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A comparision of efficacy of risperidone and olanzapine in schizophrenia patients

S. K. Shah[1], *S.P. Ojha* [2], *N.R. Koirala* [2], *V. D. Sharma* [2], *B. Yengkokpam* [1]

[1]Department of Psychiatry, College of Medical Sciences, Bharatpur, Nepal, [2]Department of Psychiatry, Institute of Medicine, Maharajgunj, Nepal

Abstract

Schizophrenia is a leading worldwide mental health problem. It is also one of the common and challenging problems in Nepal. Risperidone and olanzapine is one of the major antipsychotic drug used for schizophrenia patients, however their efficacy is not compared in Nepal. To assess the efficacy of risperidone and olanzapine in schizophrenia patients in Nepalese context. An open-label, randomized, comparative, prospective study was done for 6 weeks. Total of 63 patients attending Psychiatry OPD in Jan to July 2008 at TUTH who could be available for close follow up were enrolled with consent.

Risperidone was given in dose of 3-6 mg and Olanzapine in the dose of 15-20 mg per day. Efficacy and tolerability was assessed using PANSS, CGI, and UKU side-effect checklist. Both groups showed improvement in the entire positive, negative and general psychopathology subscales without significant difference in the two groups. Regarding tolerability, olanzapine was found to have significant sedation, weight gain while with risperidone extrapyramidal side-effects, palpitations, sexual side-effects were significant. Risperidone and olanzapine both are efficacious in the treatment of schizophrenia. Both the drugs have their own side-effects. Long-term efficacy and tolerability needs to be studied. As it has been seen in the ongoing studies, long-term use and side-effect profile, drop-out rates and the increase in metabolic syndromes need more consideration.

Key words: Antipsychotic, Olanzapine, Risperidone, Schizophrenia.

Introduction

Schizophrenia is a major psychotic disorder. The lifetime morbidity risk for schizophrenia is estimated to be 1.0%[1] and appears to be the same for men and women up to age 60 years.[2]

According to DSM-IV-TR, subtypes include paranoid type, in which preoccupation with delusions or auditory hallucinations is prominent; disorganized type, in which disorganized speech and behavior and flat or inappropriate affect are prominent; catatonic type, in which characteristic motor symptoms are prominent; undifferentiated type, which is a nonspecific category used when none of the other subtype features are predominant; and residual type, in which there is an absence of prominent positive symptoms but continuing evidence of disturbance (e.g., negative symptoms or positive symptoms in an attenuated form.[3] Although

Correspondence: S. Shah.

E-mail: sunilshah141@hotmail.com

the prognostic and treatment implications of these subtypes vary, the disorganized type tends to be the most severe and the paranoid type to be the least severe.[4]

Oral atypical antipsychotic drugs are considered in the choice of first-line treatments for individuals with newly diagnosed schizophrenia. Recent reports have shown that olanzapine and risperidone account for nearly half of all the antipsychotics prescribed. Several studies conducted to compare the efficacy and side-effect profile of the two drugs have consistently shown the comparable efficacy with their own adverse effect profile.[5] In Nepal also, there is extensive use of these two drugs and to see the results in the Nepalese population the study was conducted.

Materials and methods

The study was an open, randomized, prospective, comparative. Patients diagnosed as schizophrenia according to ICD-10 DCR between Jan, 2008 and July, 2008 in age group 18-45 yrs, giving informed consent and not having other comorbid mental or physical illness were randomized to risperidone 3-6 mg per day and olanzapine 10-20 mg per day. Patients were either drug naïve or were given one week washout if on any oral neuroleptic. If the patient developed EPS, trihexyphenidyl was started and the particular type of EPS was recorded. Lorazepam was allowed if needed for the stabilization of the patient and disturbed sleep. Drugs received by the patient for any unrelated problems were recorded.

