



A STUDY OF OFF LABEL DRUG USE IN PSYCHIATRY DEPARTMENT AT TERTIARY CARE HOSPITAL

Pharma

Dr Pratik Chabhadiya

Senior Resident, Pharmacology Department, PDU Govt. Medical college, Rajkot

Dr Amita Kubavat*

Assistant Professor, Pharmacology Department, PDU Govt. Medical college, Rajkot
*Corresponding Author

ABSTRACT

Background: US-Food and Drug Administration has defined off-label drug as “use of drugs for the indication, dosage form, regimen, patient or other use constraint not mentioned in the approved labeling.” Off-label prescription is common in Psychiatry. The aim of this study is to evaluate such off-label drug use in psychiatry department of a tertiary care teaching hospital. **Methods:** An observational, cross sectional study was conducted among 150 patients attending Psychiatry outpatient department for the period of 3 months. Data related to demographic parameters, diagnosis and prescription details were collected directly from the patient's medical records and entered in Case Record Form (CRF). The off-label drugs were categorized as per National Formulary of India and CDSCO list of approved drug use. **Results:** Total 150 patients were included in this study with mean age of 43.6 years. Most of the patients were diagnosed with Schizophrenia [N=36, 24%]. Out of 150, 90 patients [60%] received at least 1 off label drug. Total 478 drugs were prescribed, out of which 144 [30.12%] were off label according to CDSCO and 145 [30.33%] were off label according to NFI. The drugs most frequently prescribed as off label drug according to CDSCO were Vitamins & Minerals [13.59%], Clonazepam [2.92%], Trihexyphenidyl HCL [2.09%], Diazepam [1.88%]. The drugs most frequently prescribed as off label according to NFI were Vitamins & Minerals [12.76%], Aripiprazole [2.09%], and Trihexyphenidyl HCL [2.09%]. **Conclusion:** Off label drugs used among psychiatry patients was 30.12%. The most frequently used off-label drugs were Vitamins & Minerals followed by Clonazepam & Trihexyphenidyl HCL. The use of off-label drugs in psychiatric patients has been reportedly increasing which warrant national drug regulatory authorities to review and revise safe administration such drugs.

KEYWORDS

Label drug, Off-label drug, Psychiatry, Prescription.

INTRODUCTION

The exorbitant growth and use of pharmaceuticals are managed in most of the nations by a regulatory system which sharply divides use into licensed and unlicensed categories. Drug use confirming to the marketing label is known as labeled use. Off-label use is the use of pharmaceutical drugs for an unapproved indication, age group, dosage, or unapproved form of administration.^[1]

All medications are good and beneficial in treating disease, but it's important to understand what medications are intended for and how to use them appropriately. Drugs have to undergo rigorous scrutiny before marketing approval in the form of in vitro studies, animal studies and clinical trials. These data provide labeling information like approved indications, appropriate dosing and the specific populations for its use.^{[2][3]}

Since last few years, there is increased number of patients taking psychiatric medications. This use of off-label drugs was supported by strong scientific evidence in only 4% of cases. Most common mode of off-label prescribing in Psychiatry Department is unapproved indication, dose, and altered population. Off-label drug is not illegal provided the judgment is based on scientific evidence that has been accepted by professional bodies and is commonly seen in the fields of pediatrics, oncology and psychiatry.^{[4][5][6]}

Whereas, in India only two studies reported that the prevalence of prescribing off label drugs were 39.5% and 42.34% as per British National Formulary.^{[6][8]} Through extensive literature review it was revealed that till date only one study is conducted in India as per National Formulary of India (NFI). Hence, aim of this study was to evaluate the use of off-label drugs as per National Formulary of India (NFI) - 2016, 5th edition and also according to central drugs standard control organization [CDSCO] given indication for use of a particular drug.^{[9][10]} So, by this study we can evaluate proportion of off label drug use in various psychiatric diseases in psychiatry department of our hospital setup.

