

Prospective cross-sectional observational study to evaluate prescriptions pattern on CNS disorder with respect to depression, sleep disorder and mood disorder

Khairnar Avinash S, Kavathekar Snehal Arvind

UDIRT Department, MUHS Nashik

Abstract

Present Study was carried out to evaluate Prescription Patterns on CNS disorder with Respect to Depression, Sleep Disorder, and Mood Disorder. Total 186 prescriptions were collected from the medical practitioners as well as from patients and distributed for three diseases for Depression (n=83), Mood disorder (n=83) and Sleep disorder (n=20) from study centre Nashik. Prescription evaluated using WHO indicator. In Depression among 59% of SSRIs the Escitalopram (29%) prescribed. TCAs (5.59%), Antipsychotics (18.01%) prescribed. In Mood disorder olanzapine and sodium valproate are mostly prescribed drugs. SSRIs (18.12%), TCA (5.84%), Atypical antipsychotics (24.56%), Aliphatic carboxylic acid (18.12%), Lithium (5.84%) prescribed. In sleep disorder Benzodiazepines are mostly prescribed (38.46%), Newer Benzodiazepine (20.51%), SSRIs (10.25%), TCAs (10.25%) and Barbiturates (5.12%) are prescribed. Study shows a shift from older to newer drugs and overall prescription pattern are good but drug prescribed by generic name very low.

Keywords: Prescription pattern, Depression, Mood disorder, Sleep disorder, CNS disorder, Prescription Evaluation.

Introduction

Studying prescription patterns provides opportunity to monitor therapeutic trends. Many studies from western countries have reported prescription patterns of various psychotropic medications. These studies have looked into prescription patterns, prescription patterns in general practice, and specialist care (Kjosavik, SR, *et al.*, 2011) [24]. A few surveys of prescription patterns of various psychotropic from Asian centers too are available (Nakao, M, *et al.*, 2007 and Tan, CH, *et al.*, 2008) [36, 46]. Although a developing country, almost all psychotropic medications available worldwide are readily available in India. However, very few studies from India have evaluated prescription patterns of psychiatrists (Grover, S and Avasthi, A 2010) [18]. In 1977, WHO published the first model list of essential drugs and subsequently has attempted to improve drug-use practices in developing countries. An essential tool in this respect is an objective and standard method of describing drug-use patterns and prescribing behavior in health facilities through the use of prescription analysis. (Geneva, World Health Organization 1987) [47].

Depressive disorders are highly throughout the world (Kessler, RC, *et al.*, 1994) [22]. Depressive disorders often impair social and occupational function and cause a considerable social burden (Wells, KB 1999, Kim, JM, *et al.*, 2007) [50, 23]. There are more than 20 antidepressants available in the market (Murata, A, *et al.*, 2012) [35]. The occurrence of depression is associated with factors such as age, marital status, social class, and social conditions (Lehtinen, V and Joukamaa, M 1994) [27].

Sleep disturbances are associated with physical conditions such as hypertension, gastro-esophageal reflux, heart disease, hypercholesterolemia, chronic pain and obesity among others (Vgontzas, AN, *et al.*, 1998, Algul, A, *et al.*, 2009; Ohayon, MM 2009b;) [49, 4, 39]. International studies have shown prevalence rates between 4.7 and 36.2% for sleep difficulties in

general, whereas 13.1–28.1% report insomnia symptoms. Sleep problems are associated with lower social and academic performance and can have a severe impact on psychological and physical health (Angelika, A, *et al.*, 2012) [8].

The occurrence of major depression in the general population is considerable, where it has a lifetime prevalence ranging from 10% to 15 %, (Lepine, JP and Briley, M 2011) [28]. With an increased rate in females (Kuehner, C 2003) [25]. The lifetime prevalence of bipolar disorder type I is estimated at 0.6% and bipolar disorder type II at 0.4% (Merikangas, KR 2011) [32]. However, recent evidence suggests that bipolar disorder in its broadest sense has lifetime prevalence as high as 5% (Akiskal, HS 2000) [2].

There is not a single study represent the prescription patterns of Depression, Sleep and Mood Disorder in India therefore present study was planned to evaluate prescription pattern using WHO indicator on CNS disorder to provide the information about status of prescription pattern s.

Material & Methods

This study was conducted in compliance with the Declaration of Helsinki, ICH-GCP, Schedule Y, ICMR and other applied regulatory guidelines. This was prospective observational cross sectional study which aims to evaluate the prescription pattern on CNS disorders with respect to Depression, Sleep and Mood disorder in Nasik. Patients were recruited after obtaining proper voluntary written informed consent and the study was started after being approved by the UDIRT Institutional Ethics Committee (IEC). Patients were recruited from the study center Nasik. To be included in the study patients were required to fulfill the criteria for CNS disorder with respect to Depression, Sleep and Mood disorder. Both male and female of various ages between 16 to 64 years and give voluntary written informed consent were recruited. They were explained about the nature of study and patients who agreed to participate and provided

informed consent were recruited. Total 186 prescriptions were collected from the medical practitioners as well as from patients and distributed for three diseases of Depression (n=83), Mood disorder (n=83) and Sleep disorder (n=20). The documentation of clinical profile of the study involved noting down of the prescription given to the patients. The prescription data was extracted for this study.

Study of prescription patterns on CNS disorder with respect to Depression, Sleep disorder, Mood disorder were according to the WHO indicators. These indicators are highly standardized in terms of their definition and facilitate quick and reliable assessment of drugs used in health care.

Selection of indicators

The following basic drug-use indicators (core indicators) were used in the study.

- 1) Average number of medicines prescribed per prescription; purpose is to measure the degree of Poly-Pharmacy.
- 2) Percentage of medicine prescribed by generic name, purpose is to measure tendency to prescribe by generic name. Using National essential drug list the generic name of drug identify and mentioned in CRF.
- 3) Percentage of encounters when injections prescribed. Purpose is to measure the overall level of two important but commonly overused and costly forms of drug therapy.
- 4) Percentage of medicines prescribed from essential drug list. Purpose is to measure the degree to which practices conform to a National Drug Policy as indicated by prescribing from the National essential drug list or formulary for the type of facility surveyed.