Results

Total number patients enrolled in the study were 63. 32 (50.8%) patients received olanzapine and 31 (49.2%) patients received risperidone. 30 (47.6%) patients were from the age group 15-24 yrs, 26(41.3%) belonged to the age group 25-34yrs and 7(11.1%) belonged to the age group 35 and above. Chi-square test for type of drug and category of age groups was not significant (p = 0.666). The mean age of patients enrolled in the olanzapine group was 25.50 yrs while those in risperidone group was 26.32 yrs. The mean age of the patients in both the groups were not statistically significantly different (p=0.569).

Out of the total 63 patients, 44 (69.8%) were male and 19 (30.2%) were female. There was no significant difference in the sex of the patents in the two study group (p=0.848 on Chi-square test). Out of the total patients 52 (82.5%) belonged to Hindu religion and 11(17.5%) belonged to others. 21(33.3%), 18(28.6%), 23(36.5%) and 1(1.6%) are the number of patients in the study group belonging to Brahmin, Chhetri, Baisya and Sudra castes respectively. 43(68.3%) and 20(31.7%) patients were from the single and married group respectively. On Chi-square test there was no significant statistical difference in the marital status of the patients in the both study group (p=0.573).

There was no statistically significant difference in the education level of the patients allocated in the study groups (Chi-square p=0.582).Out of 63 patients 4(6.3%) were illiterate, 5(7.9%) were primary level, 12(19.0%) were from secondary level, 22(34.9%) studied up to slc 14(22.2%) studied up to intermediate and 6(9.5%) were graduates.

4(6.3%) were doing business, 7(11.1%) were farmers, 1(1.6%) was a teacher, 7(11.1%) were housewives, 15(23.8%) were student, 24(38.1%) were unemployed and 5(7.9%) were doing service. There was no

statistically significant difference in the occupational groups of the two study groups (Chi-square p=0.508). 47(74.6%) belonged to joint family and 16(25.4%) belonged to nuclear family.

A 2(3.2%) belonged to low SES, 60(95.2%) belonged to middle SES and 1(1.6%) belonged to the high SES group. There was no statistically significant difference in the socioeconomic status of the patients enrolled to the study groups (Chi-square p=0.217).

31(49.2%) were from the rural community and 32(50.8%) were from the urban community. There was no statistically significant difference in the locality of the patients in the study groups (Chi-square p=0.617). Baseline scores of patient in both the groups were comparable. With the introduction of drugs the change from baseline after 1, 2, 4 and 6 were recorded and the significance was checked with paired t test which is shown in the graphs with similar pattern of clinical improvement in both groups.

Table 1: The baseline PANSS and CGI scores (0 week) of both drug groups

PANSS and CGI	Type of drug	N	Mean	Std. deviation	Std. error of mean	t-test
Positive scale at 0 wk	Olanzapine	32	43.2188	2.43277	.43006.	p=0.741
	Risperidone	31	43.0000	2.78089	49946	
Negative scale at 0 wk	Olanzapine	32	19.3750	2.43297	.43009.	p=0.192
	Risperidone	31	18.6129	2.13974	38431	
GPS at 0 wk	Olanzapine	32	59.5625	7.63243	1.34924	p=0.008
	Risperidone	31	53.2258	10.64803	1.91244	
Total PANSS at 0 wk	Olanzapine	32	122.1563	10.54976	1.86495	p=0.575
	Risperidone	31	114.8387	10.35727	1.86022	
CGI at 0 wk	Olanzapine	32	5.4063	0.49899	.08821	p=0.498
	Risperidone	31	5.3226	0.47519	.08535	

