Review Article

Assessment the Role of Olmesartan in Esclating the Risk of Enteropathy, Review Article

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Abstract

Lmesartan, an FDA-approved angiotensin II receptor blocker (ARB), is utilized to address hypertension. It can be employed independently or in conjunction with other antihypertensive medications. In the absence of comorbidities like chronic kidney disease, cerebrovascular events, heart failure, diabetes, and ischemic heart disease, Olmesartan, along with other ARBs, may serve as monotherapy for hypertension . Olmesartan is generally well-tolerated with few side effects. However, Olmesartan-induced enteropathy was initially documented in 2012 through a case series involving 22 patients. Subsequently, additional cases linked to Olmesartan and other angiotensin II receptor blockers (ARBs) such as irbesartan, valsartan, and telmisartan have been reported .The majority of cases are characterized by celiac sprue-like villous atrophy upon intestinal biopsy. The precise pathogenic mechanism remains undetermined, but a potential explanation suggests the inhibition of the intestinal immune suppressive effect of transforming growth factor-beta (TGF-β). This inhibition could lead to an increase in intestinal T-cell inflammation, resulting in cellular damage and malabsorption. Due to a lack of awareness regarding this condition, there is a tendency for underdiagnosis and the excessive utilization of healthcare resources. This can lead to unnecessary patient suffering, including hospital admissions for a condition that typically improves upon discontinuation of the causative drug. Increased awareness is crucial to prevent these adverse outcomes and ensure appropriate management. The Medline, Pubmed, Embase, NCBI, and Cochrane databases were searched for studies of patients with non-alcoholic fatty liver disease. Incidence, etiology, and management options were analyzed. An association between olmesartan and sprue-like enteropathy has been observed in several case series and reports.

Keywords: Olmesartan, Olmesartan-induced enteropathy (oIe), Celiac disease, Angiotensin

Introduction

Olmesartan, an FDA-approved angiotensin II receptor blocker (ARB), is utilized to address hypertension. It can be employed independently or in conjunction with other antihypertensive medications. Olmesartan and other ARBs may be used as monotherapy for hypertension if concomitant conditions such as chronic renal disease, cerebrovascular events, heart failure, diabetes, and ischemic heart disease are not present [1].

Olmesartan typically has little adverse effects and is well tolerated. However, a case series comprising 22 patients first reported Olmesartan-induced enteropathy in 2012. Later, other cases associated with olmesartan and other angiotensin II receptor blockers (ARBs) including valsartan, telmisartan, and irbesartan were documented [2].

The majority of cases are characterized by celiac sprue-like villous atrophy upon intestinal biopsy. The precise pathogenic mechanism remains undetermined, but a potential explanation suggests the inhibition of the intestinal immune suppressive effect of transforming growth factor-beta (TGF-β). This inhibition could lead to an increase in intestinal T-cell inflammation, resulting in cellular damage and malabsorption [2].

Due to a lack of awareness regarding this condition, there is a tendency for underdiagnosis and the excessive utilization of healthcare resources. This may result in needless suffering for the patient, including hospital stays for conditions that usually get better when the offending medication is stopped. Raising

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awareness is essential to averting these negative consequences and guaranteeing proper handling [3].

Materials and Methods

Symptoms and Signs

- *Chronic Diarrhea:* Persistent and severe diarrhea is a hallmark symptom of Olmesartan-induced enteropathy. The diarrhea can be debilitating and may lead to significant weight loss.
- *Weight Loss:* Patients may experience unintentional weight loss, which can be substantial and contribute to overall debilitation [4].
- *Villous Atrophy:* A characteristic feature of Olmesartan-induced enteropathy is villous atrophy, observed through intestinal biopsies. This structural alteration in the small intestine can contribute to malabsorption.
- *Laboratory Abnormalities:* Laboratory evaluations may reveal signs of malabsorption, including anemia, hypoalbuminemia, electrolyte imbalances, and deficiencies in vitamins and nutrients.
- *Electrolyte Imbalance:* Diarrhea and malabsorption can lead to electrolyte imbalances, which may manifest as symptoms like weakness, fatigue, and muscle cramps [5].

Risk Factors

- *Duration of Use:* The risk of Olmesartan-induced enteropathy appears to increase with prolonged use, particularly after two years of continuous therapy.
- *Delay in Onset:* Symptoms may not become apparent until several months to years after the initiation of Olmesartan therapy. This delayed onset adds complexity to the diagnosis.
- *Cell-Mediated Immunity:* The pathogenesis is thought to involve cell-mediated immunity, and the condition may be reversible upon discontinuation of the drug [6].
- *Similarity to Celiac Disease:* Olmesartan-induced enteropathy shares clinical and histological similarities with celiac disease, necessitating the exclusion of the latter in the diagnostic process [7].