Statistical Analysis: The result presented in number and percentage (%) form for descriptive data using table and figure and charts.

Result & Discussion

Result of this study suggest that Escitalopram is the most commonly prescribed antidepressant and SSRIs are the most commonly prescribed class of antidepressants. Over the past decade, there has been an increase in the number and types of antidepressants (TCAs) were the first line drugs for depression. Recent studies show that Selective Serotonin Re-uptake Inhibitors (SSRIs) are now the initial choice of antidepressants and are more commonly prescribed antidepressant drugs (Bauer M, *et al.*, 2008). The combination of antidepressants with anti-psychotics was also prescribed for associated psychotic

symptoms with depression. The common SSRIs used were Fluoxetine/Sertraline with atypical antipsychotics like Olanzapine/Aripiprazole. Other studies also suggest that SSRIs and atypical antipsychotics together are effective for treatment of psychotic features in depression (Adli M, *et al.*, 1990)^[1]. In study found an average of drugs prescribed per prescription is 1.93 which was also in acceptable range the recommended limit is 2.0 drugs per prescription (MJ Kshirsagar, *et al.*, 1998)^[33]. Medicines prescribed from essential list for Depression is 30.43% which is lower than other studies. In Mood disorder there is not particular drug prescribed so different combination of class of drugs is used mostly SSRIs and Aliphatic carboxylic acid are used. Mostly in Aliphatic Carboxylic acid Valproic Acid and Divalproex are prescribed the other studies also shows that among the mood stabilizers, valproate was preferred over lithium (Sandeep Grover, *et al.*, 2012)^[42]. Lithium is 5.84% prescribed which is lower compare to SSRIs and Aliphatic Carboxylic acid class. This may be due to the fact that valproate is considered to be rapidly effective in the management of acute mania (Hirschfeld RM, *et al.*, 2003)^[20]. The Olanzapine also mostly prescribed drugs from essential drug list it shows that it's effective in Mood disorder. NSAIDs and Vitamins and minerals (1.75%) prescribed. In study found an average of drugs prescribed per prescription is 2.06 which were also in acceptable range the recommended limit is 2.0 drugs per prescription (MJ Kshirsagar, *et al.*, 1998)^[33]. Medicines prescribed from essential list for Mood disorder is 53.21% the drug prescribed from essential drug list is above 50% therefore we conclude that the current prescription patterned is good prescription practices. Only 20 prescription of sleep disorder was studied which are so less due to pure sleep disorder are mostly rare because sleep disorder are mostly related to other disease or co-morbidity. The class of drug Benzodiazepines and Newer non benzodiazepine hypnotics are mostly used and barbiturates are 5.12% used. Insomnia is common indication for Prescription of Benzodiazepines. Antidepressant and antipsychotics also prescribed. In study found an average of drugs prescribed per prescription is 1.95 which was also in acceptable range the recommended limit is 2.0 drugs per prescription (MJ Kshirsagar, *et al.*, 1998)^[33]. Medicines prescribed from essential list for Sleep disorder is 38.46% which is lower than other studies.

For three diseases the drug prescribed by generic name is negative result compare to other study. There are no Single injection will Prescribe by clinicians hence Percentage of encounter with an injection.