Table 2: PANSS and CGI scores after 1 wk

ANSS and CGI	Type of drug	N	Mean	Std. deviation	Std. error of mean	t-test
Positive scale at 1 wk	Olanzapine	32	36.0625	2.39539	.42345	p=0.346
	Risperidone	31	35.2581	4.12284	.74048	
Negative scale at 1 wk	Olanzapine	32	15.0313	1.99167	.35208	p=0.291
	Risperidone	31	14.5161	1.84157	.33076	
GPS at 1 wk	Olanzapine	32	48.3750	7.60199	1.34386	p=0.001
	Risperidone	31	41.6452	7.36455	1.32271	
Total PANSS at 1 wk	Olanzapine	32	99.46875	10.24848	1.81169	p=0.703
	Risperidone	31	91.41935	11.21836	2.01488	
CGI at 1 wk	Olanzapine	32	3.4375	.56440	.09977	p=0.733
	risperidone	31	3.4839	.50800	.09124	

Table 3: PANSS and CGI scores after 2 wks

ANSS and CGI	Type of drug	N	Mean	Std. deviation	Std. error of mean	t-test
Positive scale at 2 wk	Olanzapine	32	31.0938	2.34671	.41484	p=0.458
	risperidone	31	30.4516	4.23351	.76036	
Negative scale at 2 wk	Olanzapine	32	11.9063	1.51038	.26700	p=0.282
	risperidone	31	12.3226	1.53595	.27586	
GPS at 2 wk	Olanzapine	32	41.4063	7.40470	1.30898	p=0.002
	risperidone	31	35.5484	6.73715	1.21003	
Total PANSS at 2 wk	Olanzapine	32	84.40625	9.86313	1.74357	p=0.818
	risperidone	31	78.32258	11.14566	2.00182	
CGI at 2 wk	Olanzapine	32	3.0000	.25400	.04490	p=0.314
	risperidone	31	2.9032	.47292	.08494	

Table 4: PANSS and CGI scores after 4 wks

ANSS and CGI	Type of drug	N	Mean	Std. deviation	Std. error of mean	t-test
Positive scale at 4 wk	Olanzapine	32	27.0938	2.84389	.50273	p=0.756
	risperidone	31	26.8065	4.33912	.77933	
Negative scale at 4 wk	Olanzapine	32	10.0938	1.39952	.24740	p=0.009
	risperidone	31	11.0000	1.23828	.22240	
GPS at 4 wk	Olanzapine	32	35.8125	6.77489	1.19764	p=0.006
	risperidone	31	31.1290	6.31264	1.13378	
Total PANSS at 4 wk	Olanzapine	32	73.00000	9.42885	1.66680	p=0.558
	risperidone	31	68.93548	10.70182	1.92210	
CGI at 4 wk	Olanzapine	32	2.4063	.55992	.09898	p=0.715
	risperidone	31	2.3548	.55066	.09890	

Table 5: PANSS and CGI scores of patients on two drugs after 6 wks

ANSS and CGI	Type of drug	N	Mean	Std. deviation	Std. error of mean	t-test
Positive scale at 6 wk	Olanzapine	32	24.3750	3.20030	.56574	p=0.924
	Risperidone	31	24.2903	3.83139	.68814	
Negative scale at 6 wk	Olanzapine	32	9.0313	1.35562	.23964	p=0.001
	Risperidone	31	10.0968	1.04419	.18754	
GPS at 6 wk	Olanzapine	32	31.1250	6.30284	1.11420	p=0.034
	Risperidone	31	27.8065	5.81045	1.04359	
Total PANSS at 6 wk	Olanzapine	32	64.53125	9.20023	1.62639	p=0.498
	Risperidone	31	62.19355	9.73796	1.74899	
CGI at 6 wk	Olanzapine	32	2.0938	.39015	.06897	p=0.367
	Risperidone	31	2.1935	.47745	.08575	

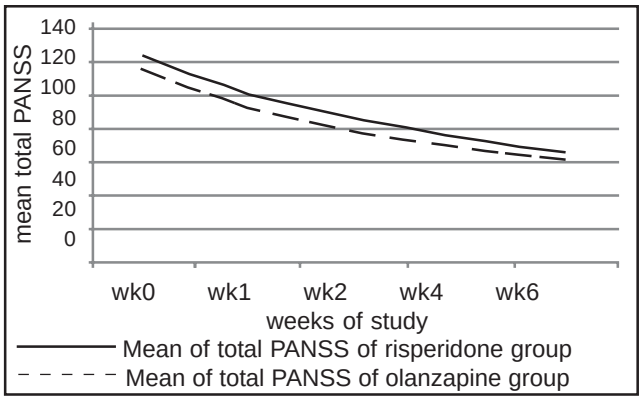

Fig 1: The above figure shows change in mean total PANSS with weeks of study.

