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RESEARCH ARTICLE

ANTI-INTEGRIN THERAPY IN INFLAMMATORY BOWEL DISEASE: ACOMPREHENSIVE REVIEW

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ABSTRACT

Inflammatory bowel disease (IBD), which includes Crohn's disease and ulcerative colitis, is a chronic immune-mediated disorder of the gastrointestinal tract characterized by episodes of inflammation and ongoing tissue damage. Standard medical treatments, such as corticosteroids, immunomodulators, and tumor necrosis factor (TNF) inhibitors, have improved patient outcomes but are limited by incomplete responses, systemic immunosuppression, and side effects. Anti-integrin therapies offer a targeted method that specifically blocks leukocyte movement into the intestinal mucosa. Integrins are cell adhesion molecules that facilitate immune cell migration and tissue infiltration. By blocking the interaction between leukocyte integrins and endothelial cell adhesion molecules, anti-integrin agents prevent inflammatory cells from entering the gastrointestinal tract. Currently approved anti-integrin drugs for IBD include natalizumab and vedolizumab, with newer options like etrolizumab under research. These medications demonstrate significant success in inducing and maintaining remission in patients with moderate to severe IBD. Notably, gut-selective agents such as vedolizumab provide enhanced safety by reducing systemic immunosuppression. This review explores the pharmacological mechanisms, pharmacokinetics, clinical effectiveness, safety profiles, and emerging therapeutic roles of anti-integrin therapies in inflammatory bowel disease.

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INTRODUCTION

Inflammatory bowel disease (IBD) is a chronic inflammatory condition of the gastrointestinal tract that mainly includes Crohn's disease (CD) and ulcerative colitis (UC). These illnesses are marked by recurrent bouts of intestinal inflammation caused by dysregulated immune responses to the gut microbiota in genetically predisposed individuals. The global prevalence of IBD has increased significantly in recent decades, especially in industrialized and developing countries (1). The development of IBD results from a complex interaction among genetic factors, environmental influences, intestinal microbiota, and immune system dysregulation. In affected individuals, immune cells infiltrate the intestinal mucosa and release pro-inflammatory cytokines, leading to chronic inflammation and tissue damage. Traditional treatments for IBD include corticosteroids, aminosalicylates, immunomodulators such as azathioprine and methotrexate, and biologic agents that target tumor necrosis factor-alpha (TNF-α). Although these treatments have improved disease management, many patients experience inadequate responses, lose effectiveness over time, or encounter adverse effects (2). Recent advances in immunology have emphasized the importance of leukocyte trafficking in the development of IBD. The movement of immune cells from the bloodstream into the intestinal mucosa is facilitated by adhesion molecules called integrins. Blocking these molecules prevents inflammatory cells from entering the intestinal tissue, thereby decreasing inflammation (3). Anti-integrin therapies are targeted strategies for managing intestinal inflammation by disrupting leukocyte migration. These biologic agents have become key treatment options for patients with moderate to severe IBD, especially those who do not respond to standard therapies (4,5). This review outlines the pharmacology, mechanisms of action, clinical uses, and safety profiles of anti-integrin therapies in inflammatory bowel disease.

METHODS

This narrative review was conducted by searching major biomedical databases, including PubMed, Scopus, and Web of Science. Search terms included "anti-integrin therapy," "vedolizumab," "natalizumab," "integrin inhibitors," "Crohn's disease," and "ulcerative colitis." Articles published in English from 2005 to 2025 were reviewed. Included were randomized controlled trials, observational studies, systematic reviews, and meta-analyses that focus on the pharmacology and clinical effectiveness of anti-integrin therapies.

Integrins and Leukocyte Trafficking in IBD

Role of Integrins in Immune Cell Migration: Integrins are transmembrane heterodimeric proteins composed of α and β subunits that facilitate cell adhesion and movement.

