Available online on 15.07.2015 at http://jddtonline.info
Journal of Drug Delivery and Therapeutics
Open access to Pharmaceutical and Medical research

RESEARCH ARTICLE

COMPARATIVE EVALUATION OF AMISULPRIDE AND ESCITALOPRAM ON SHEEHAN'S DISABILITY SCALE AMONG DEPRESSION PATIENTS IN A TERTIARY CARE TEACHING HOSPITAL IN NEPAL

Dr. Vijay Kaul[1], Dr. Shaktibala Dutta[2], *Dr. Mirza Atif Beg[3], Dr. Nand Kishore Singh[4], Dr. Shalu Bawa[5], Dr. Mohammad Anjoom[6], Dr. Srihari Dutta[7]

[1]Department of Psychiatry, Nepalganj Medical College, Nepal.

[2]Department of Pharmacology, SGRRIM&HS, Patel Nagar, Dehradun

[3]Department of Pharmacology, SGRRIM&HS, Patel Nagar, Dehradun

[4]Department of Psychiatry, SGRRIM&HS, Patel Nagar, Dehradun

[5]Department of Pharmacology, SGRRIM&HS, Patel Nagar, Dehradun

[6]Department of Pharmacology, SGRRIM&HS, Patel Nagar, Dehradun

[7]Immunization Health Specialist, Unicef, New Delhi, India Country Office India

*Corresponding Author's Email: mabeg1997@gmail.com

Received 18 May 2015; Review Completed 14 June 2015; Accepted 24 June 2015, Available online 15 July 2015

ABSTRACT

Introduction and Aim: Depression is an important global public health problem due to its relatively high lifetime prevalence and significant disability caused by it. The present study was conducted to compare improvement in functional outcome by Amisulpride and Escitalopram among depression patients using Sheehan's Disability Scaling.

Material and methods: The study was conducted in depression patients for 1 year in the Department of Neuropsychiatry, Nepalgunj Medical College & Teaching Hospital. A total of 117 depression patients were divided into 2 groups. Group I (58 patients) received Amisulpride tablet at a dose of 50 mg/day and Group II (59 patients) were given Escitalopram at a dose of 10 mg/day. The patients were required to follow up at 4, 8 and 15 weeks. The efficacy of the drugs was calculated by Hamilton depression rating scale (HAM-D). The improvement in functional outcome was compared between the two groups by using Sheehan's Disability Scale (SDS). Appropriate statistical tools using GraphPadInstat 3.0 were used for analysis. p value < 0.05 was considered significant.

Results: HAM-D score in group receiving Amisulpride at 0 and 15 weeks was 16.92±0.35 and 7.87±0.29 ($p<0.0001$). HAM-D score in group receiving Escitalopram at 0 and 15 weeks was 17.09±0.39 and 6.63±0.39 ($p<0.0001$). Sheehan's Disability Score in group receiving Amisulpride at 0 and 15 weeks was 20.35±0.31 and 11.08±0.60 ($p<0.0001$). SDS score in group receiving Escitalopram at 0 and 15 weeks was 21.53±0.55 and 11.49±0.46 ($p<0.0001$). Intergroup comparison at 15 weeks was insignificant ($p>0.05$). Gastrointestinal disturbances, sexual disturbances, amenorrhea, lactation, agitation and insomnia were the commonly encountered adverse drug reactions.

Conclusion: Both Amisulpride and Escitalopram showed improvement in Sheehan's Disability Scale at the end of study period. But intergroup comparison showed no significant difference in the two groups.

Key words: Depression, Amisulpride, Escitalopram, Sheehan's Disability Scale (SDS).

