

## OLMESARTAN-INDUCED ENTEROPATHY: BIBLIOGRAPHIC REVIEW OF THE HISTOLOGICAL FINDINGS OF THIS IATROGENIC VILLOUS ATROPHY

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**Keywords:** Antihypertensives; Enteropathy; Histology

## INTRODUCTION

Olmесartan is an antihypertensive angiotensin II receptor antagonist (ARA II), recommended for the treatment of Systemic Arterial Hypertension (SAH). However, possible rare adverse reactions have been reported in some patients, especially gastrointestinal disorders, more precisely enteropathy with macroscopic and histological changes in the duodenum.

## OBJECTIVE

Review the histology of the small intestine and changes resulting from the use of the drug Olmesartan.

## METHODOLOGY

Bibliographic survey of scientific articles in the PubMed and LILACS databases, published between 2015 and 2022, and the books: Basic Histology (13th edition, Junqueira and Carneiro) and Basic and Clinical Pharmacology (15th edition, Katzung, et al).

## DISCUSSION

Olmесartan is used to treat hypertension with high renin levels, acting on the angiotensin II AT1 receptor, which prevents vascular contraction, causing vasodilation, sodium elimination and reduced noradrenergic release. It is generally used in cases of side effects to angiotensin-converting enzyme (ACE) inhibitors. Despite the benefit, studies indicate the development of adverse reactions in certain individuals, characterized by a wide spectrum of intestinal disorders, including pain, abdominal distension, vomiting, nausea, chronic diarrhea and weight loss. The reaction appears after prolonged use, averaging 3 years. The symptoms are caused by changes in the enteric mucosa. Histologically, the duodenal

mucosa is composed of epithelium, lamina propria and muscular layer of the mucosa, which separates it from the submucosa. Facing the lumen, there are villi, which are projections of epithelium whose function is to increase the absorptive surface, formed by: simple cylindrical epithelium containing enterocytes and goblet cells, and lamina propria, providing support and allowing movement via smooth muscles and loose connective tissue, in addition of blood vessels, lymphatics and nerve fibers. This epithelium is continuous with the crypts, whose activity is proliferative, and contain Paneth, absorptive, goblet, enteroendocrine cells and stem cells. Endoscopic findings of olmesartan enteropathy indicated signs of inflammation, hyperemia and granular protrusions, mainly in the portion of the duodenal bulb. Histopathological analysis of local biopsies identifies atrophy of intestinal villi, disappearance of crypts, ulcerations, chronic inflammation of the lamina propria, characterized by an increase in eosinophils, added to the increase of intraepithelial lymphocytes and thickening of subepithelial collagen. Malabsorption syndrome is related to villous atrophy and is accompanied by electrolyte abnormalities, similar to celiac disease. The justification for these changes indicates that the drug inhibits beta growth factor, which plays a role in the homeostasis and apoptosis of enterocytes, and that damage to the microvilli of the small intestine is triggered by an abnormal immune response. Patients achieved rapid improvement in symptoms after discontinuing the use of the drug, proven through complementary exams.

## **CONCLUSION**

The continuous use of Olmesartan has, as a rare adverse effect, the development of duodenal enteropathy, observed clinically by multiple gastrointestinal disorders, and

confirmed by microscopic evaluation. Suspension of the medication leads to clinical improvement and allows reversal of histological changes, requiring regular and prolonged evaluation for patients using this drug.