Journal of Pharmaceutical Research International

33(56A): 127-129, 2021; Article no.JPRI.76667
ISSN: 2456-9119
(Past name: British Journal of Pharmaceutical Research, Past ISSN: 2231-2919, NLM ID: 101631759)

A Review on Acotiamide

S. Padmaja [a#] and G. Naveen [a*†]

[a] Department of Pharmacology, Chettinad Hospital and Research Institute, Chettinad Academy of Research and Education, Kelambakkam-603103, Tamil Nadu, India.

Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JPRI/2021/v33i56A33894

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/76667

Review Article

Received 05 October 2021
Accepted 11 December 2021
Published 13 December 2021

ABSTRACT

Functional dyspepsia (FD) is mainly treated by drugs like H2 receptors antagonists, Proton pump inhibitors, prokinetics. A novel prokinetic drug to treat FD with 2 subtypes: Epigastric pain syndrome (EPS) & postprandial distress syndrome (PDS), has been introduced recently by the approval of Acotiamide, the first in class, muscarinic receptor antagonist & cholinesterase inhibitor. It has shown improvement in gastric motility in rodents & dogs and reduced PDS symptoms in patients in Double- blinded multicentric study.

Keywords: Acotiamide, proton pump inhibitors, dyspepsia.

1. INTRODUCTION

Functional dyspepsia may change the patient's quality of life. Based on the Rome III classification criteria, the main symptoms of functional dyspepsia consist of bothersome postprandial fullness, early satiety, and epigastric burning [1]. The criteria have to be fulfilled by the presence of these symptoms for three months and onset should be at least before six months from diagnosis. The guidelines for functional dyspepsia patients were also provided in Japan, 2014 [2]. Functional dyspepsia is primarily treated by: acid inhibitors such as H_2-receptor antagonists and proton pump inhibitors (PPIs), and prokinetic drugs that accelerate disturbed gastrointestinal (GI) motility by altering visceral sensitivity [1]. The brain-gut axis was

[#] *First Year PG Student;*
[†] *Second Year PG Student;*
**Corresponding author: E-mail: drgnaveen@hotmail.com;*

acknowledged as an important factor in the causation of functional GI disorders. A Phase III trial was conducted in Europe [3].

Acotiamide is a novel prokinetic drug approved by Pharmaceuticals and Medical Devices Agency(PMDA), Japan in June 2013. It is marketed under the trade name “Acofide” by Zeria pharmaceuticals, Chuo-ku, Tokyo. Zeria has built a pipeline focused on gastrointestinal field & oncology field and has launched numerous pharmaceutical products like Acinon-H2 receptor antagonist & Asacol 400mg-for ulcerative colitis. Molecular formula of acotiamide is C21H30N4O5S. HCl .3H2O. Molecular weight is 541.06. Chemical name is N-{2-[Bis (1-methyl ethyl)amino]ethyl}-2-[(2-hydroxy-4,5-dimethoxybenzoyl)amino]thiazole-4-carboxamide monohydrochloride trihydrate. Non-proprietary name: Acotiamide Hydrochloride Hydrate. It was also approved by CDSCO on 06/07/2016 [4].

2. PHARMACOKINETICS

The maximum plasma levels of Acotiamide are attained in 1-1.5 hours after oral administration, with a plasma t1/2 of 7-10 hours. Acotiamide was metabolized to M-1 (glucuronide conjugate of acotiamide) by UGT1A8 and UGT1A9. On the other hand, in a separate in vitro metabolic study, acotiamide was metabolized to M-4 (de-isopropyl acotiamide) in the highest yield by CYP2C8, followed by CYP1A1, and then by CYP3A4 [5]. 4% of the drug is eliminated in the faeces. There is no marked CYP inhibition. The recommended dosage is 100mg three times a day before food [6].

3. PHARMACODYNAMICS

It acts by antagonizing the M1 and M2 muscarinic receptors in the enteric nervous system and also by inhibiting the anticholinesterase activity. Hence there is increased availability of ACh at postsynaptic receptors in neuromuscular junctions in the enteric nervous system. Acotiamide may also modulate gut-brain interactions through its effects on the afferent vagus nerve, altering the sensory input from the GI tract to the CNS [5].

