International Journal of Community Medicine and Public Health
Neeraja K et al. Int J Community Med Public Health. 2023 Mar;10(3):1061-1064
http://www.ijcmph.com
pISSN 2394-6032 | eISSN 2394-6040

DOI: https://dx.doi.org/10.18203/2394-6040.ijcmph20230314

Original Research Article

Effect of asenapine and iloperidone on weight gain in patients of psychosis: a prospective study

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Received: 30 January 2023
Accepted: 02 February 2023

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ABSTRACT

Background: Second generation or atypical antipsychotics are the most commonly used effective drugs for psychotic disorders like schizophrenia. But the drawback with the use of these drugs is that they tend to cause adverse effects; among which weight gain is an important one with risk of diabetes and adverse cardiovascular events. Weight gain is less with newer atypical antipsychotics. This study was conducted to compare weight gain with two newer atypical antipsychotic drugs, Asenapine and Iloperidone
Methods: It is a prospective study conducted on a total of 60 subjects who were diagnosed with schizophrenia or acute psychosis according to ICD 10 guidelines. The subjects were divided into two groups of 30 each. They received Asenapine (5-20 mg) and Iloperidone (8-24 mg) and were followed-up with weight measurements at baseline, week 1, week 3 and week 6.
Results: Out of 60 subjects, 5 patients were lost to follow-up. The mean weight gain in each of the groups was 2.18±1.84 kg with Iloperidone and 1.63±1.28kg with Asenapine, which was statistically not significant. Weight gain was dose-dependent, 3.63kg mean weight gain with 15-20 mg Asenapine and 3.45 kg with 18-24 mg Iloperidone; which was statistically significant.
Conclusions: Weight gain was seen with both the atypical antipsychotic drugs, Asenapine and Iloperidone; which was only of mild to moderate degree. Among the two study drugs, Iloperidone showed more weight gain than Asenapine.

Keywords: Asenapine, Iloperidone, Psychosis, Weight gain

INTRODUCTION

Antipsychotics form the mainstay of treatment for patients with schizophrenia, but many, especially the second-generation antipsychotics, are associated with weight gain, lipid disturbance, and glucose dysregulation, thereby contributing to the development of metabolic syndrome.[1] Approximately a third of people with schizophrenia have metabolic syndrome, with prevalence as high as 69% in those with chronic illness.[2] The prevalence of obesity, type 2 diabetes, and hypercholesterolemia in people with schizophrenia is estimated to be 3-5 times higher than in the general population.[3] Compared with the general population, people with schizophrenia are twice as likely to have a diagnosis and die as a consequence of cardiovascular disease.[4] The mortality gap between people with schizophrenia and the general population is growing, suggesting a need for improved understanding of the factors underlying cardiovascular disease in this group[5].Just as extrapyramidal side effects result in poor compliance with FGAs, weight gain is a cause for treatment noncompliance with SGAs. However, direct evidence linking weight gain to poor adherence is sparse. A systematic review and exploratory meta-analysis by De Hert et al had shown the potentially relevant short term metabolic effects for Asenapine and Iloperidone. A study by Weiden et al found that patients who are obese are 13 times more likely to discontinue medication because of weight gain than non-obese patients.[6] A meta-analysis by

De Hert et al observed that the newer antipsychotics asenapine, iloperidone, paliperidone and lurasidone caused significant weight gain. Clinically significant weight gain of more than 7% was caused by all the drugs except lurasidone.[7] Comparative effects of 18 antipsychotics on metabolic function in patients with schizophrenia by Toby et al found the evidence of weight gain with iloperidone. Iloperidone, Asenapine, and Lurasidone: a brief overview of 3 new second generation antipsychotics study by Citrome et al showed that commonly observed adverse events with asenapine in short term trial were somnolence, oral hypoesthesia, akathisia, and weight gain.[8] Commonly observed adverse events with iloperidone in short term trial were dizziness, dry mouth, fatigue, nasal congestion, orthostatic hypotension, somnolence, tachycardia and weight increase.[9] Schizophrenia imposes a great burden on both economical and quality of life. It is estimated that societal cost ranges from 37% to 214% of GDP per capita and it is ranked the sixteenth highest cause of years lived with disability out of the 25 most common diseases worldwide.[10,11]

Aim and objectives

Aim and objectives of current study were to compare weight gain propensity associated with Asenapine and Iloperidone and to compare cost effectiveness of Asenapine and Iloperidone

METHODS

Study design, location and duration

Current study is a prospective study conducted at Government medical college, Anantapuramu, Andhra Pradesh, for a period of 3 months from August 2022 to October 2022.

