A case of losartan-induced dry irritating cough

It is a well-known fact that angiotensin converting enzyme inhibitors (ACEI) alone can control blood pressure in approximately fifty per cent of the patients with mild to moderate hypertension and many consider them ‘first line’ drugs for blood pressure. Ninety per cent of patients with mild to moderate hypertension can be controlled by a combination of an ACEI with a β channel blocker, ß-adrenergic receptor blocker or a diuretic. But in five to twenty per cent of patients, ACEI can induce bothersome dry cough which usually develops between the 1st week and 6 months after initiation of therapy. Cessation of therapy is needed sometimes to control the dry cough. This adverse effect may be mediated by the accumulation of bradykinin, substance-P, and/or prostaglandins in the lungs. Once ACEI is stopped, the cough usually disappears within 4 days. Therefore, in spite of current recommendations for ACEIs to be used as first line antihypertensives, physicians are using angiotensin II receptor antagonists very commonly because of the fact that they have a comparable efficacy as angiotensin II receptor antagonists but without cough. The latter act at the AT₁ receptor level and have nothing to do with angiotensin converting enzyme, whose inhibition actually is responsible for the production of cough. Few studies have reported losartan to produce cough. Since dry cough due to losartan is rare we feel this case is worth reporting.

A 49-year-old obese woman recently diagnosed as a case of primary moderate hypertension was advised to start losartan of a reputed manufacturer at a dose of 50 mg, o.d. with salt restriction and exercise. The patient had no history of smoking, alcohol consumption, any associated pathology or concurrent drug intake. She started to have severe dry, irritating cough during the 8th week after the initiation of the drug therapy. There was no history of such an episode in the recent past. There was no history of any allergy either. Clinical examination revealed a clear chest and there was no sign of any infection, bronchitis, pulmonary tuberculosis, asthma or sinusitis. There were no symptoms and signs of gastroesophageal reflex disease. Investigations revealed normal X-ray chest and sinuses. All basic investigations like eosinophilic count, Hb, TLC, DLC, ESR, platelet count, sputum for AFB, routine urine and stool examination, blood sugar, blood urea, creatinine, LFT, RFT and ECG were found to be normal except the lipid profile which showed an increased triglyceride level (190 mg/dl).

The patient was advised to stop the drug, when the cause of the cough could not be ascertained thinking on the line that this adverse effect might be due to losartan itself and therefore no treatment was prescribed for the treatment of the cough. The patient was changed over to amlodipine (5 mg, o.d.) for the time being and it was found that the cough disappeared on the 8th day after stopping losartan in the patient. Further rechallenge was not done in the interest of the patient fearing reappearance of adverse drug reaction (ADR) and ethical constraints. Thus, the appearance of dry irritating cough in a patient taking losartan could not be explained by a concurrent disease, drug or chemicals and a dechallenge improved the condition. Hence, this ADR can be labeled ‘probably/likely’ as per causality assessment. Since this ADR was not dose dependent and unpredictable, it could be labeled as Type-II class of ADR.

Since angiotensin II receptor antagonists (losartan) are not known to produce cough this case was very unusual and unexpected. The mechanism of this adverse reaction is not clear. The reasons for cough such as overexpression of unopposed AT₁ receptor in the central nervous system and a certain degree of ‘angiotensin converting enzyme inhibiting’ property of losartan need to be explored.

Acknowledgement

The authors are grateful to Dr. Mohan Lal, Associate Professor of Cardiology, GMC, Jammu for referring this case to the Adverse Drug Reporting Center and taking keen interest in the clinical evaluation of the patient.

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