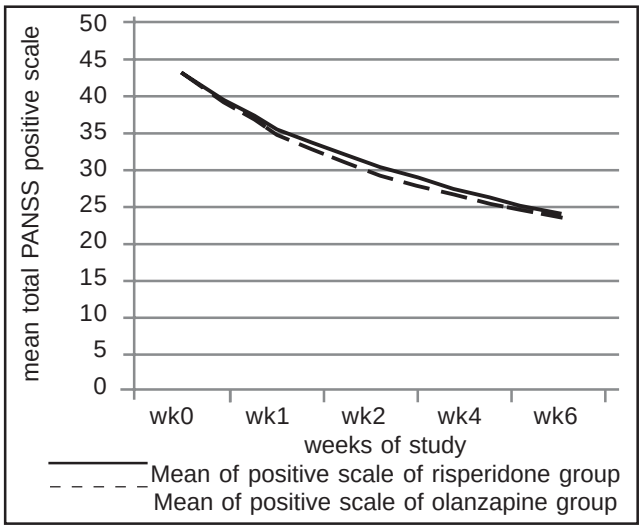

Fig 2: The above figure shows change in mean PANSS positive subscale with weeks of study

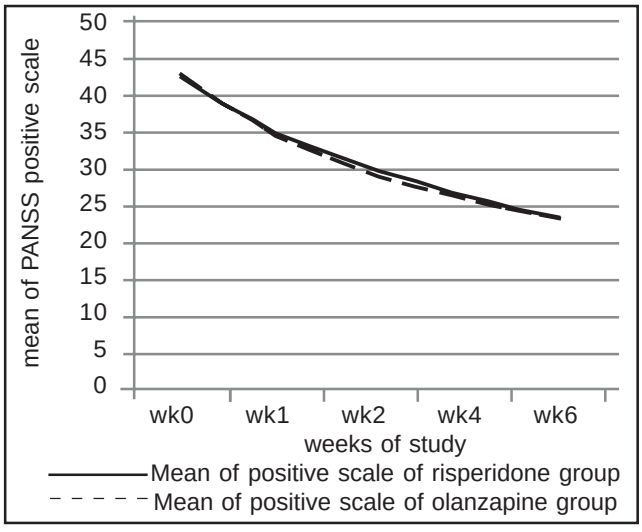

Fig 3: The above figure shows change in mean PANSS negative subscale with weeks of study

