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# EFFICACY & SAFETY OF ACOTIAMIDE IN TREATMENT OF FUNCTIONAL DYSPEPSIA AND ITS COMPARISION WITH PROTON PUMP INHIBITOR, FLUPENTHIXOL AND MELITRACEN IN NON-DIABETICS

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## ABSTRACT

**Background:** Functional dyspepsia (FD) is characterized by chronic digestive symptoms including postprandial fullness, early satiation, burning and discomfort in the stomach, bloating, nausea, vomiting, and belching. This study aims to evaluate the efficacy and safety of Acotiamide in treating Functional dyspepsia compared to proton pump inhibitors (PPIs), Flupentixol, and Melitracen in Non-Diabetic patients. **Method:** A prospective, comparative investigation was carried out for 6 months, enrolling 100 non-diabetic patients who were diagnosed with functional dyspepsia following Helicobacter Pylori eradication. Group 1 received Acotiamide while Group 2 was treated with PPI, Flupentixol, and Melitracen. Treatment effectiveness was assessed using the Hospital Anxiety and Depression Scale (HADS) and the Gastrointestinal Symptoms Rating Scale (GSRS). **Results:** Both the treatment groups demonstrated significant improvement in Gastrointestinal symptoms. Acotiamide was effective and well tolerated, with no serious side effects reported when compared to PPI with Flupentixol and Melitracen. **Conclusion**: Acotiamide is an effective and safe treatment for FD in non-diabetic patients, with comparable efficacy to the combination of rabeprazole, flupentixol, and melitracen. Acotiamide offers a well-tolerated alternative for managing FD symptoms without significant adverse effects.

**KEYWORDS:** Functional Dyspepsia, Acotiamide, Rabeprazole, Flupentixol, Melitracen, Gastrointestinal Symptom Rating Scale, Hospital Anxiety and Depression Scale.

## INTRODUCTION

Functional dyspepsia is a widespread and burdensome gastrointestinal condition that poses significant challenges for both patients and healthcare professionals. It is characterized by persistent or recurrent discomfort in the upper abdomen without any identifiable cause.[1] Common symptoms include feeling excessively full after meals, early satiety, and epigastric pain.[2] This disorder greatly impacts patients' quality of life and places considerable pressure on healthcare systems globally.[3] Conventional treatment strategies have primarily focused on suppressing gastric acid, enhancing gastrointestinal motility, and managing symptoms. However, the variability in patient responses highlights the necessity for a more comprehensive and individualized therapeutic approach.[4]

Acotiamide is a selective 5-HT3 receptor antagonist and partial 5-HT4 receptor agonist, has recently gained attention as a novel treatment option for functional dyspepsia.[5] Mechanism of action include improving gastric motility and alleviating symptoms through modulation of serotonergic pathways that regulate gastrointestinal activity.[6] Clinical studies indicate that Acotiamide effectively reduces symptoms linked to impaired gastric motility, presenting it as a promising alternative to standard therapies.[7]

Proton pump inhibitors (PPIs) have long been a mainstay for treating dyspepsia, particularly in cases driven by excessive gastric acid secretion.[8] Although effective for acid suppression, PPIs may offer limited benefits in cases of motility-related dyspepsia and carry risks of long-term side effects.[9] Additionally, flupentixol, an antipsychotic agent, and melitracen, a tricyclic antidepressant, have been investigated for their potential in managing functional dyspepsia.[10] Flupentixol acts as a dopamine antagonist, while melitracen influences central pain perception, providing alternative pathways for symptom relief. However, their application is often constrained by a higher incidence of side effects and inconsistent patient responses.[11] This study seeks to evaluate the effectiveness and safety of Acotiamide in the treatment of functional dyspepsia, comparing its outcomes with those of PPIs, flupentixol, and melitracen in non-diabetic patients. By examining the comparative effectiveness

and safety profiles of these treatments, the goal is to provide a comprehensive overview of current therapeutic options and guide clinical decision-making in managing functional dyspepsia.

