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IMPACT OF IMMUNOMODULATOR AND BIOLOGIC MEDICAL THERAPIES ON NEED FOR INTESTINAL RESECTION SURGERY IN CHILDREN WITH CROHN'S DISEASE

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INTRODUCTION

Crohn's disease, one of the types of inflammatory bowel diseases (IBD), is a chronic immune-mediated disease resulting from an inappropriate inflammatory response to an environmental stimulus in a genetically susceptible host. Current treatment for IBD frequently involves the use of immunosuppressant medications: corticosteroids, immunomodulators (azathioprine, 6-mercaptopurine, and methotrexate) and anti-tumor necrosis factor alpha biologics (infliximab and adalimumab). These medical therapies effectively treat and prevent flare-ups, but also have severe side effects. Due to the nature of this chronic disease, the general management principle tends to be surgical sparing in order to preserve as much intact bowel for as long as possible. Treatment for inflammatory bowel disease has recently changed to include the use of immunomodulators (early 1990s) and biologics (mid 2000s) to induce remission, yet, the effect of their early initiation on pediatrics' Crohn's disease course is unknown (1). The objective of this study is to evaluate the impact of early introduction of immunomodulators and biologics on surgical resection incidence in children with Crohn's disease and evaluate temporal trends in medical management from 1983 to 2012.

METHODS

In this single-center retrospective comparative study, the medical charts of patients at the Alberta Children's Hospital diagnosed with Crohn's disease from January 1, 1983 to January 1, 2012 and followed for a minimum of 1 year were reviewed.

RESULTS

There were 122 patients enrolled for a total of 380.4 person-years. From 1983 to 2012, patients with early immunomodulators use increased from 0.0% to 61.5% while maintaining stable 1 and 3 year intestinal resection incidence. Patients (n=53) with a minimum of 3 years follow up and early immunomodulators or biologics use had increased intestinal surgery incidence (100.0% vs 37.2%, P=0.0002) and increased intestinal resection incidence (60.0% vs 27.9%, P=0.03).

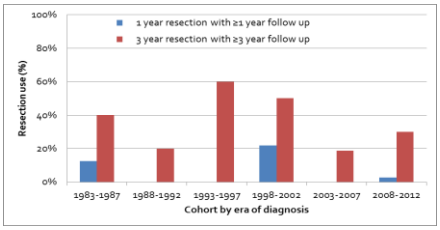

Figure 1. Intestinal resection use of cohort diagnosed with Crohn's disease during 1983 to 2012 with minimum 1 year and 3 year follow up. Change in percentage of cohorts with intestinal resection within 1 or 3 years from diagnosis shown over time. Cohort sample size ranged from 5 to 39 patients.

DISCUSSION AND CONCLUSIONS

Immunomodulators and biologics are now initiated more frequently and earlier in treating Crohn's disease. Intestinal surgery and resection incidence of children with Crohn's disease has remained stable for the last 30 years. However, intestinal surgery and resection incidence has increased in the subgroup of pediatric patients with early immunomodulators and biologics use. The debate between top-down or step up medical therapy hinges on the complex interrelationship between medication safety profile and preventing irreversible bowel damage (1). This study suggests that the traditional step-up approach is slowly being replaced in favour of the more aggressive top-down strategy. Short term surgical incidence was independent of medical therapy, indicating that the outcomes in the first year following diagnosis are difficult to control. However, this may be attributed to the fact that even though there is an increase in early initiation of immunomodulators or biologics, these two therapies have a delayed effect and are slow to begin mucosal healing. This is very important in decreasing surgical incidence rates as surgical indications, such as obstructions and perforations, are caused by unhealed mucosa. Further evidence to clarify the role of early immunomodulator and biologics intervention on disease course may help clinicians provide realistic medical management expectations for patients and their families.

REFERENCES

1. Hovde Ø, Moum B.World J Gastroenterol. 18(15): 1723-31, 2012.