INTRODUCTION:

Depression is an important global public health problem due to its relatively high lifetime prevalence and significant disability caused by it. It accounts for almost 12% of the total years which were lived with disability worldwide[1]. The WHO defines depression as a pessimistic sense of inadequacy and a despondent lack of activity. It can be defined as a mental state which is characterized by feelings of sadness, loneliness, despair, low self-esteem, and self-reproach. The accompanying signs include psychomotor retardation or at times, withdrawal from interpersonal contact and vegetative symptoms such as anorexia and insomnia. Depression is associated with marked personal, social and economic morbidity affecting 9.5% of population worldwide [2]. A recent American survey found the prevalence of current depression to be 9% and the rate of current major depression to be 3.4% [3]. Over the past several decades, pharmacologic management of depressive disorders has evolved substantially. Despite the introduction of many new antidepressant medications and a continually advancing understanding of their individual strengths and weaknesses, selecting the best possible treatment

for each individual patient remains a significant challenge for general practitioners and psychiatrists. Response and remission are key goals in the management of depression. Acceptability is also an important step towards achieving these goals, since patients require long-term (often life-long) pharmacotherapy (. First-line pharmacotherapy for depressive disorders typically chosen from among the "newer antidepressants"— either a selective serotonin reuptake inhibitor (SSRI) or a serotonin-norepinephrine reuptake inhibitor (SNRI)[5]. Escitalopram, the S-enantiomer of citalopram, is a selective serotonin reuptake inhibitor (SSRI) antidepressant that is the most selective of the SSRIs [6]. The efficacy of escitalopram has been demonstrated in major depressive disorder (MDD) in both primary care and specialist settings[7-9]. Amisulpride is a substituted benzamide derivative structurally related to sulpiride. It belongs to the second-generation antipsychotic that preferably binds to dopamine D2/D3 receptors in limbic rather than striatal structures[10]. Amisulpride is indicated for the treatment of acute and chronic schizophrenia with prominent positive and/or negative symptoms due to a dose-dependent blockade of dopamine receptors[10,11]. In addition to antipsychotic effects, preliminary reports suggest that Amisulpride may have antidepressant effects in dysthymia. Amisulpride has been shown to be as effective as comparator in clinical studies in patients with dysthymia and/or major depression [12]. The presumed selectivity of amisulpride for D2 and D3 dopamine receptors has led to the prevailing hypothesis that modulation of dopaminergic signaling is responsible for its antidepressant efficacy. Recent evidence suggests that primary-care providers do not decide on drug treatment or referral for depression on the basis of questionnaire scores alone, and that they consider practical wisdom and clinical judgment to be more important than objective assessments[13,14]. Assessment of function may, therefore, provide additional, important efficacy information over and above that provided by measuring response and remission. In this regard, emerging data show that escitalopram has an ability to improve functional outcomes in depression patients [15, 16]. Based on the above observations, the present study was conducted to compare efficacy of Amisulpride and Escitalopram by HAM-D and improvement in functional outcomes by Sheehan's Disability Scale (SDS) among depression patients in a tertiary care teaching hospital in Nepal.

MATERIAL AND METHODS:

This study was conducted in the Department of Neuropsychiatry, Nepalgunj Medical College & Teaching Hospital, Nepalgunj, for a period of 1 year from January 2013 to December 2013. Institutional Ethics Committee approval and written informed consent from the patients or legal guardians were taken prior to the commencement of the study. Inclusion Criteria: (a) All drug naive patients attending the Neuropsychiatry OPD, of both sexes who were diagnosed as F 34.1, according to ICD 10 (World Health Organization, 2008). (b) Score ≥ 14 points on the Hamilton Depression Rating Scale (1980) on the first screening visit. Exclusion Criteria: (a) Use of psychoactive substances (b) any systemic illness (c) lactating and pregnant women (d) known case of psychiatric illness as described by ICD 10 (World Health Organization, 2008), (e) History of Drug reaction.