## OBJECTIVES

- To assess the safety and efficacy of Acotiamide 100 mg BD compared with the combination of a PPI, flupentixol, and melitracen for the overall improvement of functional dyspepsia in non-diabetic patients with overlapping symptoms of postprandial distress syndrome (PDS) and epigastric pain syndrome (EPS).
- To examine the safety profiles of Acotiamide, PPIs, flupentixol, and melitracen, focusing on the incidence of adverse effects and long-term safety concerns in non-diabetic patients with functional dyspepsia.
- To evaluate the elimination of individual functional dyspepsia symptoms using the Hospital Anxiety and Depression (HAD) scale and the Gastrointestinal Symptom Rating Scale (GSRS).

## METHODOLOGY

**Study Design:** Prospective, comparative, and observational study.

**Study Population:** Non-diabetic patients diagnosed with functional dyspepsia, exhibiting overlapping symptoms of postprandial distress syndrome (PDS) and epigastric pain syndrome (EPS), will be enrolled.

**Study Site:** Outpatient Department of Gastroenterology, Princess Esra Hospital, Hyderabad.

**Sample Size:** 100 patients based on inclusion and exclusion criteria

**Interventions:** Participants were assigned to one of the following two groups.

1. Acotiamide Group: Patients will receive Acotiamide 100 mg BD.
2. Control Group: Patients will receive a combination of PPI (Rabeprazole 40mg), flupentixol (0.5 mg), and melitracen (10 mg) once daily.

### Study Criteria

**Inclusion Criteria:** Eligible patients include adults between the ages of 18 and 65 who have been diagnosed with functional dyspepsia in accordance with the Rome III criteria. patients must be non-diabetic and willing to provide informed consent. Additionally, subjects must test negative for the Rapid Urease Test (RUT).

**Exclusion Criteria:** Patients with existing organic gastrointestinal diseases, a history of gastric surgery, or those currently taking medications that influence gastrointestinal motility are excluded. Additionally, individuals with severe comorbidities, pregnant or breastfeeding women, and those receiving drugs known to induce dyspepsia, such as NSAIDs or digoxin, are not considered for inclusion.

**Ethical Considerations:** Approval was obtained from the institutional ethics committee. Informed consent was obtained from all participants before enrolment.

### Outcome Measures

- Improvement in individual symptoms measured using the Hospital Anxiety and Depression (HAD) scale and the Gastrointestinal Symptom Rating Scale (GSRS).
- Safety and tolerability assessed through adverse event monitoring and laboratory tests (complete blood count, liver function tests, renal function tests).

### Statistical Analysis

- Descriptive statistics will be used to summarize baseline characteristics.
- Outcomes will be analyzed using an intention-to-treat approach.
- Continuous variables will be compared using dependent t-tests.
- Categorical variables will be analyzed using chi-square tests or Fisher's exact tests.
- Statistical analysis was performed using SPSS version 24.

## RESULTS

Table 1 shows the comparison of age between group and founded that minimum age was 18 years and the maximum age was 70 years in both groups. Mean ± SD for Group 1 is 34.76 ± 9.78; for Group 2, it is 33.80 ± 10.97. No significant difference in age distribution was found between the two groups (p = 0.6463).

**Table 1: Age Distribution.**

| Age Interval (years) | Group 1 | | Group 2 | | P value |
|---|---|---|---|---|---|
| | N | % | N | % | |
| 11-20 | 01 | 02 | 04 | 08 | 0.6463 |
| 21-30 | 16 | 32 | 19 | 38 | |
| 31-40 | 22 | 44 | 18 | 36 | |
| 41-50 | 08 | 16 | 05 | 10 | |
| 51-60 | 02 | 04 | 03 | 06 | |
| 61-70 | 01 | 02 | 01 | 02 | |

Table 2 shows that more female patients were observed than male patients. No significant statistical difference was found between the two groups (p = 0.3952).

