EFFICACY OF ARIPIPRAZOLE IN TREATMENT OF SCHIZOPHRENIA IN POPULATION OF CENTRAL INDIA

Dr. Omprakash Raichandani¹, Dr. Abdul Faheem Khan², Mrs. Sapna Raichandani³

¹Associate Professor, Psychiatry, NSCB Medical College Jabalpur

²Head, Medical Information, Sanofi India Limited, Mumbai

³M.Pharm. Honorary Lecturer, Shri Ram College of Pharmacy, Jabalpur

Article Info: Received 06 January 2020; Accepted 28 January, 2020

DOI: <https://doi.org/10.32553/ijmbs.v4i1.968>

Corresponding author: Dr. Omprakash Raichandani

Conflict of interest: No conflict of interest.

Abstract

Background: During the past decade, there has been some progress in the pharmacotherapy of schizophrenia and schizoaffective disorder. Aripiprazole is recommended at a dose of between 10 and 15 mg/day in the treatment of schizophrenia, with a dose range considered to be effective, between 10 and 30 mg/day.

Objective: To study the efficacy and safety of Aripiprazole in low doses of 15 mg versus high doses of 30 mg in the treatment of Schizophrenia.

Methods: Total 60 new and old patients (who are not on any treatment) between 18-60 years of either gender who meet the diagnostic criteria as per DSM-IV classification for schizophrenia and schizoaffective disorder. Patients were randomly divided into 2 groups on single blind study criteria. Group-I: Aripiprazole 15 mg once a day, morning dose for 6 weeks. Group-II: Aripiprazole 30 mg once a day, morning dose for 6 weeks. Efficacy assessment included at baseline and at 6 weeks end study scoring on PANSS, EPRS and CGI.

Results: In both the groups aripiprazole showed the efficacy by improving the number of patients. In group-I, 20 patients has shown the improvement in overall scores of all scales. In group-II, 16 patients have shown the improvement in overall scores in different scales.

Conclusions: Aripiprazole is effective in schizophrenia and schizoaffective disorder, low doses of 15 mg is equally effective as high dose of 30 mg.

Keywords: Efficacy, Aripiprazole & Schizophrenia.

Introduction

Schizophrenia and schizoaffective disorder are quite common in young adult population, with high incidence rate of chronicity, morbidity and suicidal tendency. Both typical and atypical antipsychotic drugs are used for the treatment of schizophrenia. Schizoaffective disorder shares clinical characteristics with schizophrenia and affective disorder, with patients experiencing concurrent manic, mixed, or depressive episodes during psychosis.^{i, ii}

Aripiprazole is an atypical antipsychotic that is reported to be effective in the treatment of schizophrenia.ⁱⁱⁱ Atypical or second-generation antipsychotics are said to differ from conventional or typical antipsychotics in terms of their effects on the positive and negative symptoms of schizophrenia and on cognition, and in terms of their adverse effect profiles^{iv}. Aripiprazole is the prototype of a 'third generation' of antipsychotics – the so-called dopamine-serotonin-system stabilisers. It is claimed to be at least as effective as haloperidol in the treatment of positive and negative symptoms of schizophrenia, and it

may cause fewer adverse effects. Aripiprazole is reported to be useful in all phases of schizophrenia, and to enhance cognitive function.^v

Pharmacology: Aripiprazole is a quinolinone derivative with a high affinity for dopamine D₂ and D₃ receptors, and serotonin 5-HT_{1A}, 5-HT_{2A} and 5-HT_{2B} receptors. The mechanism of action of aripiprazole is not yet known, but evidence suggests that its efficacy in the treatment of the positive and negative symptoms of schizophrenia and its lower propensity for extra pyramidal symptoms (EPS) may be attributable to aripiprazole's partial agonist activity at dopamine D₂ receptors. At serotonin 5-HT_{1A} receptors, in vitro studies have shown that aripiprazole acts as a partial agonist whereas at serotonin 5-HT_{2A} receptors aripiprazole is an antagonist.^{vi}

The efficacy of aripiprazole has been demonstrated in patients with schizophrenia or schizoaffective disorder. In general, significant reductions from baseline in mean Positive and Negative Syndrome Scale total, positive and negative symptom scores, and Clinical Global Impression Severity of Illness scores were observed in patients with

acute relapse of chronic schizophrenia or schizoaffective disorder receiving recommended (10 or 15 mg/day) or higher-than-recommended (20 or 30 mg/day) dosages of aripiprazole versus those receiving placebo in three well controlled, short-term trials. Aripiprazole 10-30 mg/day was generally well tolerated. The tolerability profile of aripiprazole was broadly similar to that observed with placebo in a meta-analysis of short-term trials in patients with acute relapse of schizophrenia or schizoaffective disorder and in a 26-week trial in patients with chronic stable schizophrenia.⁶

Objectives: To study the efficacy of Aripiprazole in the treatment of Schizophrenia and to compare the efficacy and safety of Aripiprazole in low doses versus high doses of in the treatment of Schizophrenia.