Study Design: The study was an open label study conducted from January 2013 to December 2013. A total of 117 patients diagnosed with depression were randomly divided in two groups: Group I (58 patients) receivedtabletAmisulpride50 mg/day orally and Group II (59 patients) were given tablet Escitalopram 10 mg/day orally. Drug compliance was monitored rigorously, but no drug blood levels were monitored due to lack of any such facility locally. The patients were followed up at 4, 8 and 15 weeks. Adverse drug reactions were monitored at every follow up. Appropriate statistical tools using GraphPadInstat 3.0 were used for analysis. p value < 0.05 was considered significant.

RESULTS:

Out of a total of 117 patients which were included in the study, 18 patients dropped out from the study due to varying reasons: 6 patients were lost to follow up, 6 patients decided to withdraw from the study due to adverse drug reactions, 3 patients were lost due to lack of cost effectiveness, 2 patients requested therapy change and 1 patient was uncooperative. Overall, 99 patients completed the study: 48 patients in Amisulpride group and 51 patients in Escitalopram group. The mean age of the patients in the study drug groups was 46.84±1.10 years. The male: female percentage was 41(41.41%) and 58(58.59%). In our study, 31(31.31%) patients were residing in urban areas and 68(68.69%) patients were residing in rural areas. A total of 47(47.47%) patients were illiterate and 52(52.53%) patients were literate. 65(65.66%) patients were farmers, 23(23.23%) patients were employed and 11(11.11%) belonged to others category (table 1&2).

 ISSN: 2250-1177 CODEN (USA): JDDTAO

Table 1: Demographic Profile of study group

(All the values are expressed in Mean ± SEM)

Variables	Total
Age (Mean)	46.84± 1.10
Sex (M:F)	41(41.41%): 58(58.59%)
Urban: Rural	31: 68 (31.31%, 68.69%)
Illiterate: Literate	47:52 (47.47%, 52.53%)
Occupation:	
Farming	65 (65.66%)
Employed	23 (23.23%)
Others	11 (11.11%)

Table 2: Drop Outs

Variables	Amisulpride n=58	Escitalopram n=59	Total n=117
Total Drop Outs	10	08	18
Reasons:			
Lost to follow up	03	03	06
Un Cooperative	00	01	01
Adverse drug reaction	03	03	06
Requested therapy change	01	01	02
Lack of cost effectiveness	03	00	03
Total completed study	48	51	99

The efficacy of the drugs was calculated by Hamilton depression rating scale (HAM-D) and improvement in functional outcomes was measured by Sheehan's Disability Scale(SDS). All values were expressed in Mean ± SEM. At the beginning of the study, the HAM-D Score in Amisulpride group was 16.92±0.35 and in the Escitalopram group was 17.09±0.39 respectively. There was no significant difference between the two groups at the start of study (p >0.05). Patients were followed up at 4, 8 and 15 weeks. Progressive improvement was seen in both the groups over the study period (figure 1).