They are essential for leukocyte trafficking by helping immune cells adhere to endothelial cells and migrate into tissues. In the gastrointestinal tract, a key integrin involved in leukocyte movement is α4β7, which is found on lymphocytes. This integrin binds to mucosal addressin cell adhesion molecule-1 (MAdCAM-1) on endothelial cells of intestinal blood vessels. The interaction between α4β7 and MAdCAM-1 enables lymphocytes to exit the bloodstream and enter the intestinal mucosa. In patients with IBD, this process becomes overactive, leading to increased infiltration of inflammatory cells and persistent intestinal inflammation. Blocking this interaction is therefore an effective strategy to prevent leukocyte migration and reduce intestinal inflammation. (6,7,8)

Pharmacology of Anti-Integrin Agents

Mechanism of Action: Anti-integrin drugs are monoclonal antibodies that target integrins involved in leukocyte trafficking. By binding to specific integrins on lymphocytes, these agents prevent their interaction with endothelial adhesion molecules, thereby inhibiting immune cell migration into the gastrointestinal tract. This mechanism reduces intestinal inflammation without broadly suppressing the entire immune system. (9,10,11)

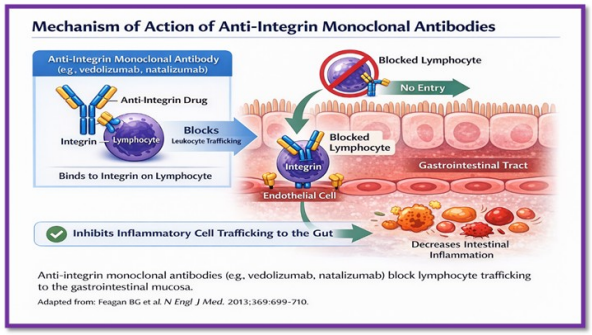

Fig. Mechanism of action of Anti-Integrin (12)

Major Anti-Integrin Agents

Natalizumab: Natalizumab is a humanized monoclonal antibody that targets the α4 integrin subunit, thereby blocking both α4β7 and α4β1 integrins. Because α4β1 integrin is involved in leukocyte migration into the central nervous system, natalizumab affects immune surveillance in the brain. Although natalizumab was initially approved for Crohn's disease, its use is limited due to the risk of progressive multifocal leukoencephalopathy (PML), a rare but serious brain infection caused by JC virus reactivation. (13,14)

Vedolizumab: Vedolizumab is a monoclonal antibody that specifically targets α4β7 integrin, which mainly plays a role in immune cell trafficking within the gastrointestinal tract. By blocking the interaction between α4β7 integrin and MAdCAM-1 in the gut, vedolizumab provides gut-selective immunosuppression. This selectivity significantly lowers the risk of systemic infections and neurological complications compared to natalizumab. Vedolizumab is currently approved for treating both ulcerative colitis and Crohn's disease (15,16).

Etrolizumab: Etrolizumab is an investigational monoclonal antibody that targets the β7 integrin subunit. Blocking both α4β7 and αEβ7 integrins may provide broader inhibition of lymphocyte migration and retention in intestinal tissues. Clinical trials are ongoing to evaluate its efficacy and safety (17,18).

Pharmacokinetics: Anti-integrin therapies are administered as intravenous or subcutaneous monoclonal antibodies. Since these drugs are proteins, they are given parenterally rather than orally. Monoclonal antibodies are mainly distributed within the vascular and interstitial compartments. These agents are broken down by proteolytic enzymes into small peptides and amino acids. Clearance occurs through the reticuloendothelial system and cellular breakdown. The long half-life of monoclonal antibodies allows for dosing intervals of several weeks (19).

Clinical Applications

Ulcerative Colitis: Vedolizumab has shown significant effectiveness in inducing and maintaining remission in patients with moderate-to-severe ulcerative colitis. Clinical trials, such as the GEMINI 1 study, have demonstrated that vedolizumab significantly increases clinical remission rates compared with placebo. Patients treated with vedolizumab also exhibited improved mucosal healing and a decreased need for corticosteroids (20).

Crohn's Disease: Vedolizumab is also effective for patients with Crohn's disease, particularly those who haven't responded to anti-TNF therapy. The GEMINI 2 trial showed that vedolizumab increased clinical remission rates and enhanced long-term disease management.(21) Anti-integrin therapies are especially beneficial for patients who have not responded to other biologic treatments, such as TNF inhibitors. Their unique mechanism of action provides a different therapeutic option.

