Olmesartan induced enteropathy affecting the entire gastrointestinal tract: a case report

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Abstract

Olmesartan, a well-known and powerful antihypertensive drug, was first described to cause enteropathy in 2012. A possible mechanism may be inhibition of the intestinal immune suppressive effect of transforming growth factor-beta (TGF-β), with a consequential increase of intestinal T-cell inflammation.

We present the case of a 60-year-old woman who developed large volume, watery diarrhoea with 8kg weight loss only two weeks after starting olmesartan 20mg daily with a secondary mild acute kidney insufficiency and hypokalaemia. Coeliac serology was negative. Endoscopy revealed no macroscopic lesions. Histology showed increased gastric, duodenal, ileal and colonic intraepithelial lymphocytes with partial duodenal villous atrophy, hence affecting the entire gastrointestinal tract.

After cessation of olmesartan, symptoms improved within a week; therefore a diagnosis of olmesartan induced enteropathy was made. Extra immunohistochemical stains to further investigate the underlying pathophysiology were inconclusive. (Acta gastroenterol. belg., 2023, 86, 95-97).

Key words: Olmesartan, chronic diarrhoea, enteropathy, adverse drug event.

Introduction

Arterial hypertension affects 20.0% of the adult Belgian population, increasing to 40.4% of adults aged 65 years and older (1). On top of lifestyle measures, five major drug classes are recommended for routine treatment: ACE-inhibitors, angiotensin receptor blockers (ARBs), beta-blockers, calcium channel blockers (CCBs), and diuretics. First choice is a combination treatment with an ACE-inhibitor or ARB plus CCB or diuretic (2).

In 2020, 22.68% of the adult Belgian population was prescribed antihypertensive treatment, of which 23.51% took an ARB and 10.31% olmesartan (data provided by Farmanet).

Olmesartan is a powerful antihypertensive drug that blocks the angiotensin II receptor type 1 (AT1), antagonizing all effects of angiotensin II mediated by the AT1-receptor (3). Olmesartan induced enteropathy (OIE) was first described in a case series of 22 patients in 2012 (4). Since then, over a hundred cases of olmesartan and few cases of other ARB (irbesartan, valsartan, telmisartan) induced enteropathy have been described (5,6).

We present a patient with OIE that affects the entire gastrointestinal tract while taking olmesartan 20mg. Symptoms developed remarkably quickly after introduction of olmesartan and improved a few days after stopping olmesartan, as expected. We performed multiple immunohistochemical stains in an effort to gain more insight in the possible pathophysiological mechanism.

Case history

A 60-year-old Caucasian female presented with anorexia and diarrhoea for two weeks. She had progressively worsening, large volume, non-bloody, non-mucoid watery diarrhoea up to twelve times daily and three times overnight. There were associated epigastric cramps, nausea and vomiting for three days. She reported non-intentional weight loss of around 8kg in the past month. She denied having a fever.

Her medical history included arterial hypertension, hypercholesterolemia, atrial flutter, lymphocytic colitis and goiter. Her daily drug therapy consisted of spironolactone 25mg, bisoprolol 2.5mg, atorvastatine 10mg and olmesartan 20mg.

Physical examination showed normal vital signs, bradyphrenia and a diffuse tender abdomen. Lab results were remarkable for minimal inflammation (CRP 14mg/L; upper limit of normal (ULN) 5mg/L; WBC 7.9x10³/µL, ULN 10.3x10³/µL), mild hypokalaemia (3.36mmol/L, lower limit of normal (LLN) 3.5mmol/L), decreased renal function (CKD-EPI 51mL/min opposed to normal baseline, LLN 60mL/min) and elevated liver enzymes (AST 111U/L, ULN 32U/L; ALT 222U/L, ULN 52 U/L; γ-GT 115U/L, ULN 36U/L; Alk P 161U/L, ULN 105U/L), tissue transglutaminase IgA and total IgA were normal, viral hepatitis serology was negative. Stool examination was unremarkable.

Abdominal ultrasound visualised a normal liver, bile ducts and gallbladder, and limited hyperperistalsis in the small intestine. Esophagogastroduodenoscopy and ileocolonoscopy showed no macroscopic lesions.

Histologic examination revealed a similar picture in all samples (Figure 1).
On further questioning, her general practitioner had prescribed olmesartan 40mg in March 2017 as well. Two months later she developed similar complaints (anorexia, watery diarrhoea without blood or mucus and 10kg weight loss). In July 2017 she was admitted to hospital with severe diarrhoea and secondary acute kidney insufficiency (AKIN stage 3), hypokalaemia and uremic stupor. She developed torsade de pointes secondary to hypokalaemia and sotalol (then prescribed for her atrial flutter) which reached higher plasma levels due to decreased renal clearance. Biopsies taken during sigmoidoscopy showed an increased number of intraepithelial lymphocytes, suggestive of lymphocytic colitis (however, no proximal biopsies were taken).

Olmesartan was stopped during hospitalisation and restarted only one month before current hospitalisation.

Discussion

Diarrhoea is accountable for 7% of adverse drug reactions through multiple mechanisms (7). In literature, OIE has an estimated incidence of <0.05% of olmesartan users (8). Overall OIE is observed to start months/years after introduction of olmesartan. Our patient developed diarrhoea after only a few weeks, which seems exceptionally early.

Rubio-Tapia et al. describe six clinical features to help decide whether gastrointestinal complaints can be contributed to olmesartan (4). These are: [1] gastrointestinal symptoms, [2] negative IgA tissue transglutaminase antibodies, [3] evidence of enteropathy with or without collagen deposition or intraepithelial lymphocytosis, [4] lack of clinical response to gluten exclusion, [5] exclusion of other causes of enteropathy, [6] evidence of clinical and histological improvement after suspension of olmesartan. Applying these criteria to our patient, all but one (criterion 4) are fulfilled. We did not start a gluten free diet, considering clinical improvement was already reached.

The mechanism of OIE remains unclear. A role for transforming growth factor beta (TGF-β) has been proposed considering the important role in immune homeostasis as a T cell regulator, interactor with the...
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Nele Van Horebeek, Romaric Croes, An Vonck and Erwin Colpaert declare that they have no conflict of interest.

References