4. USES IN SPECIFIC POPULATION: PREGNANCY

There is scanty information on the safety of drug in pregnant women. In pregnant rabbits acotiamide was administered at oral doses of 100,300,1000mg/kg from gestation days 6 to 18 [5]. Decreased body weight, decreased ovary weight, abortion, and an increase in the number of maternal animals with premature labor were observed in the 1000 mg/kg/day group. Decreased food intake was observed in the ≥300 mg/kg/day dose groups. In fetuses, decreased body weight and an increased number of dwarfs were observed in the 1000 mg/kg/day group. The effects observed in fetuses were changes secondary to the decreased body weight of maternal animals caused by decreased food intake.

5. GERIATRIC

The incidence of adverse events was similar between the non-elderly and elderly populations.

6. HEPATIC IMPAIRMENT

Acotiamide has not been studied in patients with hepatic impairment. It is not recommended for use in such patients [5].

7. NONCLINICAL TOXICOLOGIES

a) Carcinogenesis

Acotiamide was administered orally for up to 24 months in mice and rats. No acotiamide-induced neoplastic lesion was noted in mice.

b) Antigenicity

Acotiamide is not antigenic in mice, rats, or guinea pigs under the experimental conditions used [5].

8. CLINICAL TRIALS

In Europe phase III open-label study was conducted to evaluate the efficacy and safety of Acotiamide on postprandial distress syndrome [6]. Patients (defined by ROME III criteria) with active postprandial distress syndrome symptoms and without other symptoms of epigastric pain syndrome and similar GI disorders were recruited and enrolled to receive 100 mg Acotiamide three times daily for one year. 81.6% of patients took Acotiamide for >50 weeks, with a mean duration of approximately 320.3 days. There are no deaths or treatment-related severe/serious adverse events, or any clinically significant laboratory test results. Acotiamide showed improvement in the symptoms in a larger number

of patients. Clinically important minimum differences started to appear from week 1 to week 2 for the postprandial fullness and early satiety [7].

9. CONCLUSION

Acotiamide offers a promising role in functional dyspepsia, especially with postprandial distress syndrome. More clinical studies are required which have a larger population size, longer follow up periods, capturing many more clinically relevant parameters to further supplement the earlier clinical studies.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Yamawaki H, Futagami S, Wakabayashi M, Sakasegawa N, Agawa S, Higuchi K, Kodaka Y, Iwakiri K. Management of functional dyspepsia: state of the art and emerging therapies. Therapeutic advances in chronic disease. 2018;9(1):23.
2. Miwa H, Kusano M, Arisawa T, et al. Evidence-based clinical practice guidelines for functional dyspepsia. J Gastroenterol. 2015;50:125–139. Available:https://doi.org/10.1007/s00535-014-1022-3.
3. Tack J, Pokrotnieks J, Urbonas G, Banciu C, Yakusevich V, Bunganic I, Törnblom H, Kleban Y, Eavis P, Tsuchikawa M, Miyagawa T. Long-term safety and efficacy of acotiamide in functional dyspepsia (postprandial distress syndrome)-results from the European phase 3 open-label safety trial. Neurogastroenterol Motil. 2018;30(6):e13284.
   DOI: 10.1111/nmo.13284. Epub 2018 Jan 8.
   PMID: 29315999.
4. Available:https://cdscoonline.gov.in/CDSCO/Drugs
   (Accessed on 19.11.2021)
5. Masuy I, Tack J, Verbeke K, Carbone F. Acotiamide affects antral motility, but has no effect on fundic motility, gastric emptying or symptom perception in healthy participants. Neurogastroenterol Motil. 2019;31(4):e13540.
   DOI: 10.1111/nmo.13540.
   Epub 2019 Jan 20. PMID: 30663175.
6. Matsueda K, Hongo M, Tack J, Aoki H, Saito Y, Kato H. Clinical trial: dose-dependent therapeutic efficacy of acotiamide hydrochloride (Z-338) in patients with functional dyspepsia–100 mg tid is an optimal dosage. Neurogastroenterology & Motility. 2010; 22(6):618-e173.
7. Narayanan V, Bhargava A, Pallewar S. Real World Efficacy and Tolerability of Acotiamide. Relieving Meal-related Symptoms of Functional Dyspepsia. J Gastrointest Dig Syst. 2018;8:1.

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/76667