Study population and sample size

Total 60 patients of psychosis patients attending to department of Psychiatry, GMC Anantapuramu, Andhra Pradesh were taken in current study.

Inclusion criteria

Inclusion criteria for current study were; patients attending psychiatry out-patient department irrespective of gender, with age more than 18 years diagnosed with acute psychosis and schizophrenia according to ICD 10 were considered for the study and hence included, patients who accepted to give informed consent under treatment with SGA and newly diagnosed case of acute psychosis who met criteria of ICD-10.

Exclusion criteria

Exclusion criteria for current study were; the patients with known history of poor compliance to treatment (in episodic psychosis), those with severe medical or psychiatric co morbid conditions and women who were pregnant.

Procedure

Study participants were enrolled in the study as per the inclusion criteria. Demographic details, personal history, family history, drug history and clinical characteristics like body weight were recorded. The drugs were allotted as per the computerized randomization schedule. Asenapine was administered at the dose of 5-20 mg, and iloperidone at the dose of 8-24 mg. No concomitant medications were allowed. The patients were asked to come for follow up on week 1, week 3 and week 6. Weight was measured using digital weighing scale and noted in each visit. Adverse effects to asenapine and iloperidone were also recorded. Informed written consent was obtained from all the study participants in local language before their inclusion in the study.

Data analysis

The data collected was analysed by using Statistical Package for Social sciences (SPSS) for windows software version (26.0). Descriptive statistics were performed for baseline and demographic characteristics. Mean and standard deviation were calculated for continuous variables. Unpaired t- test was used to find the mean difference between two groups. The level of significance will be set at 0.05.

RESULTS

As per the inclusion criteria, a total of 60 study participants were enrolled in the study. Demographic characteristics among the 60 study participants in which 27 (45%) and 33 (55%) study participants were males and females respectively, the majority of patients were between the age groups of 26-40 years is depicted in (Table 1).

Table 1: The baseline demographic characteristics of study participants.

Demographic profile	Characteristics	N (%)
Age (years)	18-25	17(28.3)
	26-40	36(60)
	>40	7(11.6)
Gender	Male	27(45)
	Female	33(55)
Education	Illiterate	44(73.3)
	Literate	16(26.6)
Marital status	Married	36(60)
	Separated	6(10)
	single	18(30)

Majority of them were illiterates and married. Mean weight gain at sixth week between Asenapine and Iloperidone is depicted in (Table 2). Group A shows mean weight gain of

1.63±1.28 and the group B shows mean weight gain of 2.18±1.84.

Table 2: Association of mean weight gain at 6th week between Asenapine and Iloperidone.

Drug	Weight gain mean±SD	P value
Asenapine	1.63±1.28	0.161
Iloperidone	2.18±1.84	

Table 3: Association between dose of Asenapine and Iloperidone to mean weight gain.

Drug	Dose (mg/day)	Mean±SD	P value
Asenapine	5-10	1.09±0.9	<0.001
	15-20	3.63±0.9	
Iloperidone	8-12	1.14±0.97	<0.001
	18-24	3.45±1.81	

Table 4: Common side effects observed in group A.

Side effect	N (%)
Somnolence	14 (23.3)
Dizziness	16 (26.6)
Fatigue	15 (25)
Headache	15 (25)
Oral hypoesthesia	7 (11.6)

Table 5: Common side effects observed in group B.

Side effect	N (%)
Dizziness	9 (15)
Somnolence	5 (8.3)
Fatigue	11 (18.3)
Nasal congestion	5 (8.3)
Dry mouth	7 (11.6)

Table 6: Cost effectiveness of study drugs.

Name of the drug	Cost of 10 tablets	Total duration	Total cost (rupees)
Asenapine	Rs.425	6 weeks	3570/-
Iloperidone	Rs.160	6weeks	1344/-

Dose dependent weight gain with the above two groups is shown in (Table 3). Group A shows 3.63±0.9 mean weight gain at the dosage of 15-20 mg/day, whereas group B shows mean weight gain of 3.45±1.81 at the dosage of 18-24 mg/day which was statistically significant.