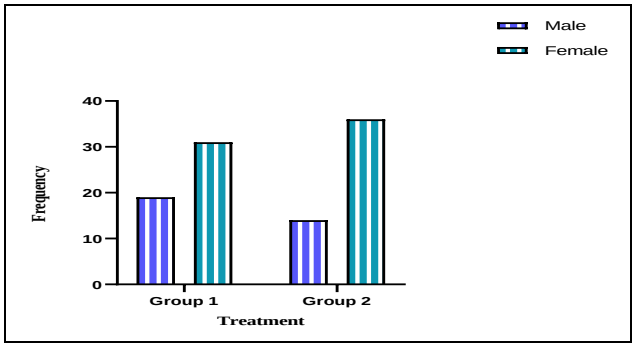


**Table 2: Gender Distribution.**

Figure 1 indicated that BMI analysis showed a comparable pattern between the groups. More overweight patients were observed. No significant difference in BMI was found between the two groups (p = 0.4225).

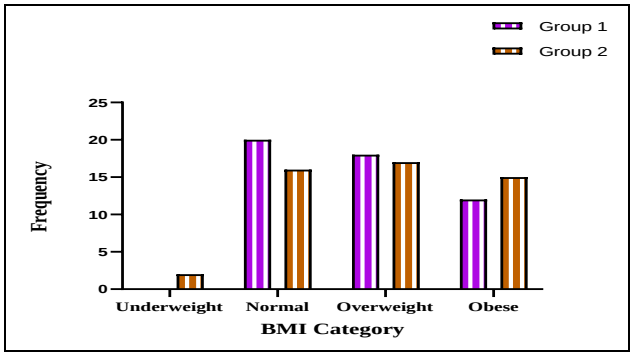


**Figure 1: BMI Distribution.**

Table 3 indicated that hypertension was the most common comorbid condition, followed by hypothyroidism in Group 1. Subjects with no known comorbidities were 80% in Group 1 and 74% in Group 2.

**Table 3: Comorbidities based Distribution.**

| Comorbidity | Group | | | |
|---|---|---|---|---|
| | 1 | | 2 | |
| | N | % | N | % |
| Hypertension | 04 | 08 | 10 | 20 |
| Hypothyroidism | 06 | 12 | 0 | 0 |
| Fatty liver | 0 | 0 | 03 | 06 |
| No | 40 | 80 | 37 | 74 |

Table 4 indicated that symptoms were analyzed for both groups. A significant difference was found in all symptoms before and after treatment in both groups, except for upper abdominal pain in Group 2.

**Table 4: Symptoms Before and After Treatment.**

| Symptom | Group1 | | | | | Group 2 | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Before | | After | | P value | Before | | After | | P value |
| | N | % | n | % | | N | % | N | % | |
| Upper abdominalPain | 50 | 100 | 01 | 02 | <0.0001* | 50 | 100 | 49 | 98 | 0.9999 |
| Upper abdominal Discomfort | 50 | 100 | 0 | 0 | <0.0001* | 50 | 100 | 43 | 86 | 0.0125* |
| Postprandial Fullness | 50 | 100 | 03 | 06 | <0.0001* | 50 | 100 | 37 | 74 | <0.0001* |
| Bloating | 50 | 100 | 02 | 04 | <0.0001* | 50 | 100 | 32 | 64 | <0.0001* |
| Early satiation | 50 | 100 | 01 | 02 | <0.0001* | 50 | 100 | 35 | 70 | <0.0001* |
| Belching | 50 | 100 | 01 | 02 | <0.0001* | 50 | 100 | 33 | 66 | <0.0001* |
| Nausea | 50 | 100 | 03 | 06 | <0.0001* | 50 | 100 | 22 | 44 | <0.0001* |
| Vomiting | 50 | 100 | 03 | 06 | <0.0001* | 50 | 100 | 13 | 26 | <0.0001* |
| Heart burn | 50 | 100 | 01 | 02 | <0.0001* | 50 | 100 | 34 | 68 | <0.0001* |
| Constipation | 50 | 100 | 06 | 12 | <0.0001* | 50 | 100 | 39 | 78 | 0.0005* |

Table 5 indicated that significant difference was found in the GSRS score before and after treatment in both groups.