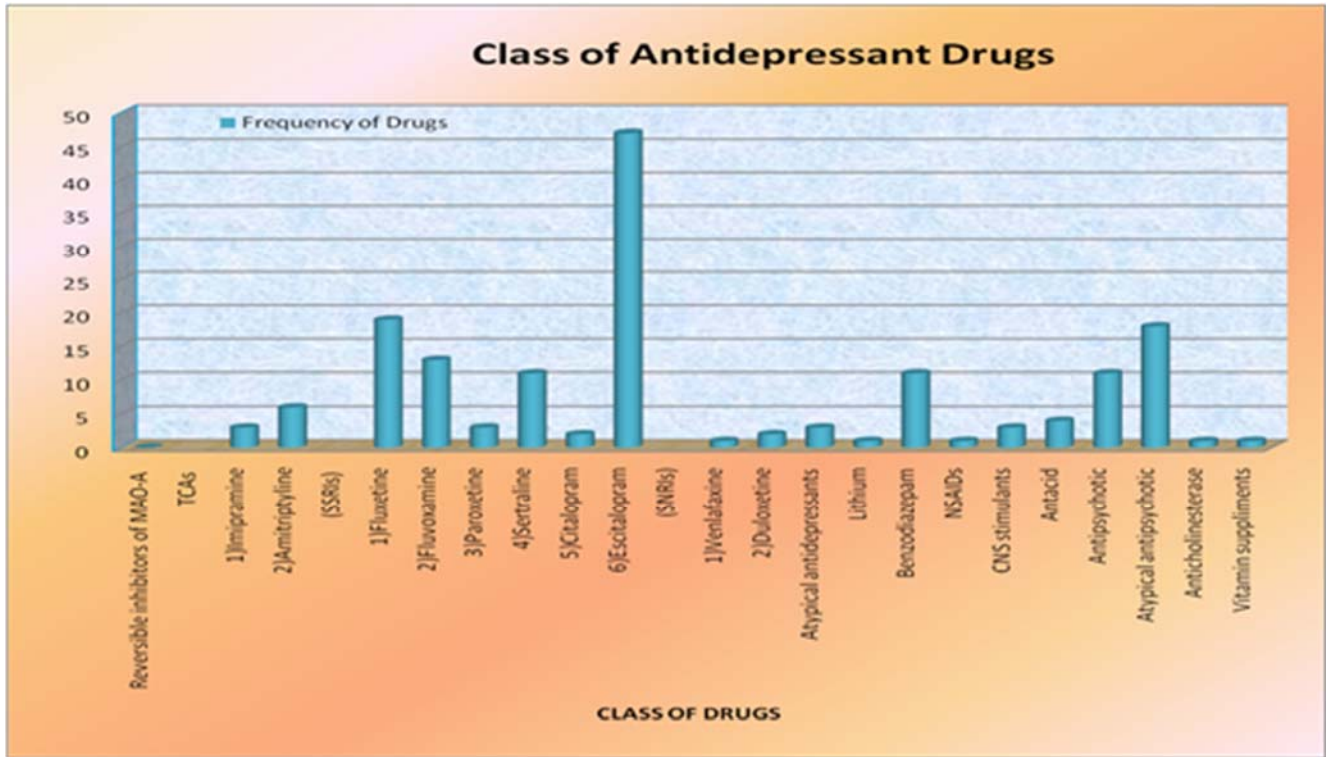


Fig 1: Classification of Antidepressants and Frequency of Drug in Depression

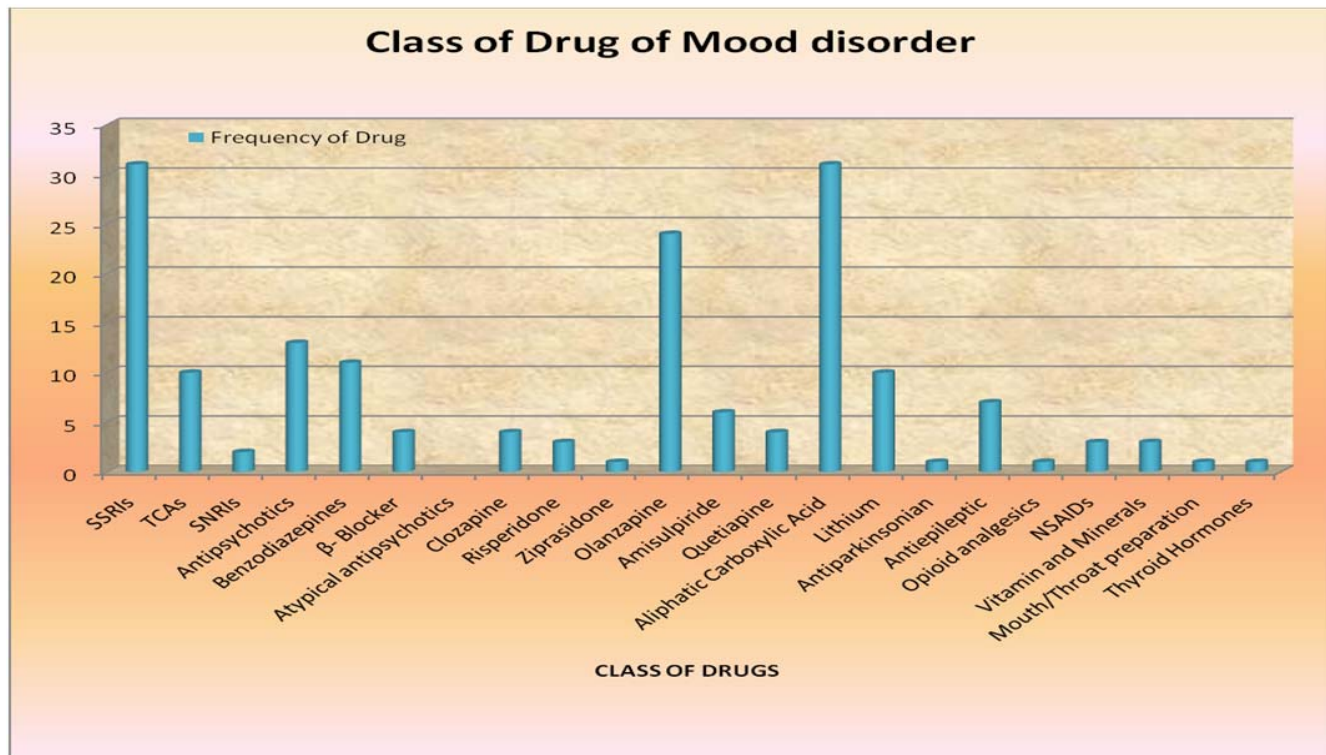