Methods and Materials:

This study was conducted in department of Pharmacology and department of Psychiatry OPD at NSCB Medical College Jabalpur (Madhya Pradesh) India of either gender aged 18-60 years. This clinical research study was conducted to determine the efficacy and safety of aripiprazole in low dose (15 mg) versus high dose (30 mg) in a patient of schizophrenia and schizoaffective disorder.

This study comprised of all the new and old patients (who are not on any treatment) of age group between 18-60 years of either gender who meet the diagnostic criteria as per DSM-IV classification for schizophrenia and schizoaffective disorder and those patients and their relatives who are willing to give consent for the treatment were taken in the study.

Selection Criteria:

- **Inclusion criteria** – (i) all the new and old patients (who are not on any treatment) of either sex who met the diagnostic criteria as per DSM-IV classification for Schizophrenia or Schizoaffective disorder were taken in the study. (ii) Those patients and their relatives who are willing to give consent for the treatment.
- **Exclusion criteria:** (i) Schizophrenic patients who are taking any antipsychotic drug treatment in last one month. (ii) If the subject is women who is pregnant or breast feeding or at risk of pregnancy during therapy. (iii) If the patient consume alcohol or have drug dependency in the last 6 months. (iv) If the patient is on ketoconazole carbamazepine, levodopa, dopamine agonist, diuretic therapy or is at risk of torsade-de-pointes. (v) Patient hypersensitive to antipsychotic drugs like aripiprazole. (vi) If the patient is suffering from hepatic, renal, metabolic or neurological disorders (Parkinson's disease or other movement disorders). (vii) ECG with long QT interval.

All the new and old patients of Schizophrenia and Schizoaffective disorder who met DSM-IV criteria and not

treated by any antipsychotic drugs in past one month is to be taken on all OPD days. Prior written informed consent from each patient and their relative's enrolled in this study were taken. The patients who were already on treatment were excluded.

Total 60 patients were taken in the study. Each patient has undergone detailed Psychiatric and medical history with clinical examination. Efficacy assessment included at baseline and at 6 weeks end study scoring on PANSS (Positive and Negative Symptoms Scale), EPRS (Extrapyrimalal Rating Scale) and CGI (Clinical Global Impression) was done. **These patients were randomly divided into 2 groups on single blind study criteria.**

- Group-I: Patients prescribed tablet Aripiprazole 15 mg once a day, morning dose for 6 weeks.
- Group-II: Patients prescribed tablet Aripiprazole 30 mg once a day, morning dose for 6 weeks.

Efficacy and safety data of aripiprazole was compared every week for 6 weeks by applying the 3 standard scales on the patients, these scales were PANNS, EPRS and CGI. Improvement was considered when reduction of >50% score on PANSS on 6th week from baseline. When rating on CGI scale is in between 2-3 at 6 weeks of treatment, it shows the improvement. The analysis of efficacy and side effects of 15 mg versus 30 mg of Aripiprazole was compared on demographic, efficacy and safety profile by using appropriate statistical tests of significance.

Results:

In this study mean age group of patients were 27-32 years, it means young age group is most commonly affected. As given in the table, there was no statistical significant difference observed among the two groups for patient's age, gender, marital status and geographical parameters of rural and urban factors. (Table-1)

Total number of patients were 60, number of dropout patients were 12, so 8 out of 60 patients (13%) didn't completed the study, they didn't follow-up. Total 4 out of the 60 (7%)

In group-I total number of patients was 26 out of which 20 (77%) patients showed improvement and in group-II 16 (73%) patients out of 22 patients showed improvement. The number of improved patients shown by effectiveness of drug reflects the efficacy of Aripiprazole. In both the groups aripiprazole showed the efficacy by improving the number of patients. In group-I 20 patients has shown the improvement in overall scores of all scales. In group-II 16 patients has shown the improvement in overall scores in different scales. (Table-2)

In group-I total number of improved patients on PANSS positive scale was 18 patients (69%) out of 26 and in

group-II 12 (55%) patients out of 22 were improved. Both groups showed significantly greater improvement in reduction on the PANSS positive scale from baseline to the end study. On PANSS negative symptom scale 16 patients (62%) out of 26 were improved in group-I and in group-II 16 patients (72%) out of 22 patients were improved. Both groups showed significantly greater improvement in negative symptoms as measured by the PANSS negative symptoms scale. More than 66% of patients showed efficacy for the aripiprazole in both the groups. On GPS scale in group-I 15 patients (58%) out of 26 were improved and in group-II 15 patients (68%) out of 22 were improved. Patients receiving aripiprazole 15 mg or 30 mg has experienced significant reduction from baseline to 6th week with a clinical improvement on GPS scale. .

On CGI scale in group-I, 20 patients (77%) out of 26 were improved and in group-II, 15 patients (68%) out of 22 were improved. In group-I CGI score at baseline is 5.7 and it goes down by 3.6 at the end of 6th week. In group-II CGI score at baseline is 6.1 and it goes down by 3.6 at the end of 6th week. In both the groups the improvement in CGI from baseline to 6th week score is 2.7 which is quite good improvement. Aripiprazole has shown improvement in 35 patients out of 48 patients after completion of 6 weeks study. No significant difference of improvement was found on age, gender, type and duration of illness between 15 mg or 30 mg dose of Aripiprazole.