Treatment

The primary therapeutic strategy for Olmesartan-induced enteropathy revolves around the swift discontinuation of Olmesartan, the implicated angiotensin II receptor blocker. Numerous reported cases consistently demonstrate clinical remission in patients following the cessation of Olmesartan therapy. Although the exact mechanism through which Olmesartan induces enteropathy remains elusive, the rapid clinical improvement observed upon discontinuation strongly implies a potential reversibility of the condition [8].

In instances where patients exhibit symptoms linked to Olmesartan-induced enteropathy, such as chronic diarrhea and villous atrophy, discontinuing Olmesartan becomes a crucial therapeutic intervention. Monitoring for the resolution of symptoms and potential mucosal recovery is imperative in assessing the efficacy of this approach. While obtaining histological confirmation may present challenges, whether due to patient preferences or other factors, the evident clinical improvement and swift mucosal recovery associated with Olmesartan-induced enteropathy underscore the critical importance of promptly recognizing and addressing this condition through the discontinuation of the implicated medication [9].

This proactive approach not only aims to alleviate symptoms but also serves to prevent the potential complications and morbidity associated with untreated Olmesartan-induced enteropathy. The emphasis on monitoring for mucosal recovery highlights the dynamic nature of the condition and the positive outcomes achievable through timely intervention, reinforcing the significance of clinical vigilance and patient-centered care in managing this relatively rare but clinically significant adverse reaction [10].

Results and Discussion

Diarrhea is a frequently observed side effect of various medications. In the United States, the prevalence of hypertension among adults aged 18 and older was reported to be 45.4% from 2017 to 2018, with a global estimated prevalence of 30% in adults. Olmesartan, classified as an angiotensin II receptor blocker (ARB), has been associated with a "sprue-like enteropathy" (meaning sharing characteristics or features similar to those associated with sprue or celiac disease) as highlighted in a 2013 FDA report.

This condition manifests as severe, persistent diarrhea and weight loss occurring months to years after the initiation of olmesartan treatment, with an elevated risk identified after two years of use [11]. The underlying mechanisms of olmesartan-induced enteropathy remain incompletely understood, but initial data point to cell-mediated immunity harm. Two proposed pathways include the inhibition of transforming growth factor by ARBs, intensifying T-cell activity, and the disproportionate activation of angiotensin II receptor type 2 (AT2) receptors after blocking AT1 receptors with olmesartan, leading to enterocyte apoptosis. Laboratory evaluations typically reveal a malabsorption process marked by anemia, hypoalbuminemia, electrolyte imbalance, and vitamin deficiencies [12]. Given the clinical and histological similarities with celiac disease, negative celiac serology is essential for diagnosing olmesartan-induced enteropathy. In a French cohort study involving 4,546,680 patients, those using olmesartan for one to two years and over two years experienced significantly higher rates of intestinal malabsorption necessitating hospitalization compared to those taking an ACE inhibitor. Treatment involves discontinuing Olmesartan, managing symptomatic diarrhea,

and ruling out alternative causes [13]. Given the possibility of symptom return, it is not advised to re-challenge with olmesartan; nevertheless, depending on the patient's priorities and medical comorbidities, it may be appropriate to explore an alternate ARB or a different class of antihypertensive drug [14]. After stopping olmesartan, clinical improvement usually happens a few days to a week later, though the duration of diarrhea resolution can vary [15].

Conclusion

Olmesartan-induced enteropathy, though uncommon, demands careful consideration in clinical contexts. This condition, marked by persistent chronic diarrhea and villous atrophy, raises concerns for individuals prescribed Olmesartan, particularly due to its widespread use as an antihypertensive medication. Of particular significance is the need to differentiate Olmesartan-induced enteropathy from celiac disease, a common cause of villous atrophy. This differentiation is crucial and is typically initiated through negative celiac serology or the absence of a response to a gluten-free diet.

To comprehensively address this diagnostic challenge, a thorough and intricate diagnostic process is essential. This involves excluding various gastrointestinal conditions and infections that could mimic the symptoms of Olmesartan-induced enteropathy. The complexity of the diagnostic pathway is compounded by the fact that symptoms may not manifest until 6 to 120 months after the initial exposure to Olmesartan. This delayed onset suggests a multifaceted pathogenesis involving cell-mediated immunity, adding a layer of intricacy to the understanding of this condition.

Despite its relatively low incidence, healthcare providers must maintain a high level of awareness. Consideration of Olmesartan-induced enteropathy is paramount in cases of unexplained chronic diarrhea. Timely recognition of the condition is crucial to facilitate the discontinuation of the offending medication and the implementation of appropriate management strategies. This proactive approach is vital to mitigate potential morbidity associated with Olmesartan-induced enteropathy, underlining the importance of staying vigilant and responsive to this relatively rare but clinically significant complication in patients undergoing Olmesartan therapy.

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