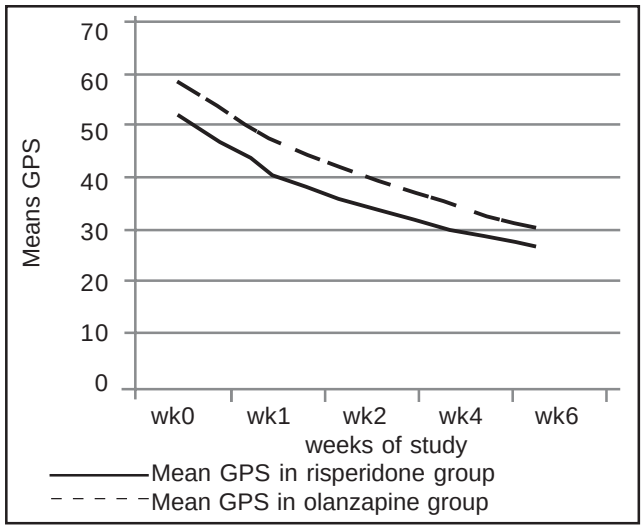

Fig 4: The above figure shows change in mean GPS with weeks of study

Discussion

The newer drugs, such as olanzapine are reputed to have fewer adverse motor effects and are as effective, if not more so, than the older drugs.[6] Risperidone was commonly associated with movement disorders and sexual dysfunction and olanzapine with considerable weight gain. No difference was found for the outcome in efficacy in the short term. One study favored olanzapine for the outcome of relapse/rehospitalisation by 12 months. Most mental state data showed the two drugs to be as effective as each other. Both drugs commonly cause adverse events: 75% given either drug experience an adverse event; 20% anticholinergic symptoms; both groups experienced insomnia although it was more frequent with risperidone; about 30% experienced sleepiness. People given either drug often experienced some extrapyramidal symptoms; 25% of people using risperidone required medication to alleviate these symptoms. People allocated to risperidone were less likely to gain weight compared with those given olanzapine and the weight gain was often considerable and of quick onset. Risperidone

participants were less likely to leave the study due to metabolic side effects and weight gain compared with olanzapine. Patients on risperidone were more likely to experience abnormal ejaculation. Both drugs are associated with high attrition rates; in the long term consistent findings show that 66% of those allocated risperidone left the study early compared with 56% given olanzapine . There was generally a high rate of attrition in the trials and there appears to be little to differentiate between risperidone and olanzapine except on issues of adverse effects. Both drugs are associated with a reduction in psychotic symptoms but both commonly cause unpleasant adverse effects.[7,8]

A Systematic Review on effectiveness and cost of risperidone and olanzapine for schizophrenia[9] concluded relative to risperidone or haloperidol, olanzapine may have a higher acquisition cost, but may decrease inpatient costs and be associated with more optimal medication use patterns.[10]

The Effects of clozapine, risperidone, and olanzapine on cognitive function in schizophrenia[11] was studied which provided strong evidence that clozapine improves attention and verbal fluency and moderate evidence that clozapine improves some types of executive function. Risperidone has relatively consistent positive effects on working memory, executive functioning, and attention, whereas improvement in verbal learning and memory was inconsistent. Preliminary evidence presented here suggests that olanzapine improves verbal learning and memory, verbal fluency, and executive function, but not attention, working memory, or visual learning and memory. The effects of the atypical antipsychotic drugs on cholinergic and 5-HT_{2a}-mediated neurotransmission as the possible basis for their ability to improve cognition.

Studies using multiple doses of risperidone[12] have shown that risperidone causes a dose-related increase in extrapyramidal side effects, with risk highest in doses greater than 6 mg/day.[13] Although precise estimates of the incidence of akathisia are not available, it appears to be less common with low-potency first-generation antipsychotics and even more infrequent with second-generation antipsychotic agents. In this regard, however, it is important to note that risperidone may cause akathisia at the higher end of the dose range.[14] The patient developed akathisia in a dose-dependent manner at dosages between 10 and 15 mg daily of olanzapine, but no EPS.[15]

Conclusion

The results of the study demonstrate the efficacy in the Nepalese context in a six week open-label randomized study. Risperidone (4-6mg) and olanzapine (15-20mg) were similarly effective in all the positive, negative and general psychopathology of schizophrenia in the acute phase. The onset of action was also similar for both the drugs. Risperidone was found to have extrapyramidal symptoms and sexual side-effects while with olanzapine excessive sedation and weight gain was seen in the six week study period. The use of anti-eps drugs was more so in patients treated with risperidone. Cost of acquisition of olanzapine is higher than risperidone but need of anti-eps drugs, need for sedatives raises the cost of treatment with risperidone lessening the cost gap between the two drugs. Long term tolerability and efficacy, continuation of the improvement in the maintenance phase, improvement in the quality of life and the metabolic disturbances being found on long term needs to be considered. Thus both the drugs are similar by efficacy in the short and long term and the cost factor also needs to be considered.

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