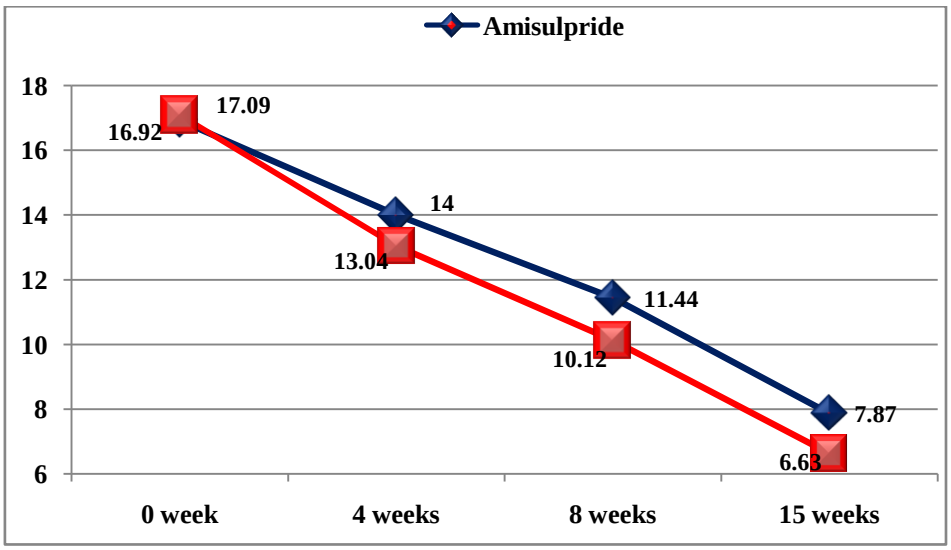

Figure 1: Progressive change of HAM-D score over study period

At the end of the study, the HAM-D score in Amisulpride group was 7.87±0.29 and in the Escitalopram group was 6.63±0.39 respectively. Intragroup comparison was done between baseline and 15 weeks and highly significant improvement was seen in both groups (p<0.0001). At the end of study period intergroup comparison was made between the two groups which was insignificant (p>0.05) (table 3). At the beginning of study, the Sheehan's Disability Scale (SDS) in Amisulpride group was 20.35±0.31 and in Escitalopram group was 21.53±0.55 respectively. Intergroup comparison was insignificant (p>0.05). At the end of study, SDS score in Amisulpride group was 11.08±0.60 and in Escitalopram group was 11.49±0.46 respectively. Intragroup comparison was done between baseline and 15 weeks which was highly significant in

both the groups (p<0.0001). Intergroup comparison at the end of study was insignificant (p>0.05) (table 4). A total of 44 adverse drug reactions (ADRs) were seen during the study period. 25 ADRs were seen in patients in Amisulpride group and 19 ADRs were seen in Escitalopram group. Gastrointestinal disturbances were seen in 5 patients in Amisulpride group and 9 patients in Escitalopram group followed by Delayed orgasm in 5 patients in Amisulpride group and 2 patients in Escitalopram group, Amenorrhoea in 4 patients in Amisulpride group, dryness of mouth in 03 patients in Amisulpride group and 02 patients in Escitalopram group, erectile dysfunction in 02 patients in Amisulpride group and 01 patient in Escitalopram group, agitation in 02 patients in both groups, giddiness, insomnia and weight gain in 1 patient in each group and lactation in 1 patient in Amisulpride group (table 5).

Table 3: Efficacy as per HAM-D

(All the values are expressed in Mean ± SEM)

Drug	**0 weeks**	**15 weeks**	**p- value**
Amisulpride	16.92± 0.35	7.87± 0.29	<0.0001
Escitalopram	17.09± 0.39	6.63± 0.39	<0.0001
p- value	> 0.05	>0.05	

Table 4: Functional outcomes as per SDS

(All the values are expressed in Mean ± SEM)

Drug	**0 weeks**	**15 weeks**	**p- value**
Amisulpride	20.35± 0.31	11.08± 0.60	<0.0001
Escitalopram	21.53± 0.55	11.49± 0.46	<0.0001
p- value	> 0.05	>0.05	

Table 5: Adverse Drug Reactions

Variables	**Amisulpride** ---------- **n=48**	**Escitalopram** ---------- **n=51**
Total patients with ADR	25(59%)	19(42.2%)
Gastrointestinal disturbances	05	09
Delayed orgasm	05	02
Amenorrhea	04	00
Dryness of Mouth	03	02
Erectile Dysfunction	02	01
Agitation	02	02
Giddiness	01	01
Insomnia	01	01
Weight gain	01	01
Lactation	01	00

DISCUSSION:

Depressive disorders lead to significant dysfunction, disability and poor quality of life in sufferers and pose a significant burden on the caregivers [17, 18]. In the present study there was a higher prevalence of depression in females which was in accordance with previous studies by Sethi et al and Ramachandran et al depicting that women were more commonly suffering from depression[19, 20]. The greater prevalence of depression among women is not fully understood, although potential contributors include different responses to stressful life events, genetic predisposition and hormonal differences [21]. The mean age group in our study was 46.84±1.10 years which was comparable with previous studies by Dutta et al and Grover et al where incidence of depression was seen predominantly in 30-51 years age group [22, 23]. More depression patients were seen in rural areas as compared to urban areas in the present study. This was comparable with previous studies by Paritala et al, Giel et al and Gautam et al where rural back ground subjects were found to be somatising more than the urban subjects[24-26]. In our study more number of literates was suffering from depression which was comparable with previous study by Paritala et al and Barsky et al [24, 27]. Farmers were the major sufferers of depression which was in accordance with previous studies by Roberts and Lee [28] which was, based on data from the Epidemiologic Catchment Area (ECA) Program, found 'farming, fishing and forestry' to have the highest lifetime risk for major depression. Other studies have also shown increased suicide rates among farmers [29, 30].

A comparative evaluation of Escitalopram and Amisulpride was done in depression patients by

measuring improvement in functional outcome using Sheehan's Disability Scale in this 15 week study. Escitalopram is an allosteric selective serotonin reuptake inhibitor (SSRI) with some indication of superior efficacy in the treatment of major depressive disorders. The results of our study revealed highly significant improvement in HAM-D in depressive patients over the study period. Intragroup comparison was made between baseline and 15 weeks in Escitalopram group, highly significant improvement was seen ($p<0.0001$). This was comparable with previous studies where efficacy of escitalopram has been proven [8, 9, 31]. Amisulpride, a selective D2/D3 receptor second generation antipsychotic is indicated for the treatment of acute and chronic schizophrenia [32]. The presumed selectivity of Amisulpride for D2 and D3 dopamine receptors has led to the prevailing hypothesis that modulation of dopaminergic signaling is responsible for its antidepressant efficacy. In the present study the antidepressant effect of Amisulpride was compared at baseline and at 15 weeks in depressive patients, highly significant improvement was observed ($p<0.0001$). This was comparable with previous studies by Ravizza L et al and Lecrubier Y et al where antidepressant role of Amisulpride has been proven[33-34]. Amisulpride has some selectivity for presynaptic dopamine autoreceptors, and exhibits limbic versus striatal selectivity, particularly at low doses, and it has been suggested that this might account for its therapeutic profile [35].

The improvement in functional impairment was measured by SDS. In the present study highly significant improvement was seen in both Escitalopram and Amisulpride groups. Previous studies by Cipriani et al. and Wade et al, have also shown favorable outcomes in SDS for Escitalopram[36, 15] and study by Smeraldi et al has shown improvement in SDS by Amisulpride, which is comparable to the present study. Proving that patients who take medications that are efficacious and acceptable have a better chance of achieving superior functional improvements compared to those who take agents that are less efficacious and/or not as well accepted[35]. At the end of the study period, intergroup comparison was made between Escitalopram group and Amisulpride group which revealed no significant difference ($p<0.05$), indicating both the drug were equally efficacious in improving depression and in improving functional outcome.

Safety analysis was done for both the groups and adverse drug reactions were assessed at each follow up. Gastrointestinal disturbances were seen most commonly with both the groups and have been proven in earlier studies [37, 38]. Endocrinological effects like Amenorrhoea and lactation were seen in Amisulpride group and have been seen in previous studies [39]. Other side effects like insomnia, agitation and dryness of mouth were seen similarly in both groups and were comparable with previous studies [40, 41].

Study Limitations: The study was an open label study. Both doctors and patients were aware of the treatments. Hence there could be chances of bias. Sample size was small and the patients were followed up for only 15 weeks.

CONCLUSION:

Both Escitalopram and Amisulpride were highly effective in improving functional outcome in depression patients. But intergroup comparison revealed no significant difference between the two groups. A double blind study with larger sample size and longer duration of follow up can substantiate the findings of the present study.