**Table 5: GSRS Score.**

| Group | Review | Minimum | Maximum | Mean ± SD | P value |
|---|---|---|---|---|---|
| 1 | Before | 05 | 14 | 10.66 ± 2.72 | <0.0001* |
| | After | 0 | 07 | 2.70 ± 1.83 | |
| 2 | Before | 07 | 14 | 12.18 ± 1.94 | <0.0001* |
| | After | 03 | 14 | 9.54 ± 2.67 | |

Table 6 indicated that Hospital Anxiety and Depression Scale was evaluated and analyzed for both groups. A significant difference was found in the HAD score before and after treatment in Group 1 but not in Group 2.

**Table 6: HAD Score.**

| Group | Review | Minimum | Maximum | Mean ± SD | P value |
|---|---|---|---|---|---|
| **1** | Before | 07 | 20 | 14.66 ± 2.89 | <0.0001* |
| | After | 03 | 13 | 7.20 ± 2.40 | |
| **2** | Before | 07 | 21 | 12.98±3.82 | 0.5283 |
| | After | 06 | 19 | 12.70 ± 3.81 | |

Table 7 indicated that most common adverse drug reaction reported was gastrointestinal upset, with no significant difference between the groups (p = 0.6031).

**Figure 8: Adverse drug reaction.**

| ADR | Group | | | | P value |
|---|---|---|---|---|---|
| | Group 1 | | Group 2 | | |
| | N | % | n | % | |
| GI upset | 06 | 12 | 06 | 12 | 0.6031 |
| Headache | 01 | 02 | 0 | 0 | |
| No | 43 | 86 | 44 | 88 | |

## DISCUSSION

This study aimed to evaluate the efficacy and safety of acotiamide in the treatment of functional dyspepsia (FD) in non-diabetic patients, comparing its effects to those of proton pump inhibitors (PPIs), flupentixol, and melitracen. The findings present valuable insights into the demographic characteristics, symptom alleviation, and overall safety profile associated with each treatment approach.

### Age and Gender Distribution

The age distribution between the two treatment groups was well-matched, with no statistically significant differences detected (p = 0.6463). This parity minimizes the risk of age-related biases impacting the evaluation of efficacy and safety outcomes. Furthermore, analysis of gender distribution indicated a greater proportion of female patients in both groups, reflecting the higher prevalence of functional dyspepsia (FD) among females. The absence of a significant difference in gender distribution (p = 0.3952) enhances the robustness and credibility of the comparative analysis.

### Body Mass Index (BMI) and Comorbidities

BMI analysis showed that most patients were either overweight or obese, with no significant differences between the two groups (p = 0.4225). This indicates that BMI does not confound the treatment outcomes. Comorbidities, such as hypertension and hypothyroidism, were present but did not differ significantly between groups, suggesting that the observed treatment effects can be attributed more directly to the medications themselves rather than underlying health conditions.

### Symptom Relief

A significant reduction in all FD symptoms was observed in both treatment groups, highlighting the effectiveness of acotiamide as well as the comparators. However, Group 1 (acotiamide) demonstrated superior symptom relief across several metrics. For instance, upper abdominal pain was almost completely resolved in Group 1 (p < 0.0001), while Group 2 (comparators) showed only a marginal reduction (p = 0.9999). This trend was consistent across other symptoms such as upper abdominal discomfort, postprandial fullness, and bloating, where acotiamide outperformed the alternative treatments, showcasing its potent prokinetic effects.

### GSRS and HAD Scores

The Gastrointestinal Symptom Rating Scale (GSRS) and Hospital Anxiety and Depression Scale (HAD) further corroborated these findings. Group 1 showed a significant improvement in GSRS scores (p < 0.0001), indicating substantial alleviation of gastrointestinal symptoms. In contrast, Group 2, although improved, did

not achieve the same level of symptom relief. Similarly, the HAD scores improved significantly in Group 1 ($p < 0.0001$), suggesting a notable reduction in anxiety and depression symptoms associated with FD. This improvement was not mirrored in Group 2 ($p = 0.5283$), underscoring the additional benefit of acotiamide in addressing the psychological aspects of FD.

