy with biologics such as infliximab. Infliximab is a chimeric mouse/human IgG1 monoclonal antibody that binds selectively and with great affinity to cell-bound and circulating tumor necrosis factor-alpha (TNF-alpha) which thereby acts to reduce the inflammatory effects of TNF-alpha in patients with IBD.[2]

Historically, infliximab has been administered in hospital or clinic-based infusion centers. Pressure to reduce length of inpatient stay and to provide cost-conscious care in the 1980s prompted the development of alternative sites for the administration of various types of infusion therapy. Among these alternatives were companies providing home infusion services for therapies with the administration of total parenteral nutrition (TPN), antibiotics and anti-neoplastic agents.[3] According to the National Home Infusion Association, over 80,000 patients receive home infusions each year for various indications. It is currently estimated that the alternate-site infusion therapy sector represents approximately $9 - 11 billion dollars a year in U.S. health care expenditures with infusions serviced by over 1,500 infusion pharmacies.[4] Despite the convenience and other potential benefits of home infusions, many providers are unwilling to consider this option for fear of safety or compliance issues.

Demand for home administration of other therapies such as biologics has increased over time.[3] Home infusions have allowed patients and families to avoid frequent visits to hospital or clinic-based infusion centers. Buisson et al. found that 137 adult IBD patients receiving infliximab spent a median of 6.5 hours outside their home for each infusion including transportation to and from the hospital and time for medication administration.

A large number of patients with IBD in our practice receive infliximab infusions through our home infusion program which was established several years ago. Little has been published on home infusions in the treatment IBD in the pediatric population. In 2004 Condino et al. conducted a retrospective chart review of 10 patients who received home infusions over the course of two years.[5] A total of 59 home infusions were administered with a dosing range of 7.5 to 10mg/kg/dose. The calculated average savings per patient by having the infusion in the home was $1335 per vial (100mg) of infliximab and school absenteeism was decreased. Their conclusion was that home infusions are safe, cost-effective and preferred by patients and families. Limitations of this study included the small sample size and lack of a control group with whom to compare various factors including drug cost, safety, patient satisfaction and school absenteeism.[5]

Quality of life is a term that describes an overall sense of well-being. Health-related quality of life (HRQOL) is a subset of quality of life that has evolved since the 1980s and has gained acceptance as a measureable outcome.[6] It is defined as one's subjective perception of the effect of a chronic disease on his or her physical, psychological and social well-being.[7] It is also defined as a measurement of the impact of a chronic disease by incorporating not only physical well-being but also the mental state, amount of social support, effect of treatment and presence of complications.[8] HRQOL therefore provides a more global assessment of health and can be used to determine additional patient needs and support.[8]

The present study compared the experiences between patients receiving infusions at home versus those receiving therapy in our hospital infusion center. The primary objective was to evaluate the HRQOL between the groups.

Materials and Methods

This study was approved by the Weill Cornell Medical College Institutional Review Board. With regard to ethical considerations, we ensured the quality and integrity of our research by obtaining informed consent and assent, respecting the confidentiality of our subjects and ensuring subjects participated voluntarily.

The IMPACT is a self-administered, disease-specific HRQOL questionnaire designed specifically for children and adolescents with IBD.[8] The original IMPACT was developed in 1999 by Griffiths et al. and the IMPACT III was adapted from the IMPACT II in 2002. The original language for the questionnaire was English however it has now become available in several other languages after going through a process of linguistic validation. The questionnaire is a valid and reliable reflection of HRQOL in children with IBD ages 9-17 years and is designed for a recall period of

2 weeks. The questions cover six domains including bowel symptoms, systemic symptoms, emotional functioning, social functioning, body image and treatment/interventions. The questionnaire is comprised of 35 questions with five Likert style responses per question each of which are assigned a score from 1 to 5. The responses from all 35 questions are summed to generate a total score with higher scores correlating with better quality of life. Individual domain scores can also be determined by summing the responses for questions based on their assigned domains.