ACKNOWLEDGEMENT:

Authors would like to thanks to the administration and Institutional Ethics Committee of Nepalganj Medical college, Nepal for their support in conducting this study. At the same time they can't forget the unconditional support of the staff members of psychiatry department.

REFERENCES

1. Revised global burden of disease (GBD) 2002 estimates. Geneva, World Health Organization 2005;667.
2. Sadock B, Ruiz P, (Editors). In Comprehensive textbook of psychiatry-Kaplan and Sadock's, ninth Edition, Volume 1-Wolters Kluwer, Lippincott Williams and Wilkins, 2009;P.923.
3. Lépine JP, Briley M. The increasing burden of depression Neuropsychiatric Dis Treat. 2011;7 (Suppl 1):3–7.
4. Kennedy SH,Rizvi SJ. Comparative Efficacy of Newer Antidepressants for Major Depression: A Canadian Perspective. The Canadian Journal of Diagnosis / September 2009.
5. Anderson IM, Ferrier IN, Baldwin RC, et al. Evidence-based guidelinesfor treating depressive disorders with antidepressants: A revision ofthe 2000 British Association for Psychopharmacology guidelines. J Psychopharmacol 2008;22:343–96.
6. Owens MJ, Knight DL, Nemeroff CB. Second-generation SSRIs: human monoamine transporter binding profile of escitalopram and R-fluoxetine. Biol Psychiatry 2001;50:345-50.
7. Montgomery SA, Huusom AKT, Bothmer J. A randomised study comparing escitalopram with venlafaxine XR in primary care patients with major depressive disorder. Neuropsychobiology 2004;50:57-64.
8. Burke WJ, Gergel I, Bose A. Fixed-dose trial of the single isomer SSRI Escitalopram in depressed outpatients. J Clin Psychiatry 2002;63:331-36.
9. Waugh J, Goa KL. Escitalopram: A review of its use in the management of major depressive and anxiety disorders. CNS Drugs. 2003;17:343–62.
10. McKeage K, Plosker GL. Amisulpride. A review of its use in the management of Schizophrenia. CNS Drugs 2004;18(13):933-56.
11. Scatton B, Claustre Y, Cudennec A, et al.Amisulpride: from animal pharmacology totherapeutic action. Int. ClinPsychopharmacol 1997;12(Suppl 2):S29-36.
12. Racagni G, Canonico PL, Ravizza L, Pani L, Amore M. Consensus on the use of substituted benzamide in psychiatric patients. Neuropsychobiology 2004;50:134–43.
13. Kendrick T, Dowrick C, McBride A, et al. Management of depression in UK general practice in relation to scores on depression severity questionnaires: analysis of medical record data. BMJ 2009;338:b750.
14. Dowrick C, Leydon GM, McBride A, et al. Patients' and doctors' views on depression severity questionnaires

