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Commentary

Efficacy of Novel Anti-Anginal Agents: Current and Emerging Therapies

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DESCRIPTION

Angina pectoris, a key symptom of Ischemic Heart Disease (IHD), occurs when myocardial oxygen demand surpasses supply, typically due to coronary artery stenosis or spasm. Despite advancements in the management of Coronary Artery Disease (CAD), including lifestyle modification, anti-platelet therapy, and traditional anti-anginal agents like nitrates, beta-blockers, and calcium channel blockers, a significant proportion of patients continue to experience symptoms and are at risk of progression to more severe cardiovascular events. Consequently, novel anti-anginal agents have been developed to address the clinical needs for more effective and better-tolerated therapies. This commentary explores the efficacy of current and emerging anti-anginal agents, focusing on their mechanisms, clinical outcomes, and potential advantages over traditional therapies.

Conventional anti-anginal therapies

The fundamental principle of angina management has long been based on nitrates, beta-blockers, and calcium channel blockers. Nitrates, by dilating the coronary vasculature, reduce myocardial oxygen demand, while beta-blockers lower heart rate and reduce contractility, thus decreasing oxygen consumption. Calcium channel blockers provide vasodilation and reduce afterload. While these agents remain effective for many patients, they are associated with limitations, including

- Tachyphylaxis with prolonged nitrate use, leading to diminishing efficacy over time.
- Beta-blocker-induced fatigue, bradycardia, and a potential negative impact on exercise capacity.
- Peripheral edema and constipation associated with calcium channel blockers, especially in elderly patients.

Emerging anti-anginal therapies

In recent years, several novel agents have emerged, provides alternatives to conventional therapies. These drugs target various physiological pathways that contribute to angina, including metabolic modulation, vascular tone regulation, and autonomic control. Below, we discuss the most notable agents that have been investigated for their efficacy in treating angina.

Ranolazine: Multiple clinical trials have demonstrated that ranolazine significantly reduces anginal episodes and improves exercise tolerance in patients with stable angina, particularly in those who remain symptomatic despite conventional therapy. The MERLIN-TIMI 36 trial confirmed that ranolazine also offers a modest reduction in cardiovascular events, particularly in patients with Non-ST Elevation Myocardial Infarction (NSTEMI). However, ranolazine is not without drawbacks, including its potential to cause QT interval prolongation and drug interactions due to its metabolism via CYP3A4.

Ivabradine: It has shown efficacy in clinical trials such as the Systolic Heart failure treatment with IF inhibitor Trial (SHIFT), where it significantly reduced hospitalization for heart failure and cardiovascular death in patients with chronic heart failure. In the context of stable angina, studies have shown that ivabradine improves exercise capacity, reduces anginal frequency, and enhances quality of life in patients with elevated heart rates despite treatment with beta-blockers or in those who are intolerant to beta-blockers. However, ivabradine is associated with potential side effects like bradycardia and visual disturbances, limiting its use in certain populations.

Nicorandil: Nicorandil instable angina trials have shown that nicorandil effectively reduces anginal symptoms, enhances exercise tolerance, and improves long-term outcomes in patients with stable angina. Its unique mechanism makes it particularly useful in patients with vasospastic angina and those who are not adequately managed by nitrates alone. However, oral ulceration and hypotension are common side effects that limit its tolerability, particularly in long-term use.

Anti-inflammatory therapies

Emerging evidence suggests that inflammation plays a key role in the pathogenesis of angina, particularly in microvascular angina and in the context of atherosclerotic plaque rupture. Agents

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targeting inflammatory pathways, such as canakinumab (an IL-1β inhibitor), have shown effects in reducing cardiovascular events in patients with high-risk CAD. While these drugs are primarily focused on reducing major cardiovascular events, they may also have the potential to alleviate symptoms of angina by reducing the inflammatory burden within coronary vessels. However, further studies are required to assess the long-term efficacy and safety of such therapies in the angina cohort.

Gene and cell-based therapies

Gene therapy and stem cell-based approaches are in the early stages of development for the treatment of angina. These therapies aim to promote angiogenesis and enhance myocardial perfusion by delivering genes or cells that improve coronary blood blood flow. Initial animal models and small clinical trials have demonstrated some success, particularly with Vascular Endothelial Growth Factor (VEGF) gene therapy.

CONCLUSION

The perspective of anti-anginal therapies has expanded significantly with the development of novel agents targeting various aspects of angina pathophysiology. Ranolazine, ivabradine, and nicorandil have emerged as effective options, particularly in patients with refractory angina or those who cannot tolerate traditional therapies. Additionally, anti-inflammatory agents and gene therapies represent compelling frontiers in the treatment of angina, though further investigation is required to establish their safety and long-term benefits.