Adverse Effects and Safety

Infusion Reactions and Infections: Some patients may experience infusion-related reactions like headache, fever, or rash. Since anti-integrin therapies target immune cell movement, there is a potential risk of infections. However, gut-selective agents such as vedolizumab have a relatively low risk of systemic infections (22).

Progressive Multifocal Leukoencephalopathy: The most serious adverse effect associated with natalizumab is progressive multifocal leukoencephalopathy (PML). This condition results from reactivation of the JC virus in the central nervous system. Due to this risk, careful patient monitoring is essential when using natalizumab. Vedolizumab has not been significantly associated with PML. (23)

Emerging Therapeutic Developments: Research continues to explore new integrin-targeting therapies with improved efficacy and safety.Potential developments include:

- Oral integrin inhibitors
- Combination biologic therapy
- Personalized therapy based on molecular biomarkers

These advances may further improve outcomes for patients with inflammatory bowel disease.

DISCUSSION

Anti-integrin therapies represent a significant advancement in treating inflammatory bowel disease. By targeting leukocyte trafficking rather than broadly suppressing the immune system,

Table 1. Comparison of Anti-Integrin Drugs Used in Inflammatory Bowel Disease

Feature	Natalizumab	Vedolizumab	Etrolizumab
Drug class	Humanized monoclonal antibody	Humanized monoclonal antibody	Monoclonal antibody (investigational)
Target integrin	α4 integrin (blocks α4β1 and α4β7)	α4β7 integrin	β7 integrin (blocks α4β7 and αEβ7)
Mechanism of action	Prevents leukocyte adhesion and migration into tissues, including the CNS and GI tract	Blocks interaction between α4β7 integrin and MAdCAM-1, preventing lymphocyte trafficking to the intestinal mucosa	Inhibits both lymphocyte trafficking and retention in the intestinal epithelium
Selectivity	Non–gut selective	Gut-selective immunosuppression	Gut-focused but broader β7 blockade
Main clinical use	Moderate-to-severe Crohn's disease (limited use)	Moderate-to-severe Crohn's disease and ulcerative colitis	Under investigation for IBD treatment
Route of administration	Intravenous	Intravenous or subcutaneous	Intravenous or subcutaneous (clinical trials)
Major advantage	Strong inhibition of leukocyte trafficking	High efficacy with improved safety due to gut specificity	Potential broader intestinal immune modulation
Major adverse effect	Progressive multifocal leukoencephalopathy (PML) due to JC virus reactivation	Infusion reactions, mild infections	Safety is still being evaluated
Risk of CNS infection	High risk (PML reported)	Very low risk	Unknown (under study)
Current regulatory status	Approved but restricted	Widely approved and commonly used	Investigational drug in clinical trials

these agents provide a more selective and potentially safer way to control intestinal inflammation. Vedolizumab, in particular, has demonstrated strong clinical effectiveness with a favorable safety profile. Its gut-specific mechanism decreases the risk of systemic immunosuppression and neurological issues. Despite these benefits, challenges remain, such as the high cost of biologic therapies and the need to identify patients who are most likely to benefit from treatment. Future research should focus on optimizing treatment strategies, discovering predictive biomarkers, and developing new integrin-targeting drugs (24,25,26).

Limitations

This narrative review summarizes current knowledge about anti-integrin therapies but may not include all recently published studies. As research in this area continues to evolve, ongoing clinical trials could offer additional insights into the long-term safety and effectiveness of these agents.

CONCLUSION

Anti-integrin therapies have become a significant class of biologic drugs used to treat inflammatory bowel disease. By specifically blocking leukocyte migration into the gastrointestinal tract, these agents effectively reduce intestinal inflammation while minimizing systemic immunosuppression. Vedolizumab has established itself as a primary treatment option for patients with moderate to severe ulcerative colitis and Crohn's disease, especially those who have not responded to conventional therapies. Ongoing research will help clarify the role of integrin inhibitors and could lead to the development of more effective and safer treatments for inflammatory bowel disease.

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