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ORIGINAL ARTICLE

Psychotropic Medicines for Non-Psychiatric Indications: A Cross-sectional, Observational Study

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Abstract

Background Off-label use of medicines is quite prevalent in some settings like paediatric department, psychiatry department, intensive care units and oncology departments. The off-label use of psychotropics is also substantial, however, there is scanty data regarding their use in our setup. **Objective**: To study the prescription pattern of psychotropic medications for non-psychiatric indications. **Methods:** A 6-month prospective, cross-sectional, observational study was conducted in a Tertiary Care Teaching Hospital. Patients who were prescribed at least one psychotropic medication were included in the study. Their demographic data, clinical history and all the medicines prescribed were noted. These prescriptions were analysed for the off-label use of psychotropic medications for non-psychiatric indications.

Results: A total of 200 prescriptions containing psychotropic medications were analysed in the study. Nortriptyline (41%), clonazepam (31%) and gabapentin (20%) were the most commonly prescribed psychotropic medications for non-psychiatric indications. Hypertension (29%) was the most common co-morbid condition. The most common non-psychiatric indications for which these drugs were prescribed were neurological headache (35%), restless leg syndrome (14%) and nonspecific arthralgia (10%). **Conclusion:** The off-label use of psychotropic medications was found to be substantial in our study population, warranting the attention of drug regulatory authorities to review the status of these drugs.

Key Words

Psychotropic Medicines, Off label use, Prescription Pattern, Non-Psychiatric Indications

Introduction

Physicians prescribe drugs for unapproved indications especially for the treatment of those diseases which are resistant to standard therapy or there is an absence of standard therapy.[1] Such use of medicines for an unapproved indication or contraindication, age group, dosage, or form of administration is called off-label use.[2] It usually lacks the support of efficacy and safety data obtained from clinical trials with only 30% off label use bearing scientific evidence. [3] The physicians in the United States of America have the freedom of prescribing drugs in an off-label manner as it is approved by the Food and Drug Administration (FDA) and their federal courts. [4] However, the drug cannot be marketed for its off-label indications. A gap between the prescribing information provided by the regulatory authorities, failure of the best treatment options, need for newer treatment alternatives, time and cost are the main constraints for pharmaceutical companies which prevent them from conducting trials for many indications. This gives birth to drug use for unapproved indications.[5]

Off-label use is quite prevalent in some settings like paediatric, psychiatric, intensive care units and oncology department. CNS drugs, cardiac medications, anti-infective agents, and ear-nose-throat medications are

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among the commonly prescribed drugs in an off-label manner. Among the CNS drugs, anticonvulsants, antipsychotics and antidepressants top the list. Gabapentin, Clonazepam, Amitriptyline hydrochloride and trazodone hydrochloride are the most frequently prescribed off-label drugs. [6,7] Thus, there is substantial off-label use of psychotropics. However, there is a lack of data regarding their use in our setup. Hence, the need was felt to undertake the present study to assess their off-label use in medical OPD in a tertiary teaching hospital of north India.

Materials and Methods

A cross-sectional, observational study was carried out in the department of Pharmacology in collaboration with the Department of Medicine for a period of 6 months from November 2015 to May 2016 in a tertiary care teaching hospital of North India. The study was initiated after approval by the Institutional Ethics Committee vide number I33/C/IECJ/15. All the adult patients attending the Out Patient Department of Internal Medicine and willing to give consent were screened. Those patients who were prescribed at least one psychotropic medication were included in the study. Demographic details, a complete history and prescription details were recorded in a prescribed format. These were evaluated for the off-label use by noting the psychopharmacological agent prescribed and the condition for which it was given.

Results

A total of 11,236 patients attending the Medicine OPD were screened. Out of these, 200 patients having prescriptions with at least one psychotropic medicine were picked up. Thus, the point prevalence of such prescriptions containing off-label drug use came to be 1.78%. A total of 789 medicines were prescribed of which 213 (27%) were psychopharmacological agents. Thirteen prescriptions were with 2 psychotropic medicines (*Table 1*).

The mean age of these patients was 47.41 ± 13.89 years. Almost 2/3rd of the patients were women (65 %). A preponderance of patients from urban areas was seen with an urban: rural ratio of 1.4:1. Among males, a huge majority were smokers (82%). An almost equal proportion of vegetarian (48%) and non-vegetarian (52%) patients were seen (*Table 2*).

Of the total patients, 27% had one associated co-morbid condition and 11% had two associated co-morbid conditions. 68% were without any associated co-morbid condition (*Table 2*). Among these, hypertension (29%) was found to be the most common followed by diabetes mellitus and hypothyroidism (5% each). Dyslipidaemia was seen in 4% and coronary artery disease in 2% (*Table 2*).The psychopharmacological drug used most commonly in off label manner was nortriptyline prescribed in 82 (41%) patients, followed by clonazepam in 62 (31%), gabapentin in 40 (20%), chlordiazepoxide in 10 (5%), amitriptyline in 10 (5%), escitalopram in 2 (1%), alprazolam 2 (1%) and fluoxetine 2 (1%) patients (*Table 3*).

