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# Efficacy and Safety Assessment of Acotiamide and Levosulpiride in Functional Dyspepsia

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***Abstract:***
***Aim:*** *To assess the Efficacy and Safety of Acotiamide and Levosulpiride in Functional Dyspepsia*
***Methods:*** *Total 60 patients were selected for the study.Patients were divided into 2 groups.*
*Group A received 100mg acotiamide TDS before meal for 8wks.Group B received levosulpiride 25 mg TDS for 8 wks.Treatment outcome categorized as excellent:Complete relief of symptoms,*
*Good:improvement with only occasional symptoms,nil:no improvement. Safety parameters were assessed by noting the tolerability of adverse effects.*
***Result:*** *Patients treated with Acotiamide showed more improvement in symptoms of FD and better tolerated in comparision to Levosulpiride.*
***Conclusion:*** *Acotiamide found to be quiet safe and effective drug in patients of Functional Dyspepsia in comparision to Levosulpiride.*
***Keywords:*** *Acotiamide,Levosulpiride,Functional Dyspepsia*

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## I. Introduction

Functional Dyspepsia (FD) is a clinical syndrome defined as the presence of symptoms thought to originate from the gastroduodenal region in the absence of organic,systemic,or metabolic disease likely to explain to explain the symptoms.(1) FD is a common morbid condition and has a great impact on quality of life,healthcare usage,and socioeconomic costs.(2)Dyspepsia has been recently considered as a biopsychosocial disorder with dysregulation of the brain-gut axis central in origin of disease.(3)The pathophysiology of functional dyspepsia is unknown,but a number of mechanism have been suggested.There is considerable evidence to suggest an association between disordered motility and symptom production in functional dyspepsia.Motor dysfunction includes antral hypomotility and delayed gastric emptying,myoelectrical abnormalities of the gastric rhytm,abnormal tone (impaired gastric accommodation), or maldistribution of food within stomach.(4)The underlying pathophysiology of FD is incompletely understood and may be heterogenous,possibly including mechanism such as hypersensitive to gastric distension.(5)Impaired meal accomodation.(6,7)and delayed gastric emptying.(8,9)According to Rome III Consensus,the main symptoms of FD include bothersome postprandial fullness,early satiety,epigastralgia,and epigastric burning and FD is further subdivided into two categories:meal induced postprandial distress syndrome(PDS,Characterized by postprandial fullness and early satiation)and epigastric pain syndrome(EPS,characterized by epigastric pain and burning)(1)
The role of Helicobacter pylori in symptom production in the absence of mucosal lesions is controversial,although H.pylori eradication is recommended in patients in whom no other causes of symptoms has been identified.(10).

According to motor and/or sensory functional abnormalities causing dyspeptic symptoms treatment options with prokinetics,serotonergic agents,antacids and pain modulating medications have been proposed,although proton-pump inhibitor drugs (PPIs),histamine -2 receptor antagonists, and prokinetic agents are the most commonlyused.(11,12) Levosulpiride(substituted benzamide:a levo-isomer of Sulpiride) acts selectively at Dopamine type 2 receptors,which exerts antidopaminergic activity at both D1 and D2 receptor subtypes and has action on both central and peripheral levels.(13)Levosulpiride ,a selective dopamine $D_2$ receptor antagonist with prokinetic activity,is therapeutic option in management of functional dyspepsia on the basis of dopaminergic pathways controlling gastrointenstinal motility.(14)
Acotiamide is a new prokinetic agent which exerts its gastrokinetic activity by enhancement of acetylcholine release via acting as an antagonist on the M1 and M2 muscarinic receptors in the enteric nervous system and inhibiting acetylcholinesterase activity.(15,16)Furthermore,it may also act directly on the gut and indirectly on central nervous system by way of the brain-gut axis.(17)

## II. Materials & Method

The study was conducted in Apollo Hospital Bhubaneswar at Gastroenterology OPD
Total 60 patients were selected.Study period was 4wks.Patient were divided into 2 groups .
30 patients in each group.
Group A received 100mg acotiamide TDS before meal for 8 weeks
Group B received levosulpiride 25 mg TDS for 8 weeks
Patients diagnosed as Functional Dyspepsia aged between 25-50 were included in the group.At least three of the following symptoms post prandial bloating,abdominal pain,discomfort,belching,regurgitation,nausea,vomiting,heart burn,early satiety & abdominal fullness must be present at least twice a week within the preceding 3 weeks.(18)
Patients having Organic lesion,Gall stone,pancreatic disease,intenstinal dysfunction,pregnant women,nursing mother and patients treated with the drugs and medications that were known to affect GI motility were excluded from study.