Fig 2: Classification of drugs and Frequency of Drug in Mood Disorder

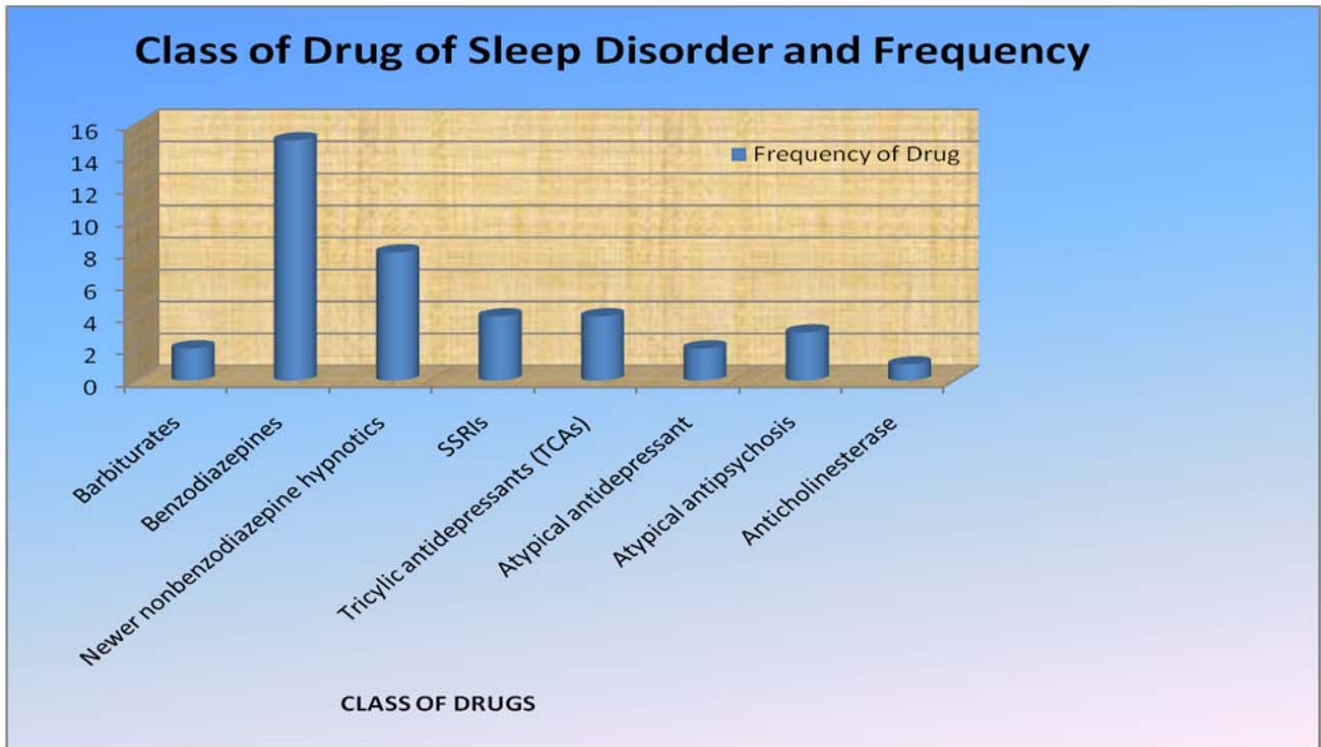


Fig 3: Class of Drug and Their Frequency of Sleep Disorder

