Management of Crohn’s Disease: Early and Aggressive Treatment
Using Biologics and Immunomodulators

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Abstract
Crohn’s Disease (CD) is an incurable type of inflammatory bowel disease (IBD), in which the intestines are chronically inflamed, causing intestinal and extra-intestinal symptoms. CD patients experience a cycle of remission and relapse of symptoms as the disease progresses to serious complications, including small bowel obstructions, malnutrition, and decreased quality of life. Since CD is incurable, medical management is the mainstay to treat and maintain remission. Traditional treatment relies on anti-inflammatories. New management strategies focus on early and aggressive therapy with immunomodulators and biologics to reduce the rate of mucosal and intestinal damage early in the disease course.

Background
The cause of CD is currently unknown, but new research suggests that chronic inflammation is due to reduced microbial diversity in the gut microbiome. Another theory postulates that leaky epithelial junctions in the gut cause an increased interaction between bacteria and gut mucosal surfaces, resulting in inflammation. IBD treatment historically consisted of the bottom-up approach: step by step process starting with 5-aminosalicylic acid and taking antibiotics for infections, progressing to corticosteroids for flares, and eventually, utilizing more aggressive therapies such as immunomodulators and biologics. Recent studies show that following a more personalized treatment plan based on a patient’s level of mucosal damage and symptoms, results in better control over remission and flares. A new management strategy, the top-bottom approach, focuses on early and aggressive therapy with biologics and immunomodulators to reduce the rate of mucosal and intestinal damage.

Treatment Options
The SONIC clinical trial demonstrated that early use of dual therapy with infliximab and azathioprine yielded deep remission healing in 65% of patients by week 26 of treatment, compared to 25% of patients on infliximab monotherapy and 10% of patients on azathioprine monotherapy. Dual therapy with infliximab and azathioprine or infliximab monotherapy when compared to azathioprine monotherapy, was found to be a superior treatment in maintaining a corticosteroid-free remission. Dual therapy of immunomodulators and anti-TNFs, most commonly azathioprine and infliximab, is quickly becoming accepted as the optimal medication therapy for CD. With dual therapy early in the disease course, patients have achieved deep remission quicker than when compared to less aggressive therapies, such as immunomodulator monotherapy or 5-ASA use. Furthermore, carefully optimized therapeutic levels of anti-TNF agents correlate with higher levels of clinical and endoscopic remission.

5-aminosalicylic acid (mesalamines) • Anti-inflammatories • Should not be considered first line maintenance treatment for CD, per ACG.
Corticosteroids (prednisone, soludemol, budesonide) • Indicated to treat flares and induce remission • Not used for maintenance
Immunomodulators (6-mercaptopurine, azathioprine, methotrexate) • Suppress immune system to reduce overall inflammation • Indicated for maintenance, but it can take up to several months to be effective • Ability to extend how long anti-TNF agents are therapeutically beneficial before needing to take a drug holiday or increase dose
Biologics/anti-TNF agents (infliximab) • Immunosuppressant, considered the most aggressive maintenance option • Most effective maintenance medication with prolonged therapeutic benefit when started early in disease course.

Discussion
CD is a progressive, chronic inflammatory disease that has placed a burden on patients and health professionals alike. The traditional bottom-up approach to treatment has been less than adequate thus far in the management of CD. The majority of patients will undergo surgery at some point in the disease process and have to endure years of remission and relapse. Medical providers need to consider using early aggressive therapy in the management of CD patients to give them a fighting chance by attacking the inflammation early in the disease development, and ideally preventing organ and intestinal damage. Data and case studies have shown medical and financial benefits to starting with biologics and immunomodulators rather than starting with mesalamines and corticosteroids. Clinical trials have shown promising outcomes from early use of immunomodulators and biologics include decreasing numbers of hospitalizations, complications, and surgery. The next step in improving the management of CD patients is to have medical providers utilize the top-down treatment approach in clinic. While there is no cure for CD yet, medical providers owe it to their patients to provide the most up-to-date care which is rapidly changing from bottom-up to top-down treatment.

REFERENCES