**Adverse Drug Reactions (ADR)**

Both groups reported minimal adverse drug reactions, with gastrointestinal upset being the most common. The incidence of ADRs was comparable between the groups ($p = 0.6031$), indicating that acotiamide is as safe as the traditional treatments. The low occurrence of headaches in Group 1 (2%) compared to Group 2 (0%) is not statistically significant but may suggest a slightly better tolerability profile for acotiamide.

## CONCLUSION

Our study concluded that Acotiamide demonstrates significant efficacy and tolerability in the management of Functional Dyspepsia (FD) compared to the combination therapy of Rabeprazole, Flupentixol, and Melitracen. Acotiamide effectively alleviates FD symptoms and presents a safety profile on par with proton pump inhibitors and psychotropic agents. The notable improvement in both gastrointestinal and psychological parameters underscore Acotiamide's potential as a holistic treatment for FD. These results support Acotiamide's integration into current therapeutic strategies, offering patients a reliable and well-tolerated alternative to conventional treatment options.

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**CONFLICT OF INTEREST:** Nil.

## REFERENCES

1. Corsetti M, Fox M. The management of functional dyspepsia in clinical practice: what lessons can be learnt from recent literature?. F 1000 Res., 2017; 6: 1778. Published, 2017 Sep 28; doi:10.12688/f1000research.12089.1.
2. Voiosu TA, Giurcan R, Voiosu AM, Voiosu MR. Functional dyspepsia today. *Maedica (Bucur)*, 2013; 8(1): 68-74.
3. Kim SE, Kim N, Lee JY, et al. Prevalence and Risk Factors of Functional Dyspepsia in Health Check-up Population: A Nationwide Multicenter Prospective Study. *J Neurogastroenterol Motil*., 2018; 24(4): 603-613. doi:10.5056/jnm18068.
4. Chaves J, Pita I, Libânio D, Pimentel-Nunes P. Pharmacological Treatment of Functional Dyspepsia: An Old Story Revisited or a New Story to Be Told? A Clinical Review. *GE Port J Gastroenterol*, 2022; 30(2): 86-97. Published, 2022 Nov 4; doi: 10.1159/000526674.
5. Ueda M, Iwasaki E, Suzuki H. Profile of acotiamide in the treatment of functional dyspepsia. *Clin Exp Gastroenterol*, 2016; 9: 83-88. Published, 2016 Apr 6; doi:10.2147/CEG.S72172.
6. Terry N, Margolis KG. Serotonergic Mechanisms Regulating the GI Tract: Experimental Evidence and Therapeutic Relevance. *Handb Exp Pharmacol*, 2017; 239: 319-342. Doi: 10.1007/164_2016_103.
7. Xiao G, Xie X, Fan J, et al. Efficacy and safety of acotiamide for the treatment of functional dyspepsia: systematic review and meta-analysis. *Scientific World Journal*, 2014; 2014: 541950. doi:10.1155/2014/541950.
8. Freedberg DE, Lebwohl B, Abrams JA. The impact of proton pump inhibitors on the human gastrointestinal microbiome. *Clin Lab Med*., 2014; 34(4): 771-785. doi:10.1016/j.cll.2014.08.008.
9. Pinto-Sanchez MI, Yuan Y, Hassan A, Bercik P, Moayyedi P. Proton pump inhibitors for functional dyspepsia. *Cochrane Database Syst Rev*., 2017; 11(11): CD011194. Published, 2017 Nov 21; doi:10.1002/14651858.CD011194.pub3.
10. Lu Y, Chen M, Huang Z, Tang C. Antidepressants in the Treatment of Functional Dyspepsia: A Systematic Review and Meta-Analysis. *PLoS One*, 2016; 11(6): e0157798. Published, 2016 Jun 16; doi:10.1371/journal.pone.0157798.
11. Wang Y, Shrestha N, Shen Y, Luo F. Effectiveness and Safety of Flupentixol and Melitracen Tablets for the Treatment of Patients with Persistent Idiopathic Facial Pain: A Retrospective Observational Study. *Pain Physician*, 2024; 27(4): 263-272.