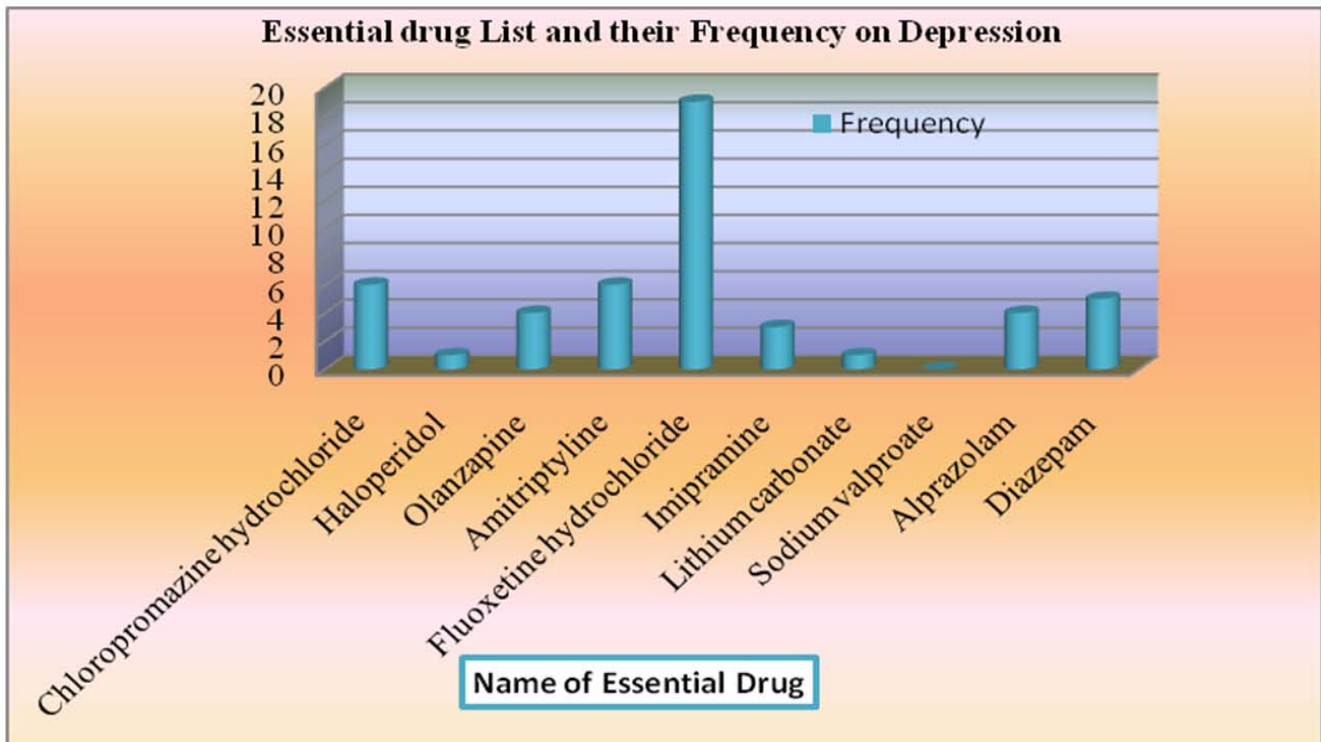


Fig 4: Essential Drug List and their Frequency on Depression

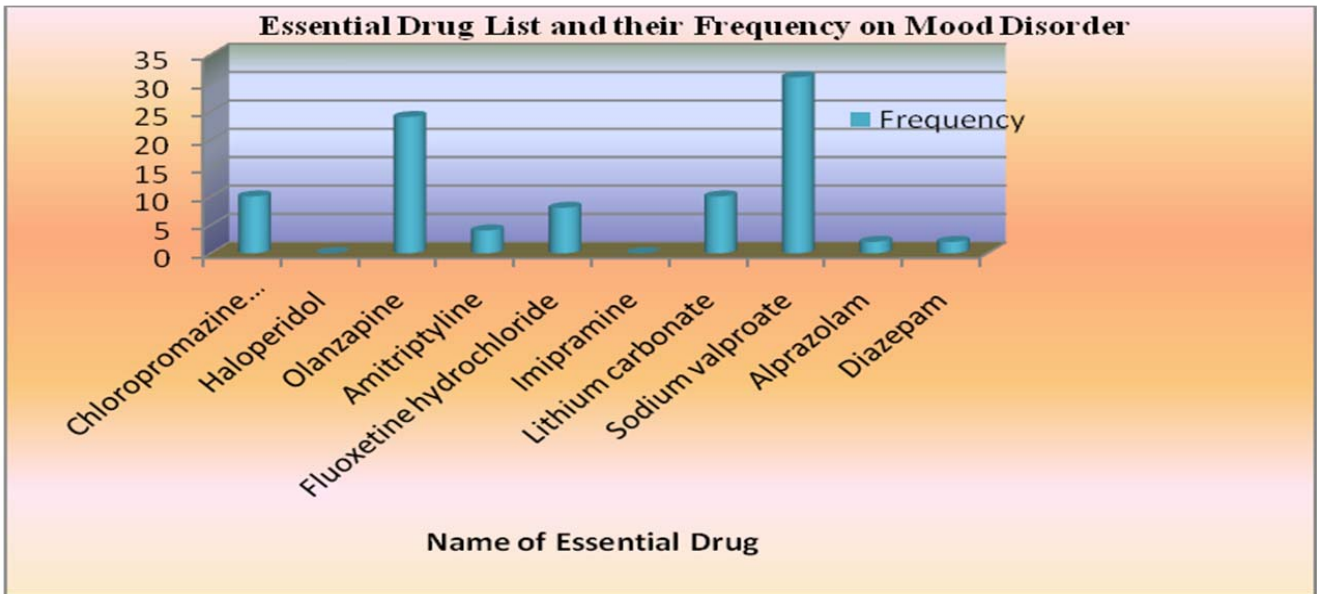


Fig 5: Essential Drug List and their Frequency on Mood Disorder