## III. Study Design

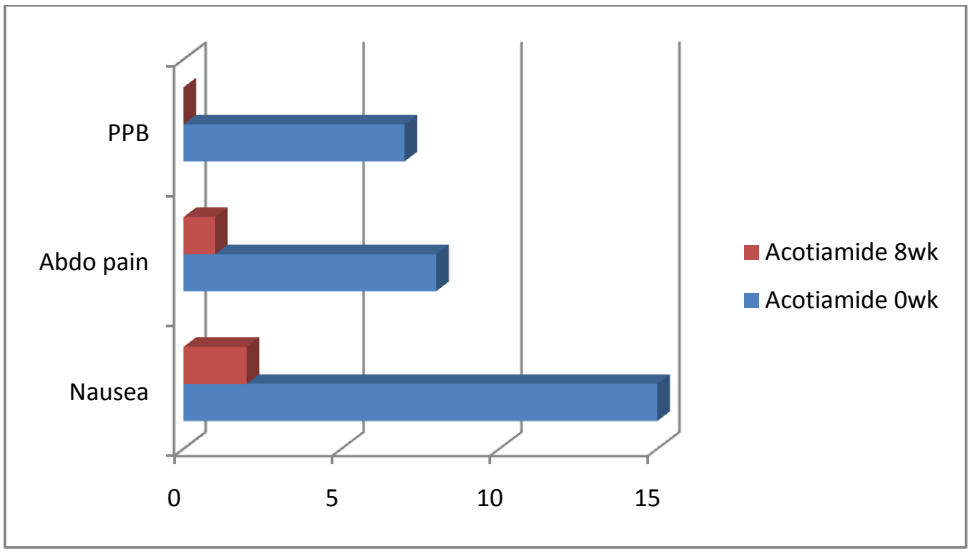
This is a prospective,cohort study conducted for 8 weeks.Enrolled patients were treated with acotiamide or levosulpiride for 8 weeks.Patients were assessed at $4^{nd}$ and $8^{th}$ week.
Efficacy Parameters:
Severity of Symptoms were assessed by following grading system(13)
Using a 3 Point Scale 1=mild,2=moderate,3=severe on enrollment and on completion of 4 week and 8week treatment period outcome categorized as excellent [Complete relief of symptoms],good[improvement with only occasional symptoms] and nil[no improvement].
Safety Parameters:
Based on adverse effects:
To assess tolerability adverse effects related to systems like GIT,CVS,CNS,Endocrine and others noted at each visit .
Based on investigation:
Serum prolactin level were done at 0 week and at end of 8 week.

## IV. Statistical Analysis

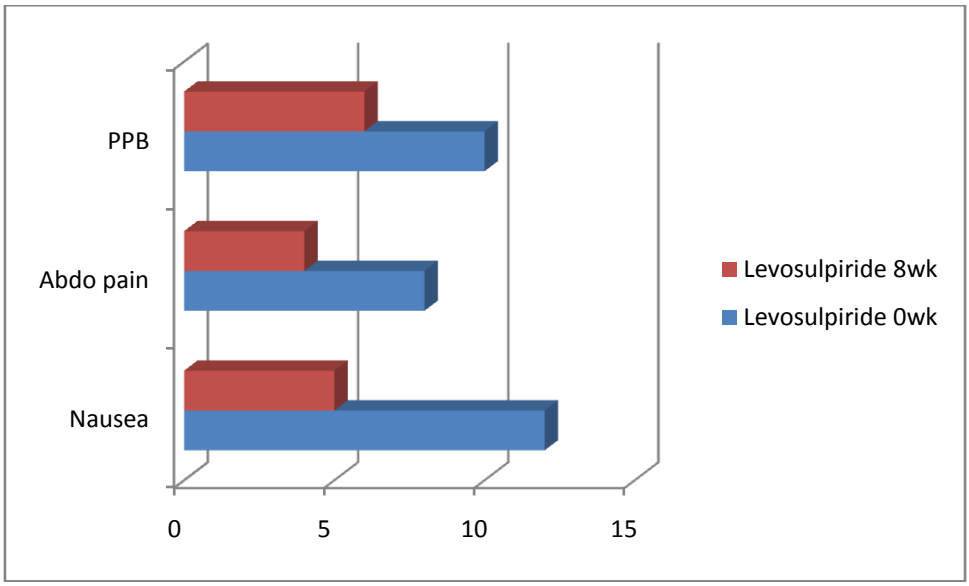
Data is expressed as numbers and percentage.The Chi square test was used for analysis of data.
$p< 0.05$ considered as statistically significant and $p< 0.001$ as highly significant.

## V. Result

There is more improvement of features of Nausea,Abdominal Pain & Post Prandial Bloating (PPB) with administration of Acotiamide in comparision to Levosulpiride which is represented in Graph-1 & 2.