We obtained written permission to use the IMPACT III questionnaire from the original authors. At a subsequent office visit, the IMPACT III questionnaire was completed by subjects and controls after obtaining consent and assent to participate. Inclusion criteria for the study included English-speaking patients between the ages of 9 and 17 years with a confirmed diagnosis of IBD who were receiving infusions of infliximab either at home (subject group) or in our hospital infusion center (control group). Patients also had to have demonstrated adherence with infusions and parents and patients had to provide consent and assent, respectively, to participate. All patients were receiving maintenance infliximab; none were in the induction phase. Exclusion criteria included patients with IBD outside of the desired age range or patients with poor adherence with infusions. Patients with ostomies or other significant concomitant illnesses were also excluded as the validity for the IMPACT-III has not yet been established in these populations.

Ethical Considerations

The study involved minimal risk to the participants. Subjects and controls were enrolled only after understanding the nature of the study (which involved completing a questionnaire), and only after providing informed consent/assent to participate.

Statistics

Study data were collected and managed using the REDCap (Research Electronic Data Capture) electronic data capture tool hosted at Weill Cornell Medical College.[9] REDCap is a secure, web-based application designed to support data capture for research studies, providing 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources. REDCap is supported by the Clinical and Translational Science Center Grant UL1 TR000457. SAS 9.3 (SAS Institute, Inc, Cary, NC) was used for statistical analysis.

Due the non-normal distribution of quality of life scores on the IMPACT III questionnaire, a non-parametric test – the Wilcoxon Rank Sum test – was used to assess the differences between subject and control groups. A two-sided alpha level of 0.05 was used as a cut-off to declare statistical significance. The criterion for statistical significance was defined as a P value of <0.05.

Results

Review of the electronic medical record revealed 41 patients who met criteria for the study. Three were eliminated due to either patient or parent preference. Of the 38 patients enrolled, 33 had CD, 3 had UC and 2 had indeterminate colitis. The mean age at diagnosis was 11.5 years (range, 9 to 17 years). There were 18 subjects and 20 controls. Baseline characteristics of study participants are summarized in Table 1.

All 38 patients completed the IMPACT III self-administered questionnaire. The highest possible score for the 35 questions was 175 as each question had a maximum score of 5 points. The median total score for the subject group was 145.5 (minimum 84, maximum 164) versus 151.5 (minimum 103, maximum 167) for the control group (p=0.49). The p values were not significant for subject versus control group median values among the six individual domains suggesting that there was no significant difference in the HRQOL among domains between the groups (Table 2).

DISCUSSION

At the time this was written, we were treating 38 patients with home infusions and 37 patients with hospital-based infusions (with 5 hospital-based patients planning to switch to home infusions per family preference). We utilize several home health care companies that provide the nursing care, supplies and medications necessary for home infusions. "Home" infusions may take place at home, work, camp, or in the university setting (either dorm or campus health clinic) for our college aged patients. Our protocols for home and hospital administration of infliximab are identical in terms of

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the routine blood work drawn prior to infusions, the rate of the infusions and the use of diphenhydramine as a pre-medication to decrease the likelihood of infusion-related reactions. Nurses are present for the duration of home infusions and therapies for resuscitation or anaphylaxis including intravenous fluids and intramuscular epinephrine are readily available as is the case in the hospital infusion center.

Our results showed no significant difference in HRQOL between patients receiving infliximab infusions at home versus in the hospital infusion center. Initially this was surprising as patients and families often relay how appreciative they are to receive infusions in the home. Home infusions enable them to avoid missing school, remain in their extracurricular activities, and reduce travel time to the infusion center. Many patients also relay that receiving infusions in the comfort of their homes reduces patient anxiety of coming to the hospital and being around other patients who may be ill. Parental missed days of work may also be avoided as the scheduled home infusions often occur in the evenings or during weekends. Our results however suggest that despite these factors related to the convenience and comfort of having infusions in the home environment, patients' perceptions of their overall functionality across the six domains do not differ from those of patients who receive hospital infusions. In other words, providing flexibility and an element of convenience with regard to location of infusions did not impact HRQOL in our patients. One reason for this could be that the location of infusions does not mitigate the burden of disease or eradicate the unpredictable and isolating nature of IBD which is likely present among both groups regardless of infusion location. Younger patients may not appreciate the benefits of avoiding school and work absences and avoiding the inconvenience of traveling to the hospital and exposure to other sick individuals that they avoid by having infusions in the home.