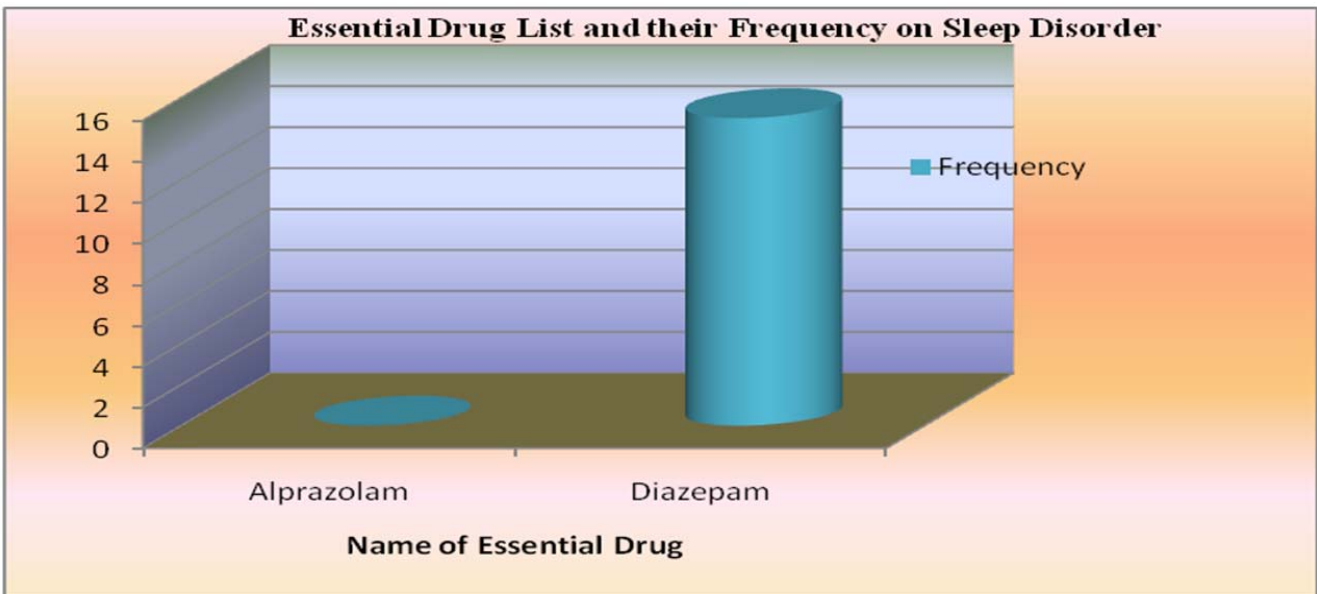
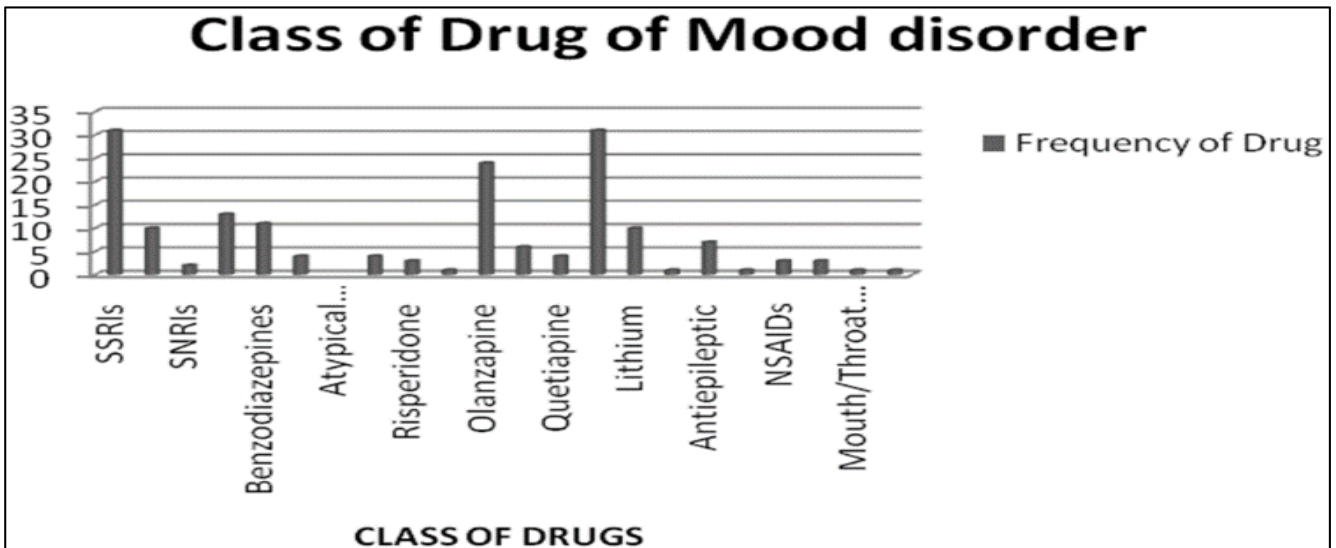
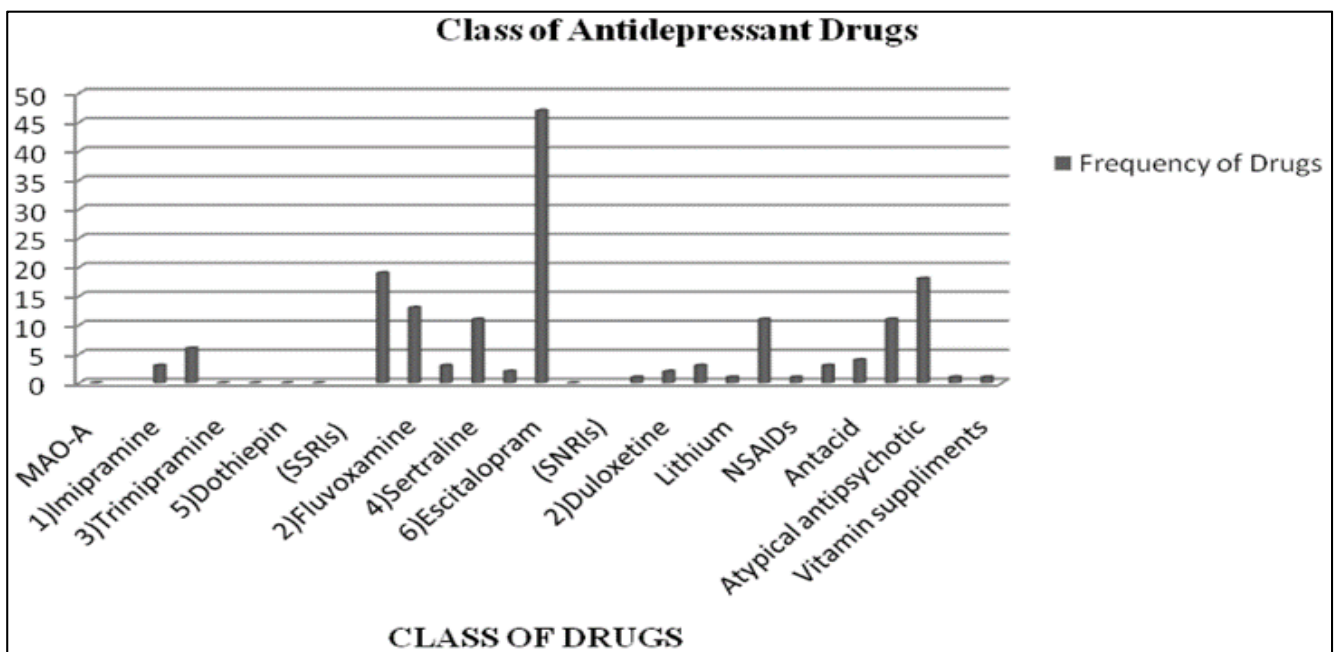
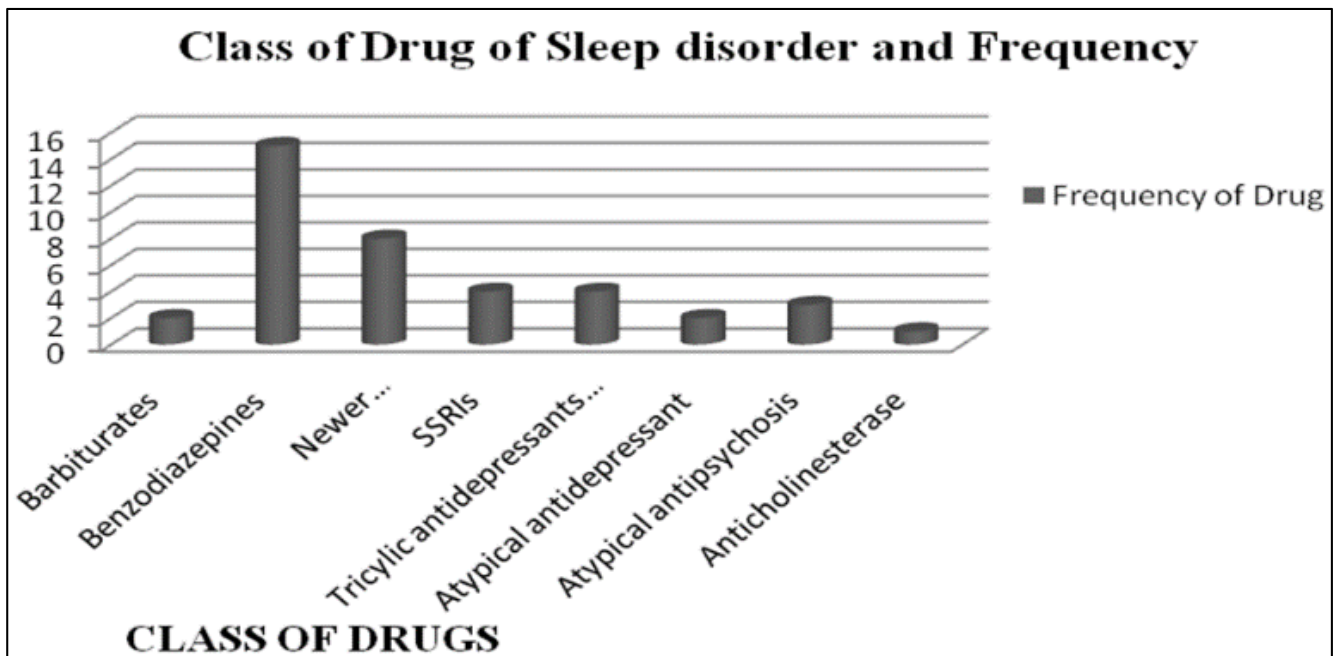