MATERIAL & METHODS

A cross sectional observational study was conducted among 150 psychiatric patient attending outpatients and Inpatient Department at Pandit Dindayal Upadhyay Medical College, Rajkot, Gujarat. The study was conducted for 3 months. Before conducting the study approval was obtained from Institutional Ethics Committee, PDUMC, Rajkot, Gujarat. 100 Patients attending the psychiatric outpatient

department and 50 indoor patients were included in the study. The purpose of the study was explained to the patients and the informed consent was obtained from those who are willing to participate in the study.

Data related to demographic parameters (age, gender, locality), diagnosis of psychiatry conditions and drugs details (dose, route, frequency and duration of administration) were collected directly from the patient's medical records. Assessment of indication of prescribed drugs (label or off label) according to diagnosis will be done using central drugs standard control organization [CDSCO] – online database and NFI (National Formulary of India) – 5th edition. Assessment will also be done according to treating consultant's reference for use of that particular drug in that specific condition.

RESULTS

Total 150 prescriptions of patients [55% Male, 45% Female] were included in this study with mean age of 43.6 ± 12.52 years.

As per shown in Figure no. 1, most frequent diagnosis in psychiatry department was schizophrenia [24%] followed by major depressive disorder [23%]. Other psychiatric diseases seen were bipolar 1 disorder, alcohol withdrawal syndrome, other specified anxiety disorder, other specified schizophrenia spectrum, generalized anxiety disorder, persistent depressive disorder, cannabis withdrawal, brief psychotic disorder etc.

In figure no. 2, drug prescribing frequency is shown. Total 478 drugs were prescribed in 150 prescriptions. Figure 2. indicates clonazepam, olanzapine and multivitamin B complex were most frequently prescribed drugs. Followed by fluoxetine, escitalopram, sodium valproate, folic acid, diazepam, Aripiprazole etc.

In figure 3, drug use is displayed as label or off-label according to National formulary of India [NFI]. In which labeled and off label use is shown. Total 478 drugs were prescribed in 150 prescriptions among which 145 [30.33%] drugs are from off label prescription according to NFI. The drugs most frequently prescribed as off label according to NFI were Vitamins & Minerals [12.76%], Aripiprazole [2.09%], Trihexyphenidyl HCL [2.09%], Clonazepam [2.0%].

In figure 4, drug use is displayed as label or off-label according to central drugs standard control organization [CDSCO]. Total 478 drugs were prescribed in 150 prescriptions among which 144 [30.12%] drugs

are from off label prescription according to CDSCO. The drugs most frequently prescribed as off label according to CDSCO were Vitamins & Minerals [13.59%], Clonazepam [2.92%], Trihexyphenidyl HCL [2.09%], Diazepam [1.88%].