Limitations of the study: However, less sample size, single blinded study, lacking placebo as a control group are few drawbacks and limitations in this study, but the findings are worth considering in choosing the appropriate antipsychotic medications in the treatment of schizophrenia and schizoaffective disorder.

Table 1: Demographic profile

Parameters	Group-I (Low dose 15 mg)	Group-II (High dose 30 mg)
Age (mean)	32 Years	27 Years
Gender		
Males	22	19
Females	08	11
Marital status		
Married	12	10
Unmarried	18	20
Geography		
Rural	15	20
Urban	15	10
Dropouts patients	04 patients	08 patients
	EPS	EPS
	Patient didn't follow-up	EPS
	Patient didn't follow-up	EPS
	Patient didn't follow-up	5 Patient didn't follow-up

Table 2: Average score of overall efficacy, positive and negative symptoms and average mean score of positive and negative symptoms

Groups	Overall Efficacy		Total patients
	Effective	Not-effective	
Group-I (15 mg)	20	6	26
Group-II (30 mg)	16	6	22
Average score in positive symptoms			
Group-I (15 mg)	18	08	26
Group-II (30 mg)	12	10	22
Average score in negative symptoms			
Group-I (15 mg)	16	10	26
Group-II (30 mg)	16	06	22
Average mean score of positive symptoms			
	Group-I (15 mg)	Group-II (30 mg)	
Total no. of improved patients	18	12	
Baseline	82	90	
At 6 weeks	38	42	
Average mean score of negative symptoms			
Total no. of improved patients	16	16	
Baseline	70	86	
At 6 weeks	36	40	

$P < 0.05$

Table 3: General Psychopathological Scale (GPS), PANSS and CGI Scales

Groups	GPS		Total no. of patients	
	Improved	Not improved		
Group-I (15 mg)	15	11	26	
Group-II (30 mg)	15	07	22	
Groups	Total PANSS		Total no. of patients	
	Effective	Not effective		
Group-I (15 mg)	20	06	26	
Group-II (30 mg)	16	06	22	
Groups	CGI		Total no. of patients	
	Improved	Not improved		
Group-I (15 mg)	20	06	26	
Group-II (30 mg)	15	07	22	
Mean score of GPS, PANSS and CGI				
	15 mg dose		30 mg dose	
Symptoms	Baseline	6 th week	Baseline	6 th week
GPS	50	34	48	32
PANSS Mean score				
Positive	39	21	40	21
Negative	34	18	35	16
Total	73	39	75	37
CGI mean score				
Group-I (15 mg)	5.7	3.6	1	2.7
Group-II (30 mg)	6.1	3.6	1	2.7

$P < 0.05$

Conclusions

There was no statistical significant difference between two groups found on age, gender, rural and urban factors. On comparing the dose of aripiprazole 15 mg with 30 mg once daily is effective and well tolerated in patients with schizophrenia and schizoaffective disorder. Clinical and therapeutic efficacy is more with 15 mg dose of aripiprazole with fewer side effects and with 30 mg dose of

aripiprazole there is high incidence of side effects due to which it results in low efficacy. It means low dose is equally effective as high dose.

On comparison of total PANSS score of both the groups there is >50% improvement in symptoms of patients from baseline to 6 week of study. The result also shows the improvement in PANSS positive and negative scale score which is also reduced by >50%. Improvements in GPS scale score >50% shows the efficacy of aripiprazole in both the groups. CGI >2.7 (=2 is much improved) improvement in score shows the efficacy of aripiprazole in both the groups. To recommend, it would be advisable to use aripiprazole in low doses to prevent the side effects, by using low doses the cost of the treatment is also low

References

1. ⁱGlick ID, Mankoski R et al. The efficacy, safety, and tolerability of aripiprazole for the treatment of schizoaffective disorder: results from a pooled analysis of a sub-population of subjects from two randomized, double-blind, placebo-controlled, pivotal trials. *J Affect Disord.* 2009 May;115(1-2):18-26.
2. ⁱⁱAripiprazole Prescribing Information 2014 updated revised version.
3. ⁱⁱⁱHG. El-Sayeh et al. Aripiprazole for schizophrenia: Systematic review. *BJP* 2006, 189:102-108.
4. ^{iv}Gelder, M., Lopez-Ibor Jr, J. J. & Andreason, N.C. (2000) Antipsychotic and anticholinergic drugs. In *New Oxford Textbook of Psychiatry*, Volume 2.
5. ^vRivas-Vasquez, R. A. (2003) Aripiprazole: a novel antipsychotic with dopamine-stabilising properties. *Professional Psychology: Research and Practice*, 34, 108-111.
6. ^{vi}Swainston Harrison T. Aripiprazole: a review of its use in schizophrenia and schizoaffective disorder. *Drugs.* 2004;64(15):1715-36.