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ELDER CARE

A Resource for Interprofessional Providers

Anti-TNF Agents for Inflammatory Bowel Disease in Older Adults

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Between 10-30% of patients with inflammatory bowel disease (IBD), comprised of Crohn's disease (CD) and ulcerative colitis (UC), are at least 60 years old, and 10-15% of patients with IBD are first diagnosed in older age groups. The rate of IBD is growing worldwide with an increasing number of older adults affected by IBD.

IBD in older adults has unique characteristics. While younger patients with IBD tend to have progression of their disease over time, IBD in older adults is fairly stable, with inflammation that does not progress as it does in younger individuals. This results in less aggressive disease, fewer strictures, and fewer bowel perforations.

Despite this, older patients make up a disproportionate number of IBD-related hospitalizations and have the same rate of surgery as their younger counterparts. The reasons for this are not clear, but may be due to clinicians being hesitant to use more aggressive immunosuppression in older adults. Or, perhaps many older adults have decreased functional status and end up in the hospital when unable to care for themselves with symptoms that a younger and more functional individual could manage at home.

Steroid Therapy - Overused in Older Adults?

Use of long-term corticosteroid therapy, typically given for moderate-to-severe disease, is disproportionately high as a treatment for IBD in older adults, despite its known adverse effects. Adverse effects of particular importance to older adults include osteoporosis, impaired glucose tolerance, mental status changes, cataracts, and an increased risk of infections.

The disproportionately high rate of steroid use in older adults suggests that other treatments, particularly the new so-called biologics (Table), which can induce and maintain remission in IBD, are likely underused in older adults.

The biologics discussed in this issue of *Elder Care* are immunosuppressive drugs that inhibit the action of tumor

necrosis factor (TNF), a cytokine that induces inflammation. Anti-TNF agents are the biologics with which we have the most experience in treating IBD in older adults. Newer biologics with which we have less experience include vedolizumab and ustekinumab, inhibitors of inflammatory pathways that involve integrin and interleukins.

All of these drugs are alternatives to steroids that have the potential to limit steroid use while reducing intestinal inflammation. The results may be a lower rate of disease complications and improved quality of life.

Effectiveness in Older Adults

When used in younger patients with IBD, anti-TNF agents increase steroid-free remission periods, decrease hospitalizations, delay or prevent surgery, and improve quality of life. However, only a few small observational studies have specifically evaluated their use in older adults. One study involving 95 patients over 65 years old found that biologics induced remission at similar rates in both younger and older individuals. Another study also found similar rates of improvement, based on endoscopic examination, in older vs younger individuals. But, a third study found that patients over 60 years had a lower response rate than younger individuals (61% vs 83%), and they were 3 times more likely to stop therapy.

Safety in Older Adults

Infections Information on safety of anti-TNF agents in older adults is drawn partly from experience treating patients for IBD, but more from patients treated with these drugs for rheumatologic disorders. All of these studies show an increased risk of infection in older adults.

The infections that occur in older adults may also be more serious, such as sepsis. One study found that the rates of severe infection with anti-TNF agents are four-fold higher (12% vs. 3%) and infection-related deaths are increased by a factor of ten (11% vs. 1%).

TIPS FOR MANAGEMENT OF INFLAMMATORY BOWEL DISEASE (IBD) IN OLDER ADULTS

- Although many clinicians think of IBD as a condition that occurs in younger adults, don't forget that 10-15% of patients newly diagnosed with IBD are over 60 years of age.
- While steroids are widely used for acute disease control in IBD, their side effects from long-term use can cause problems, especially for older adults. Consider biologics as an alternative therapy.
- Test patients for latent tuberculosis before starting therapy with biologics.
- When following patients who are taking biologics for IBD, be alert for adverse effects including infections and psoriasis-like skin disorders. There is also concern that biologics might increase the risk of cancer, particularly melanoma.

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Other studies of anti-TNF agents have shown a 5-10% rate of infections requiring hospitalization. It is important to note, however, that the risk of infection is even higher among patients receiving steroids as a treatment for IBD. Preliminary studies with ustekinumab and particularly vedolizumab have shown that the infection risk with these drugs may be lower than with anti-TNF agents.

The infection risk includes activation of latent tuberculosis, hepatitis B, and certain endemic fungal infections. Patients being considered for therapy with biologics should be tested for these conditions prior to treatment.

Malignancy There has been concern that, because of their immunosuppressive effects, biologics might increase the risk of cancer. However, studies have only shown a slight association with an increased cancer risk – and only with non-melanoma skin cancer, non-Hodgkin’s lymphoma, and possibly melanoma. (Patients taking biologics should use sunscreen and undergo interval dermatological exams.)

Furthermore, a large prospective study recently completed in North America found no increased risk of cancer in patients exposed to anti-TNF agents versus other immunosuppressants for IBD, such as azathioprine and 6-mercaptopurine. In addition, studies in the rheumatology literature indicate that patients with a history of malignancy while on these drugs do not have increased risk of cancer

when they are restarted. Of note, all of these studies examined only short-term outcomes, so the long-term cancer risk remains unknown.

Other Adverse Events Anti-TNF agents have been associated with psoriasis, psoriasis-like rash, and injection site reactions. They can also worsen heart failure and are contraindicated in moderate-to-severe heart failure (New York Heart Association class III or IV).

They can also cause hypersensitivity reactions, especially when discontinued and then restarted. Rarely, biologics have been associated with demyelinating disease.

Information on the aforementioned adverse effects is drawn primarily from studies involving younger individuals. There are no specific data based on studies in older adults.

Final Comment

The burden of IBD in older adults is significant and patients often require immunosuppression with biologics to manage their disease. Limited studies suggest that anti-TNF agents are effective for treating IBD in older adults, and they allow less use of steroids, but at the cost of a possible increased risk of infection and malignancy. Data on effectiveness and safety drawn specifically from studies in older adults are limited, however, and more studies are necessary to better define the role of biologics for treating IBD in older adults.

Table 1. Biologic Agents for Treating Crohn’s Disease (CD) and Ulcerative Colitis (UC)

Anti-TNF Agents	CD	UC	Contraindications	Adverse Events
Adalimumab (Humira) *	x	x	<ul style="list-style-type: none"> Heart failure (New York Heart Association Class III/IV) No live-virus vaccines should be given while taking these drugs 	<ul style="list-style-type: none"> Cytopenias Demyelinating disease Hypersensitivity Increased rate of infection and melanoma Injection site reaction Psoriasis
Certolizumab pegol (Cimzia) *	x			
Golimumab (Simponi) *		x		
Infliximab (Remicade) **	x	x		
Integrin/Interleukin Inhibitors				
Ustekinumab (Stelara) ** first dose, then *	x		<ul style="list-style-type: none"> No live-virus vaccines should be given while taking these drugs 	Increased rate of infection, liver injury, arthralgia
Vedolizumab (Entyvio) **	x	x		Increased rate of infection and non-melanoma skin cancer
*Given subcutaneously at home **Given intravenously by health care professional ***Given subcutaneously by health care professional				

References and Resources

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