Figure 1. Disease distribution

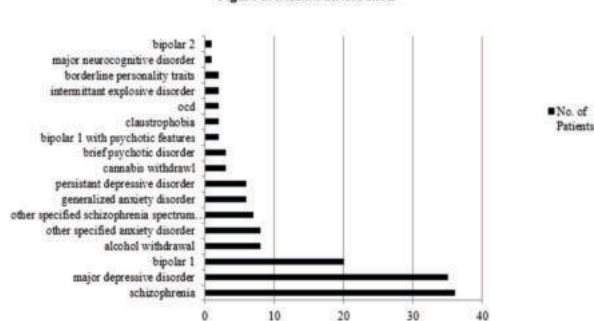


Figure 2. Most frequently prescribed drugs

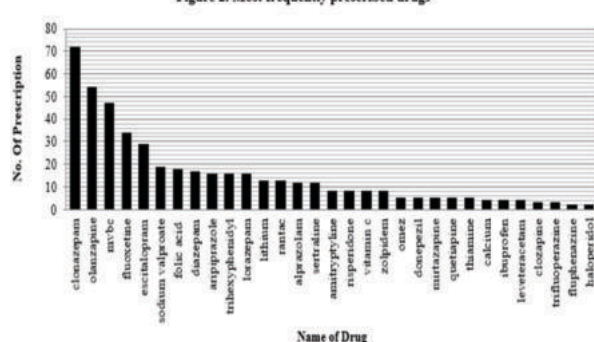


Figure 3. Drug use according to NFI

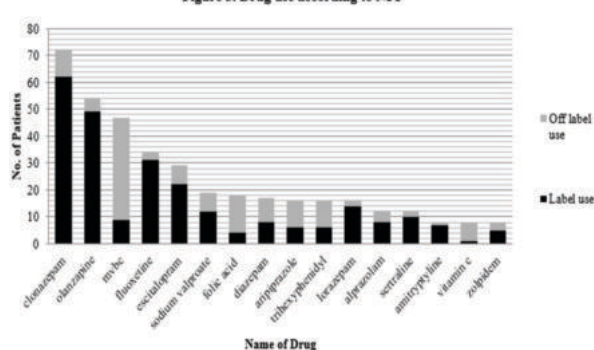
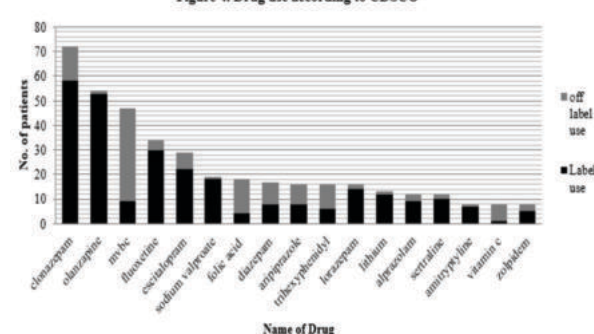


Figure 4. Drug use according to CDSCO



DISCUSSION

Many psychiatrists believe that off-label prescribing is sometimes necessary when attempting to treat certain patients, for example the patients whose symptoms have proven resistant to a range of treatment approaches. The extent of off-label prescribing in psychiatric practice is not fully known, but survey findings and research studies suggest that it is common across psychiatric prescriptions.^[6]

In our study, we have assessed prescription according to national formulary of India and CDSCO drugs database. But if we assess clinically, by taking opinion of prescribing psychiatrists, then there

will be labeled prescriptions only. As In conditions where most prescribing is for unlabeled indications (for example, in many aspects of practice in old age psychiatry) it is simply not possible to fully document the reasons for every prescribing decision in every patient.

In our study, most commonly diagnosed psychiatric disorder was schizophrenia followed by major depressive disorder which was also seen in previous studies.^{[8][11]} In present study clonazepam, olanzapine and multivitamin B complex were most frequently prescribed drugs. While in a study done by Vadher MD et al. lorazepam, fluoxetine & trihexyphenidyl were most frequently prescribed.^[12]

We assessed off-label drug use according to CDSCO & NFI both. There were few studies which have assessed drug use according to NFI and also British national formulary whereas studies analyzing drug use according to CDSCO were not found. In our study, 30.33% drugs are from off label prescription according to NFI. Whereas in previous studies off-label prescription percentage was 19.85%^[12], 39.5%^[6] and 46.41%^[8].

In present study, the drugs most frequently prescribed as off label according to NFI were Vitamins & Minerals [12.76%], Aripiprazole [2.09%], Trihexyphenidyl HCL [2.09%], and Clonazepam [2.0%]. Whereas in a study done by Vadher MD et al. trihexyphenidyl HCL [10.2%], clozapine [8.1%], clonazepam and sodium valproate [4.6%] each were there in off-label prescription.

The limitation is that the present study was conducted only in single tertiary care hospital. Hence, it is advisable that further studies should be conducted at various clinical setups to make the result more generalized and justifiable. Though, few drugs, that are prescribed by clinicians very frequently but they are not included in NFI for that diagnosis which make them off-label as per our study. Hence, It is also recommended that the revision should be made in National Formulary of India to include these drugs as labeled.