Fig 6: Essential Drug List and their Frequency on Sleep Disorder





Conclusion

The study has several limitations. We focused only on prescriptions and this necessarily does not reflect the true clinical situation. Study shows a shift from older to newer drugs and overall prescription pattern are good but drug prescribed by generic name very low need to improve the prescription.

References

- Adli M, Rossius W, Bauer M. Olanzapine in the treatment of depressive disorders with psychotic symptoms. *Nervenarzt*. 1990; 70:68-71.
- Akiskal HS, Bourgeois ML, Angst J, Post R, Moller H, Hirschfeld R. Re-evaluating the prevalence of and diagnostic composition within the broad clinical spectrum of bipolar disorders. *J Affect Disorder*. 59 Suppl. 2000; 1:5-30.
- Alan M, Gruenberg Reed, Goldstein D, Harold Alan Pincus. *Classification of Depression: Research and Diagnostic Criteria: DSM-IV and ICD-10. Biology of Depression. From Novel Insights to Therapeutic Strategies.* WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim, 2005, ISBN: 3-527-30785-0.
- Algul A, Ates MA, Semiz U, Basoglu C, Ebrinc S, Gecici, O. Evaluations of general psychopathology, subjective sleep quality, and health-related quality of life in patients with obesity. *International Journal of Psychiatry in Medicine*. 2009; 39:297-312.
- American Academy of Sleep Medicine 2005, *International classification of sleep disorders, second edition: diagnostic and coding manual.* Chicago, Illinois: American Academy of Sleep Medicine, 298 pages.
- American Psychiatric Association *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition.* Washington, DC: APA, 1994, 943.

7. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders Text Revision (DSM-IV-TR), 4th ed. Washington, DC: APA, 2002, 943.
8. Angelika A, Schlarb Dorota Reis, Annette Schroder. Sleep Characteristics, Sleep Problems, and Associations to Quality of Life among Psychotherapists. Hindawi Publishing Corporation, Sleep Disorders, 2012, Article ID 806913, 7 pages doi:10.1155/2012/806913
9. Baldessarini RJ, Leahy L, Arcona S, Gause D, Zhang W, Hennen J. Patterns of psychotropic drug prescription for U.S. patients with diagnoses of bipolar disorders. *Psychiatry Serv* 2007; 58:85-91. [PubMed: 17215417]
10. Bauer M, Monz BU, Montejo AL, Quail D, Dantchev N, Demyttenaere K. prescribing patterns of antidepressants in Europe: results from the Factors Influencing Depression Endpoints Research (FINDER) study. *Eur Psychiatry*. 2008; 23:66-77. [PubMed:18164600]
11. Borbely AA. A two-process model of sleep regulation. *Human Neurobiology* 1982; 1:195-204.
12. Borbely AA. Process underlying sleep regulation. *Hormone Research* 1998; 49:114-117.
13. Brieger P, Marneros A. Dysthymia and cyclothymia – serious consequences of rarely diagnosed disorders. *Versicherungsmedizin*. 1998; 50:215-218. [German.]
14. Buysse DJ, Ancoli-Israel S, Edinger JD, Lichstein KL, Morin CM. Recommendations for a standard research assessment of insomnia. *Sleep* 2006; 29:1155-1173.
15. Cramer V, Torgersen S, Kringlen E. Mood disorders and quality of life. A community study. *Nord J Psychiatry*. 2010; 64:58-62.
16. Daan S, Beersma D, Borbely AA. The timing of human sleep: Recovery process gated by a circadian pacemaker. *American Journal of Physiology*. 1984; 246:R161-R178.
17. Ford DE, Kamerow DB. Epidemiologic study of sleep disturbances and psychiatric-disorders - an opportunity for prevention. *Journal of the American Medical Association*. 1989; 262:1479-1484.
18. Grover S, Avasthi A. Anti-psychotic prescription pattern: A preliminary survey of Psychiatrists in India. *Indian J Psychiatry*. 2010; 52:257-9. [PMCID: PMC2990827] [PubMed: 21180412]
19. Guan B, Deng Y, Cohen P, Chen H. Relative impact of Axis I mental disorders on quality of life among adults in the community. *J Affect Disorder*. 2011; 131:293-298.
20. Hirschfeld RM, Baker JD, Wozniak P, Tracy K, Sommerville KW. The safety and early efficacy of oral-loaded divalproex versus standard-titration divalproex, lithium, olanzapine, and placebo in the treatment of acute mania associated with bipolar disorder. *J clin Psychiatry*. 2003; 64:841-6. [PubMed: 12934987]
21. Hublin C, Partinen M. The extent and impact of insomnia as a public health problem. *Primary Care Companion to the Journal of Clinical Psychiatry*. 2002; 4:8-12.
22. Kessler RC, McGonagle KA, Zhao S, Nelson CB, Hughes M, Eshleman S. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States. Results from the National Comorbidity Survey. *Arch Gen Psychiatry* 1994; 51:8-19.
23. Kim JM, Stewart R, Kim SW, Yang SJ, Shin IS, Kim YH. Interactions between life stressors and susceptibility genes (5-HTTLPR and BDNF) on depression in Korean elders. *Biol Psychiatry* 2007; 62:423-428.
24. Kjosavik SR, Hunskaar S, Aarsland D, Ruths S. Initial prescription of antipsychotics and antidepressants in general practice and specialist care in Norway. *Acta Psychiatr Scand*. 2011; 123:459-65. [PubMed: 21401533]
25. Kuehner C. Gender differences in unipolar depression: an update of epidemiologic findings and possible explanations. *Acta Psychiatr Scand* 2003; 108:163-174.
26. Leboyer M, Kupfer DJ. Bipolar disorder: new perspectives in health care and prevention. *J Clin Psychiatry*. 2010; 71:1689-1695.
27. Lehtinen V, Joukamaa M. Epidemiology of depression: prevalence, risk factors and treatment situation. PMID, 1994, 8053370.
28. Lepine JP, Briley M. The increasing burden of depression. *Neuropsychiatry Dis Treat*. 2011; 7(11):3-7.
29. Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJ. *Global Burden of Disease and Risk Factors*. Washington: The World Bank, 2006.
30. Maria Luca, Giuseppa Prossimo, Vincenzo Messina, Antonina Luca, Salvatore Romeo, Carmela Calandra. Epidemiology and treatment of mood disorders in a day hospital setting from 1996 to 2007: an Italian study, *Neuropsychiatric Disease and Treatment* 2013; 9:169-176.
31. Maughan B, Collishaw S, Stringaris A. Depression in childhood and adolescence. *J can Acad Child Adolescent Psychiatry*. 2013; 22:35-40.
32. Merikangas KR, Jin R, He JP. Prevalence and correlates of bipolar spectrum disorder in the world mental health survey initiative. *Arch Gen Psychiatry*. 2011; 68:241-251.
33. MJ Kshirsagar, Langade D, Patil S, Patki PS. Prescribing patterns among medical practitioners in Pune, *Bull World Health Organ* 1998; 76(3):271-275.
34. Morin CM, Ware JC. Sleep and psychopathology. *Applied & Preventative Psychology*, 1996; 5:211-224.
35. Murata A, Kanbayashi T, Shimizu T, Miura M. Risk factors for drug nonadherence in antidepressant – treated patients and implication of pharmacist adherence instructions for adherence improvement. *Patient Preference Adherence* 2012; 6:863-9.
36. Nakao M, Takeuchi T, Yano E. Prescription of benzodiazepines and antidepressants to outpatients attending a Japanese university hospital. *Int J Clin Pharmacol Ther*. 2007; 45:30-5. [PubMed: 17256448]
37. Nicola Louise Barclay. Genetic and Environmental Influences on Sleep Quality: Quantitative and Molecular Genetic Approaches to an Understanding of Individual Differences, 2011.
38. Ohayon MM, Smirne S. Prevalence and consequences of insomnia disorders in the general population of Italy. *Sleep Medicine* 2002; 3:115-120.
39. Ohayon MM. Nocturnal awakenings and comorbid disorders in the American general population. *Journal of Psychiatric Research*. 2009b; 43:48-54.
40. Pilcher JJ, Ginter DR, Sadowsky B. Sleep quality versus sleep quantity: Relationships between sleep and measures of health, well-being and sleepiness in college students. *Journal of Psychosomatic Research*. 1998; 42:583-596.
41. Roth T. Insomnia: definition, prevalence, etiology, and consequences. *Journal of Clinical Sleep Medicine*. 2007; 3(5):S7-S10.
42. Sandeep Grover, Vineet Kumar, Ajit Avasthi, Parmanand Kulhara. An audit of first prescription of new patients attending a psychiatry walk-in-clinic in north India *Indian*

- J Pharmacol. 2012; 44(3):319-325. doi:10.4103/0253-7613.96302
43. Sclar D, Robison L, Schmidt J, Bowen K, Castilli L, Oganov A. Diagnosis of depression and use of antidepressant pharmacotherapy among adult in the United States. *Clinical Drug Investig* 2013; 32:139-44.
 44. Servellen G, Heise B, Ellis R. Factors associated with antidepressant medication adherence and adherence enhancement programs: A systematic literature review. *Mental Health in Family Med* 2011; 8:255-71.
 45. Smith S. Gender differences in antipsychotic prescribing. *Int Rev Psychiatry*. 2010; 22:472-84. [PubMed: 21047160]
 46. Tan CH, Shinfuku N, Sim K. Psychotropic prescription practices in East Asia: Looking back and peering ahead. *Curr Opin Psychiatry*. 2008; 21:645-50. [PubMed: 18852575]
 47. The rational use of drugs. Report of the Conference of Experts, Nairobi 25-29 November 1985. Geneva, World Health Organization, 1987.
 48. Thomas H, Chan T. Assessment and management of depression in primary care settings. *Nursing Older People* 2012; 24:32-40.
 49. Vgontzas AN, Bixler EO, Tan TL, Kantner D, Martin LF, Kales A. Obesity without sleep apnea is associated with daytime sleepiness. *Archives of Internal Medicine* 1998; 158:1333-1337.
 50. Wells KB, Sherbourne CD. Functioning and utility for current health of patients with depression or chronic medical conditions in managed, primary care practices. *Arch Gen Psychiatry* 1999; 56:897-904.
 51. Weyerer S, Dilling H. Prevalence and treatment of insomnia in the community: Results from the Upper Bavarian field study. *Sleep* 1991; 14:392-398.
 52. Xiang YT, Wang CY, Si TM, Lee EH, He YL, Ungvari GS. Use of anticholinergic drugs in patients with schizophrenia in Asia from 2001 to 2009. *Pharmacopsychiatry*. 2011; 44:114-8. [PubMed: 21491361]