Symptoms of FD with administration of Acotiamide(Graph-1)




Symptoms of FD with administration of Levosulpiride (Graph-2)

N-60 Gr A-30 Gr B-30

| | GROUP A | GROUP B |
|---|---|---|
| MILD | 4(13.3%) | 8(26.6%) |
| MODERATE | 10(33.3%) | 15(50%) |
| SEVERE | 16(53.3%) | 7(23.3%) |

Severity at presentation/0wk (Table 1)

| | GROUP A | GROUP B |
|---|---|---|
| EXCELLENT | 15(50%) | 9(30%) |
| GOOD | 8(26.6%) | 15(50%) |
| NIL | 7(23.3%) | 6(20%) |

Control of symptoms after 4 wks of therapy (Table 2)

| | GROUP A | GROUP B |
|---|---|---|
| EXCELLENT | 22(73.3%) | 12(40%) |
| GOOD | 6(20%) | 8(26.6%) |
| NIL | 2(6%) | 10(33.3%) |

Control of symptoms after 8 wks of therapy (Table 3)

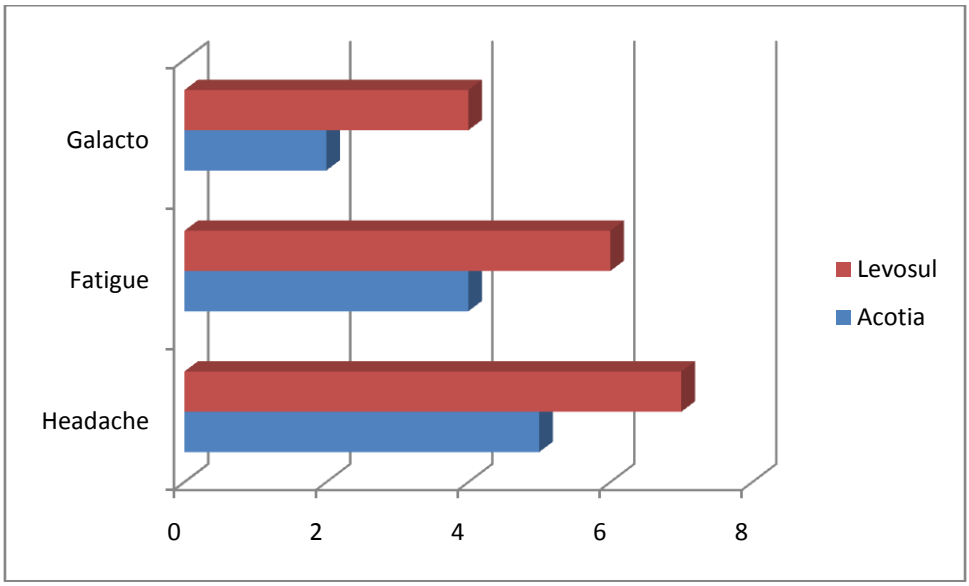
It is observed from the above tables that the symptoms of improvement is more with administration of acotiamide in comparision to levosulpiride.

Comparision of adverse effects between Gr A & Gr B has been shown in Table 4.

| | GROUP A | GROUP B |
|---|---|---|
| Headache | 5(16.6%) | 7(23.3%) |
| Fatigue | 4(13.3%) | 6(20%) |
| Galactorrhoea | 2(6.6%) | 4(13.3%) |

Adverse Effects of Group A & B (Table 4)

From Table 4 it is observed that the incident of adverse effects are more in Group B patients in comparision to Group A patients.This result has been graphically represented in Graph 3.




Adverse effects of Gr A & Gr B (Graph-3)

## VI. Discussion

In this prospective,cohort study Acotiamide and Levosulpiride were administered to patients of functional dyspepsia daily for 8 weeks.Then Safety and efficacy parameters were assessed. Levosulpiride (substituted benzamide:a levo-isomer of Sulpiride) acts selectively at Dopamine type 2 receptors,which exerts antidopaminergic activity at both D1 and D2 receptor subtypes and has action on both central and peripheral levels.(13)Acotiamide is a new prokinetic agent which exerts its gastrokinetic activity by enhancement of acetylcholine release via acting as an antagonist on the M1 and M2 muscarinic receptors in the enteric nervous system and inhibiting acetylcholinesterase activity.(15,16) Both groups(Group A &B) were compared taking into consideration of severity of symptoms & tolerability of adverse effects.

## VII. Conclusion

There is more improvement of features of Functional Dyspepsia in patient treated with Acotiamide in comparision to Levosulpiride .It is observed that Acotiamide is better tolerated in comparision to Levosulpiride in patients with Functional Dyspepsia. Acotiamide found to be quiet safe and effective drug in patients of Functional Dyspepsia in comparision to Levosulpiride

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