CONCLUSION:

Off label drugs used among psychiatry patients was 30.12%. The most frequently used off-label drugs were Vitamins & Minerals followed by Clonazepam & Trihexyphenidyl HCL. The use of off-label drugs in psychiatric patients has been reportedly increasing which warrant national drug regulatory authorities to review and revise formulary & enhance safe administration of such drugs.

REFERENCES:

- Stafford R. S. (2008). Regulating off-label drug use--rethinking the role of the FDA. *The New England journal of medicine*, 358(14), 1427-1429. <https://doi.org/10.1056/NEJMp0802107>
- Sugarman, P., Mitchell, A., Frogley, C., Dickens, G. L., & Picchioni, M. (2013). Off-lisence prescribing and regulation in psychiatry: current challenges require a new model of governance. *Therapeutic advances in psychopharmacology*, 3(4), 233-243. <https://doi.org/10.1177/2045125312472530>
- Thakkar, K. B., Jain, M. M., Billa, G., Joshi, A., & Khobragade, A. A. (2013). A drug utilization study of psychotropic drugs prescribed in the psychiatry outpatient department of a tertiary care hospital. *Journal of clinical and diagnostic research : JCDR*, 7(12), 2759-2764. <https://doi.org/10.7860/JCDR/2013/6760.3885>
- Radley, D. C., Finkelstein, S. N., & Stafford, R. S. (2006). Off-label prescribing among office-based physicians. *Archives of internal medicine*, 166(9), 1021-1026. <https://doi.org/10.1001/archinte.166.9.1021>
- Sugarman, P., Mitchell, A., Frogley, C., Dickens, G. L., & Picchioni, M. (2013). Off-lisence prescribing and regulation in psychiatry: current challenges require a new model of governance. *Therapeutic advances in psychopharmacology*, 3(4), 233-243. <https://doi.org/10.1177/2045125312472530>
- Kharadi, D., Patel, K., Rana, D., & Patel, V. (2015). Off-label drug use in Psychiatry Outpatient Department: A prospective study at a Tertiary Care Teaching Hospital. *Journal of basic and clinical pharmacy*, 6(2), 45-49. <https://doi.org/10.4103/0976-0105.152090>
- Wittich, C. M., Burkle, C. M., & Lanier, W. L. (2012). Ten common questions (and their answers) about off-label drug use. *Mayo Clinic proceedings*, 87(10), 982-990. <https://doi.org/10.1016/j.mayocp.2012.04.017>
- Jacob, M. K., Ammu, A., Eapen, B. A., Behnan, A., Prabha, S., & Devassy, K. A. (2016). Evaluation of off label drug use in the outpatient department of a psychiatry hospital. *Int J Pharm Sci Rev Res*, 40, 206-10.
- Indian Pharmacopoeia Commission. (2016). *National formulary of India (5th ed)*.
- Drugs - CDSCO [Internet]. Retrieved August 31 2022. <https://cdscoonline.gov.in/CDSCO/Drugs>. Ministry of Health and Family Welfare, Government of India.
- Piparva, K. G., Parmar, D. M., Singh, A. P., Gajera, M. V., & Trivedi, H. R. (2011). Drug utilization study of psychotropic drugs in outdoor patients in a teaching hospital. *Indian journal of psychological medicine*, 33(1), 54-58. <https://doi.org/10.4103/0253-7176.85396>
- Vadher, M., Patel, K., Vadher, D., Parkar, S., & Raval, C. (2017). Drug utilization study of off-label drug use in outpatient department of psychiatry: a prospective study at a tertiary care teaching hospital. *International Journal of Basic & Clinical Pharmacology*, 6(3), 581-586. doi:<http://dx.doi.org/10.18203/2319-2003.ijbcp20170817>