Acotiamide

Samir Patil[1]

ABSTRACT

Functional dyspepsia is a common functional gastro-intestinal disorder with prevalence of 12-15% in general population. Many drugs including H2 Blockers, proton pump inhibitors, prokinetic agents, antidepressants have been tried in the management of functional dyspepsia. Acotiamide is the world's first approved treatment for functional dyspepsia diagnosed by Rome III criteria. The drug modulates upper gastrointestinal motility to alleviate abdominal symptoms resulting from hypomotility and delayed gastric emptying. This review summarises pharmacological profile of acotiamide.

Functional dyspepsia is a very common condition encountered in day to day clinical practice which is often difficult to treat. Acotiamide is a novel drug which is now available for the treatment of functional dyspepsia. It is the first drug in the world which is approved for functional dyspepsia. It was first approved in Japan and It has been found to be useful in symptoms associated with Post prandial syndrome.[1]

Mechanism of action :

The drug modulates the upper Gastrointestinal motility and regulates stress.

The salt is acotiamide hydrochloridetrihydrate (Z-338), [N - (N9, N9 diisopropylaminoethy l) - [2 - (2 - hydroxy - 4, 5 - dimethoxy - benzoylamino) - 1, 3 - thiazole - 4 - y l] carboxamide monohydrochloride trihydrate]. It has a strong affinity formuscarinic M 1-3 receptors and has less affinity for serotonin 5-HT, 5-HT and 5-HT receptors, and weak affinity for dopamine D2 receptors.[2] In the enteric nervous system, the release of Acetyl Choline (ACh) from myenteric and submucosal plexus neurons is inhibited by the presynaptic M1receptor and M2 receptor in the mucosal or submucosal neurons. Acotiamide mechanism of augmentation of gastrointestinal motility is due to exertion of acetylcholine release by acting as an antagonist of the M1 and M2 muscarinic receptors from enteric cholinergic nerve terminals and inhibiting acetylcholinesterase activity[3]

Acotiamide does not increase ACh release simply by inhibiting acetylcholinesterase (AChE) acotiamide may also act directly on the gut and indirectly on the CNS through the brain gut axis.[3]

Pharmacologic effects :

- It enhances electrically stimulated contractions and the release of ACh in the [3H] - 6 choline-preincubated gastric antrum and body.
- It reversibly inhibits human erythrocyte Ach E activity, although the IC is 50 approximately 100 - fold less than that of neostigmine and physostigmine.
- Acotiamide alters the expressions of stress - related genes such as GABA receptors, GABA transporters and neuromedin U in medulla oblongata or hypothalamus hence it possibly has a role in the regulation ofstress through the hypothalamicpituitaryadrenocortical axis activity.[4]

Indications :

It is helpful in the treatment of functional dyspepsia. It is useful especially in symptoms f postprandial fullness, upper abdominal bloating and early satiety

Dosage and administration :

The adult dosage is 100 mg of acotiamide hydrochloride hydrate administered orally three times daily before a meal.[5]

[1]Consultant in Gastroenterology and Liver diseases
GI Endoscopy and Liver clinic, SMP Hospital, Nagpur

Address for Correspondence -
Dr. Samir Patil
E-mail : samirspatil@gmail.com

Safety data :

The only adverse drug reaction observed in = 2.0% of subjects was "diarrhea" (4.1%) [18 of 442 subjects] in the placebo group and 4.7% [21 of 450 subjects] in the 300 mg/day group). There were no deaths.[6]

Warning and precaution :

If symptoms do not improve after 1 month of treatment with acotiamide, consideration should be given to treatment discontinuation.

If symptoms persist, the possibility of organic disease should be taken into account and consideration should be given to performing other tests.

If symptoms have remained improved over a sufficiently long period of time, consideration should be given to treatment discontinuation.

Geriatric Use :

Acotiamide should not be administered without careful consideration for a long period of time Safety in special population. Elderly patients as there is limited data available in the elderly.

Safety in pregnancy and nursing has not been established.

Bibliography :

1. Nowlan ML, Nolan ML, Scott LJ. Acotiamide: first global approval. Drugs. 2013; 73 (12) : 1377-83.
2. Matsushita M, Masaoka T, Suzuki H. Emerging treatments in neurogastroenterology: Acotiamade, a novel treatment option for functional dyspepsia. Neurogastroenterol Motil. 2016; 28 (5) : 631-8.
3. Suzuki H, Hibi T. Acotiamide (Z-338) as a possible candidate for the treatment of functional dyspepsia. Neurogastroenterol Motil. 2010; 22 (6) : 595-9.
4. Ueda M, Iwasaki E, Suzuki H. Profile of acotiamide in the treatment of functional dyspepsia. Clin Exp Gastroenterol. 2016; 9 : 83-8.
5. Karamanolis GP, Tack J. Current management of functional dyspepsia : impact of Rome III subdivision. Ann Gastroenterol. 2012; 25 (2) : 96-9.
6. Matsueda K, Hongo M, Tack J, Saito Y, Kato H. A placebo-controlled trial of acotiamide for meal-related symptoms of functional dyspepsia. Gut. 2012; 61 (6) : 821-8.