Biologic agents in the management of inflammatory bowel disease: is it worth it?

Tommy Choy (Meds 2015), Jessica Jackson (Meds 2015)
Faculty Reviewer: Dr. John Howard, MD, FRCPC (Department of Medicine and Paediatrics)

INTRODUCTION

Inflammatory Bowel Disease (IBD) represents a group of disorders that affects the gastrointestinal (GI) tract. In this disease, an abnormal immune response in the body causes inflammation and ulceration of the GI tract. The two main forms of IBD include Crohn’s disease (CD) and ulcerative colitis (UC), which differ in their presentation and treatment.1 Crohn’s disease can affect any part of the GI tract, and the entire thickness of the intestinal wall is generally involved. Ulcerative colitis, on the other hand, is limited to the rectum and colon and the exterior layers of the intestinal wall are generally not affected. IBD is a lifelong disease that has a substantial impact on the quality of life of patients and has a tremendous impact on a patient’s wellbeing. There are currently no cures available for IBD and treatment is aimed towards keeping the patient symptom-free.1

IBD is most commonly found in the developed world, although cases have begun appearing more frequently in developing countries.2 Globally, Canada and Sweden have the highest incidence of both CD and UC.3 It is estimated that more than 5000 cases of CD and 4000 cases of UC are diagnosed in Canada each year, with a total of more than 200,000 Canadians living with one of these diseases at any given time.

The heavy burden that IBD imposes on patients in turn leads to substantial financial costs for the Canadian healthcare system. Due to the nature of IBD, these costs include both direct costs associated with treating the disease and indirect costs such as lost productivity and time missed from work. In a 2008 report by the Crohn’s and Colitis Foundation of Canada, it was found that the indirect cost associated with IBD is approximately $1 billion dollars annually, with CD comprising roughly $600 million of that value due to its higher prevalence.3 Direct medical costs for IBD in Canada are estimated at over 750 million, with CD accounting for two-thirds of that value.3 Although these costs will continue to increase as the prevalence of IBD grows, the distribution of the direct medical costs have recently undergone significant changes due to the introduction of new treatment options. The remainder of this article will address these specific changes.

TREATMENT – PRE BIOLOGIC ERA

Prior to the introduction of biologics, the major categories of medication prescribed for the treatment of IBD included aminosalicylates, corticosteroids and immunomodulators.4 In the event of failed medical therapy, surgery was also considered. Resections were ideally conservative and only undertaken for symptomatic patients.5

In both CD and UC, roughly one-third of total costs are concentrated in the most severe patients (2% of all patients), who are often resistant to traditional drug therapy.6 Medication costs are relatively inexpensive when compared to the surgical interventions and related hospitalizations required by these patients. In fact, surgical interventions account for the greatest portion of the cost of IBD.8 Parenteral nutrition is another costly intervention, which was reported to be responsible for majority of overall pharmacy costs, despite infrequent use.5 Pharmaceuticals used to represent less than 10% of overall health care cost related to the treatment of IBD, but this value has increased in the post-biologic era.5

COST EFFECTIVENESS OF BIOLOGIC AGENTS

Overall, most studies done to investigate the cost effectiveness of biologic treatment of IBD have demonstrated a decrease in necessary hospitalizations and surgical interventions. One study done at the University of Chicago demonstrated a decrease in all surgeries by close to 40%, emergency room visits by over 60% and decrease in hospitalization by over 50%.6 Another study in Spain reported that the cost of hospitalization was reduced from 60 percent down to 6% of total annual health expenditures for the treatment of IBD.10 Despite these positive outcomes, these studies also indicated that the overall cost of IBD management actually increased as a result of biologics usage. That being said, a more costly intervention can still be cost effective as long as there is a sufficient increase in health outcome. For example, the National Institute
for Health and Clinical Excellence (NICE) suggests that an incremental cost-utility ratio of 20,000 to 30,000 pounds (roughly $32000 to $48000 CAN dollars) per quality adjusted life year (QALY) gained can be considered cost effective.11

Early studies reported induction therapies of infliximab for acute attacks to be greatly cost effective according to the above NICE guideline, however, these were all short-term one year studies.12 This short time frame likely led to an overestimate of the cost-effectiveness ratio due to the chronic nature of IBD. Indeed, subsequent studies where the study time horizon was expanded to 5 years revealed that the use of biologic agents in acute attacks approached cost effectiveness. Lindsay et al. reported that Infliximab was cost effective for both luminal and fistulising forms of CD, however, body weight was an important factor affecting cost effectiveness.13 An evidence review group in the United Kingdom reviewed the use of infliximab in exacerbations of UC and found an incremental cost-utility ratio of roughly $32,000 US dollars, with the results being sensitive to the patients’ colectomy rates.14 A systematic review on the use of infliximab in CD was done by the National Institute for Health Research and it reported that infliximab was cost-effective for episodic treatment of active CD.11

Contrary to the evidence found in induction therapies, studies have reported poor results for the use of biologics in lifelong maintenance therapies. French authors reported that the incremental cost per QALY for infliximab in lifetime maintenance therapy of CD was more than 10 times that of the ratio for induction therapy.15 Similarly, Bogder et al. found continuous therapy of infliximab to only be economically feasible for up to 4 years.16 Evidence for models with a shorter time horizon has also been mixed. “The Crohn’s Trial of the Fully Human Antibody Adalimumab for Remission Maintenance trial” data reported that for a 5 year horizon, maintenance of adalimumab will result in an incremental ratio of less than $48,000 per QALY in CD.17 The Active Colitis Treatment trials18 also reported similar findings for the use of infliximab in UC patients.18 On the other hand, Kaplan et al. from the United States have found an incremental ratio of $332,000 per QALY for infliximab use in CD19, and a systematic review done by the Canadian Agency for Drugs and Technologies in Health reported an incremental ratio of over $200,000 for both infliximab and adalimumab in CD and $350,000 for using infliximab in UC.20

Part of the reason for the heterogeneity of results can be attributed to differences in the cost of administering the agents between countries. Although the cost for 100mg of infliximab is fairly stable at a price range of ($700-900 US dollars), patients in the United States, but not the UK must pay a substantial fee for the services of an infusion center.6 Greater cost containments in both drug and administration costs will likely be needed to ensure cost effective care. Another significant caveat of these studies is the fact that indirect costs were not accounted for in their cost effectiveness models. This is likely to cause a gross overestimation of the cost effectiveness ratios for biologic agents.6 Lastly, it should be noted that meta analyses were not performed as a result of significant heterogeneity between studies, so a definitive answer on the matter is unavailable.11,20

CONCLUSION

Biologic agents have been shown to provide clinical benefit in patients with moderate to severe attacks of CD and UC. In turn, the increasing use of these agents in treatment of IBD has raised concerns about whether or not these drugs are a cost-effective use of health care resources. Current evidence suggests that biologic agents are likely to be cost effective when used to treat moderate to severe acute attacks of CD and UC. Evidence for its use in maintenance therapy is inconclusive and more research in this area is recommended.

REFERENCES