incentivised in UK quality and outcomes framework: qualitative study. BMJ 2009;338:b663.
15. Wade A, Gembert K, Florea I. A comparative study of the efficacy of acute and continuation treatment with escitalopram versus duloxetine in patients with major depressive disorder. Curr Med Res Opin 2007;23(7):1605-14.
16. Demyttenaere K, Andersen HF, Reines EH, et al. Impact of escitalopram treatment on Quality of Life Enjoyment and Satisfaction Questionnaire scores in major depressive disorder and generalized anxiety disorder. Int Clin Psychopharmacol 2008;23(5):276-86.
17. Chadda RK. Social support and psychosocial dysfunction in depression. Indian J Psychiatry. 1995;37:119–23.
18. Chaudhary PK, Deka K, Chetia D. Disability associated with mental disorders. Indian J Psychiatry 2006;48:95–101.
19. Sethi BB, Prakash R. Depression in Industrial population. An overview of Indian research in depression. Indian J Psychiatry 1979;21:359–61.
20. Ramachandran V, Menon MS, Arunagiri S. Socio-cultural factors in late onset depression. Indian J Psychiatry 1982;24:268–73.
21. National Institute of Mental Health. Women and depression, discovering hope, Berthesda, MD: US Department of Health and Human Services, National Institute of Health, National Institute of Mental Health; 2009.
22. Dutta SB, Beg MA, Sindhu S, Singh NK. Role of pharmaco-epidemiology in psychopharmacology: a study in psychiatric out-patient department of a tertiary care teaching hospital at Dehradun, Uttarakhand. Int J Basic ClinPharmacol 2014;3(4):637-43.
23. Grover S, Avasth A, Kalita K, Dalal PK, Rao GP, Chadda RK, et al. IPS multicentric study: antidepressant prescription patterns. Indian J Psychiatry 2013;55(1):41-45.
24. Paritala CB, Nallapaneni RN,Chennamsetty SK. A cross-sectional study to assess the prevalence of somatisation and associated sociodemographic factors in depression. AP J Psychol Med 2014;15(1):93-8.
25. GeilR, Hardings TW. Psychiatric priorities in developing countries. Br J Psychiatry 1976;128:513-22.
26. Gautam SK, Kapur RL. Psychiatric patients with somaticcomplaints, Indian J Psychiatry 1977;19:75-80.
27. Barsky AJ. Amplification, Somatisation and the Somatoform disorders. Psychosom 1992;33:28-34.
28. Roberts RE, Lee ES. Occupation and the prevalence of major depression, alcohol, and drug abuse in the United States. Environ Res 1993;61:266–78.
29. Boxer PA, Burnett C, Swanson N. Suicide and occupation: A review of the literature. J Occup Med 1995;37:442–52.
30. Malmberg A, Simkin S, Hawton K. Suicide in farmers. BritJPsychiat 1999;175:103–105.
31. Montgomery SA, Baldwin DS, Blier P, et al. Which antidepressants have demonstrated superior efficacy? A review of the evidence. Int Clin Psychopharmacol 2007;22:323–29.
32. Perrault G, Depoortere R, Morel E, Sanger DJ, Scatton B. Psychopharmacological profile of amisulpride: an antipsychotic drug with presynaptic D2/D3 dopamine receptor antagonist activity and limbic selectivity. J Pharmacol Exp Ther 1997;280:73–82.
33. Ravizza L. Amilong investigators. Amisulpridein medium-term treatment of dysthymia: a sixmonth, double-blind safety study versus amitriptyline. J Psychopharmacol 1999; 13(3)248-254.
34. Lecrubier Y, et al. Amisulpride vs. imipramine and placebo in dysthymia and major depression. J Affect Disorder 1997;43(2):95-103.
35. Smeraldi E. Amisulpride vs. fluoxetine in patients with dysthymia or major depression in partial remission: a double-blind, comparative study. J Affect Disord 1998;48(1):47-56.
36. Cipriani A, La Ferla T, Furukawa TA, et al. Sertraline versus other antidepressive agents for depression. Cochrane Database Syst Rev 2009; (2):CD006117.
37. Kasper S, Baldwin DS, Larsson LS, Boulenger JP. Superiorityof escitalopram to paroxetine in the treatment of depression. EurNeuropsychopharmacol 2009;19:229–37.
38. Rosenzweig P, Canal M, Patat A, et al. A review of the pharmacokinetics, tolerability and pharmacodynamics of amisulpiride in healthy volunteers. Hum Psychopharmacol 2002;17(1):1-13.
39. Curran MP, et al. Amisulpride: a review of its use in the management of schizophrenia. Drugs 2001;61:2123-50.
40. Gartlehner G, Gaynes BN, Hansen RA, et al. Comparative benefitsand harms of second-generation antidepressants: Background paperfor the American College of Physicians. Ann Intern Med 2008;149:734–75.
41. Chabra V, Bhatia MS. Amisulpride: A Brief Review. Delhi Psychiatry Journal 2007;10(2):140-43.

 ISSN: 2250-1177 CODEN (USA): JDDTAO