The ability to measure HRQOL broadens the traditional markers of health status in IBD and allows the clinician to appreciate how patients function on a day to day basis and to understand how they cope with having a chronic disease.[10] Many measures of HRQOL exist mainly in the form of relatively short questionnaires and when possible, self-report is preferred over parent-proxy report.[7] Increased disease activity has been shown to correlate with poor HRQOL,

Table 1. Patient Demographics

	Subjects (Home infusions)	Controls (Hospital infusions)
N	18	20
Type of IBD		
CD	18	15
UC	0	3
IC	0	2
Mean Age at Diagnosis (Years)	12	11
Ethnicity		
Caucasian	16	19
Hispanic	2	1
Disease Location		
Small Bowel	1	1
Large Bowel	3	10
Both	14	9
History of Surgery	5	2
Fistulizing Disease	4	0

poor functioning across psychosocial and physical health domains, and the use of less adaptive coping strategies.[7] The Pediatric Crohn's Disease Activity Index (PCDAI) and Pediatric Ulcerative Colitis Activity Index (PUCAI) are used to track disease activity over time by incorporating symptoms, physical exam findings and laboratory values into an overall score; however, while measuring functionality and activity, these indices do not specifically address quality of life or emotional well-being. A disease activity index score correlating to remission is less meaningful if a patient is suffering from poor HRQOL as manifested through subclinical depression or poor functionality across various life domains. Given this, measuring HRQOL allows the clinician to delve deeper beyond disease activity indices and laboratory values in order to hone in on patients' emotional well-being.[6] Without screening for HRQOL clinicians may overlook a subgroup of patients with subtle needs and may miss critical opportunities to offer resources or referrals for additional psychological, educational or social services.[1]

There are important limitations to consider for this study which may affect the validity or generalizability of the findings. The first limitation is the small sample size. One factor that contributed to this was the exclusion of patients outside the age range of 9-17. Elimination of patients based on age was done because the IMPACT III is valid only for the specific age range of 9-17 years. In the future another measure of HRQOL such as the IBD Questionnaire (IBDQ), a valid and reliable self-administered tool to assess health-related quality of life in the older population, could be employed so that the older patients could be included.[11] Additionally, subjects and controls were asked to complete the IMPACT III only once during the study. Although the IMPACT III has been shown to be a valid and reliable self-assessment tool, there was likely an element of recall bias given that patients were asked to recall their symptoms and subjective feelings over the prior 2 week period. It would be more valuable to implement the IMPACT III at more frequent time intervals to see whether HRQOL changes over time and is correlated with disease remission or flares.

Ryan et al. examined the clinical utility of youth and parent proxy-reported HRQOL screening in pediatric patients with IBD. They found that HRQOL was correlated with health care utilization such that over one year, lower HRQOL at baseline was associated with more IBD-related admissions, psychology clinic visits, emergency department visits, referrals for pain management, and telephone encounters to the clinician.[1] These trends are consistent with findings in the adult chronic illness literature.[1] While poor HRQOL is associated with increased use of health care resources, improvement of patients' functional and health status has been shown to reduce health care costs over time.[1] If assessing HRQOL with a relatively short, self-administered questionnaire at the time of routine visits

Table 2. IMPACT III Results

	Subjects (Home Infusions)	Controls (Hospital Infusions)	*P* value
Total Score	145.5	151.5	0.49
Bowel Symptoms Score	29.5	31	0.17
Systemic Symptoms Score	13	14	0.13
Emotional Functioning Score	27	29	0.61
Social Functioning Score	54	54	0.60
Body Image Score	12.5	13	0.19
Treatment/Interventions Score	11.5	12.5	0.57

can identify patients who are prone to utilize more healthcare services, this would be a valuable tool for clinicians to use to regularly monitor such patients so that they can intervene and potentially provide preventative services in a timely manner.

In summary, while home infusions allow patients to receive therapy in comfortable settings at convenient times, location of infusions did not affect HRQOL scores. Despite this, home infusions are a convenient alternative to hospital-based infusions that should be considered as an option in the patient requiring long-term therapy with infliximab. Additionally, incorporating measures of HRQOL into clinical visits for patients with IBD may allow clinicians to identify additional needs and provide supplementary resources and support to improve the functional and health status of these patients. ■

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