Common side effects in group A patients in which majority of them had dizziness (26%) as most common side effect and oral hypoesthesia (11.6%) as least common side effect are depicted in (Table 4).

Common side effects in group B patients in which majority of them had fatigue (18.3%) as most common side effect and less common side effects were found to be somnolence (8.3%) and nasal congestion (8.3%) is shown in (Table 5).

The cost effectiveness of both drugs, in which Iloperidone is found to be more cost effective than Asenapine is shown in (Table 6). Mean weight gain at 1st, 3rd and 6th weeks by Iloperidone is more than that of Asenapine is depicted in (Figure 1).

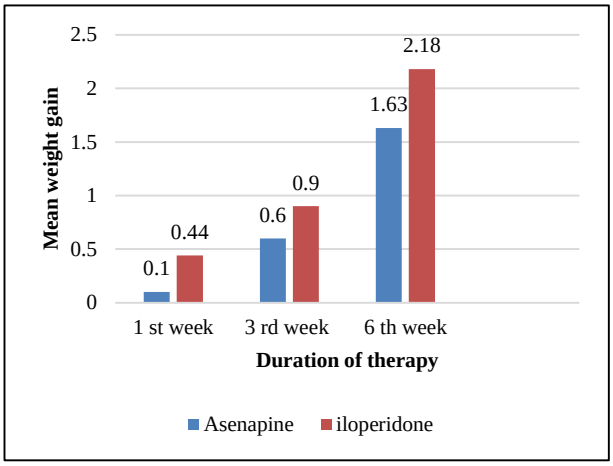

Figure 1: Weight gain in both the groups at 1st, 3rd, 6th weeks of therapy (n=60).

DISCUSSION

The present study showed that treatment with antipsychotic drugs like Asenapine and Iloperidone at higher doses increased risk of weight gain. De Hert et al in their study had shown that there were potentially relevant short term metabolic effects and significant weight gain for Asenapine and Iloperidone similar to the present study.[7] Comparative effects of antipsychotics drugs by Toby et al found evidence of weight gain with Iloperidone.[12] The present study showed that most common adverse drug reactions reported in Group A were somnolence, dizziness, fatigue, headache, oral hypoesthesia and the most common adverse drug reactions reported in Group B were somnolence, dizziness, fatigue, nasal congestion and dry mouth. A study by Leslie et al showed that commonly observed adverse events with Asenapine were somnolence, oral hypoesthesia, akathisia and weight gain.[13] Commonly observed adverse events with Iloperidone were dizziness, dry mouth, fatigue, nasal congestion, orthostatic hypotension, somnolence, tachycardia and increased weight. Present study on cost effectiveness of drugs shown that asenapine costs more than iloperidone for the duration of six weeks. Comparative evaluation of cost effectiveness between typical antipsychotic and atypical antipsychotics in the treatment of stable schizophrenia by Garg et al shown that atypical antipsychotics were found to be more cost effective compared to typical antipsychotics.[14]

Limitations

Limitation of current study was that it was difficult to accurately determine whether they gained weight from medication and/or as a result of other lifestyle changes.

CONCLUSION

This study showed weight gain with both Asenapine and Iloperidone and higher doses were associated with increased weight gain. The majority of patients in both the groups showed a weight gain of around 1-3 kg. This weight gain could be attributed to antagonism of 5-HT2C/5-HTIA/H1/D2 receptors. Mean weight gain was more with Iloperidone in all the three visits. Hence, Iloperidone has more propensities to produce weight gain when compared to Asenapine. Hence these side effects should be taken into consideration before prescribing especially in obese patients. Long term large scale studies are required to confirm this research work. Adverse effects are also seen with the study drugs.

ACKNOWLEDGEMENTS

Authors are thankful to all the patients, their attendants, faculty of Psychiatry department, GMC, Anantapuramu for their participation and support.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Neeraja K, Keerthi C, Sonia SS. Effect of asenapine and iloperidone on weight gain in patients of psychosis: a prospective study. Int J Community Med Public Health 2023;10:1061-4.