Neurological headache, observed in 70 (35%) prescriptions was the most common non-psychiatric indication for which psychotropic medicines were prescribed. The other indications included restless leg syndrome (14%), non-specific arthralgia (10%), sinus tachycardia (10%), cervical and lumbar spondylosis (9%), rheumatoid arthritis (6%), uneasiness in the chest (6%), gastritis (5%), neuropathic pain (5%), osteoarthritis of the knee (4%), giddiness and vertigo (4%). One patient each with insomnia (1%) and rickettsial fever (1%) were prescribed psychotropic medicines (*Table 4*).

Discussion

Off-label use of psychotropics such as second-generation antipsychotics is quite prevalent in children and adolescents; more so in younger children aged 5-9 years than adolescents aged 15-17 years of age. [8,9] The mean age of our study population (47.41 ± 13.89 years) was higher compared to another study which reported a mean age of 40.36 years.[10] Our study showed a male: female ratio of 1:2 which was similar to another study by Fletscher-Covaleda *et al.* [11] Contrasting results with a male preponderance were seen with another study by Kharadi *et al*. [10] These differences could be attributed to the geographical variation in the study population.

About one-third of patients were with one or more associated co-morbidity, of which hypertension was the most common, followed by diabetes mellitus and hypothyroidism. The presence of 3 or more co-morbid conditions is positively associated with off-label prescribing. [12]

Psychotropics are commonly prescribed in an off-label manner with a rate of 12.9% reported by Vijay et al. [12] The prevalence of prescription of psychotropic drugs in our Medicine outpatient department was 1.78%. In the present study, drugs prescribed in an off-label manner were nortriptyline, clonazepam and gabapentin. Amitriptyline, escitalopram and clonazepam were reported to be the drugs most commonly prescribed in an off-label manner by Pant *et al*. [13] Similar findings were also reported by Eguale *et al.* [6] Similarly, Kharadi *et al.* [10] and Lucke *et al.* [14] reported that benzodiazepines were the most commonly prescribed drugs in an off-label manner. In another study conducted in Colombia, amitriptyline was observed to be the most common psychotropic drug prescribed in an off-label manner. [11]

Table 1.Showing Prescription Detail

Total no. of patients screened	11,236
Total no. of patients' prescriptions with psychotropic medicine picked up	200
Point prevalence of prescriptions with psychotropic medication	1.78%
Total no. of drugs prescribed	789
Psychotropic medicines prescribed	213 (27%)
Prescriptions with = 2 psychotropic medicines	13

Table 2. Demographic and baseline details of study population (N = 200)

Parameter	Values
Mean Age in years ± SD	47.41 ± 13.89
Female: Male Ratio	Approx. 2:1
Urban: Rural Ratio	1.4:1
Smoker Vs Non-Smoker	36 (18%) 164 (82%)
Veg Vs Non-Veg	96 (48%) 104 (52%)
No. of associated comorbid conditions (n=200)	**No. of patients (Percentage)**
0 Co-morbid Condition	136 (68)
1 Co-morbid Condition	54 (27)
= 2 Co-morbid Conditions	22 (11)
Most common co-morbid conditions: (n=200)	
Hypertension	58 (29%)
Diabetes mellitus	10 (5%)
Hypothyroidism	10 (5%)
Dyslipidaemia	08 (4%)
Coronary Artery Disease	04 (2%)

Table 3. Most Frequently Prescribed Psychotropic Medicines (n=200)

Medicine	ATC code	No. of patients	Percentage
Nortriptyline	N06AA10	82	41
Clonazepam	N03AE01	62	31
Gabapentin	N03AX12	40	20
Chlordiazepoxide	N05BA02	10	5
Amitriptyline	N06AA09	10	5
Escitalopram	N06AB10	02	1
Alprazolam	N05BA12	02	1
Fluoxetine	N06AB03	02	1

Table 4. Common Non Psychiatric Indications of Psychotropic Medicines (n=200)

Indication	No. of patients	Percentage
Neurological headache	70	35
Restless leg syndrome	28	14
Nonspecific arthralgia	20	10
Sinus tachycardia	20	10
Spondylosis (cervical & lumbar)	18	9
Rheumatoid arthritis	12	6
Uneasiness in chest	12	6
Gastritis	10	5
Neuropathic pain	10	5
Osteoarthritis of knee	08	4
Giddiness & vertigo	08	4
Insomnia	02	1
Rickettsial fever	02	1

In a study conducted in the pediatric population, it was observed that off-label prescribing was more common with first-generation antipsychotics in comparison to second-generation antipsychotics. [9]

In the present study, neurological conditions like neurological headache and restless leg syndrome followed by non-specific arthralgia were the most common conditions for which these drugs were prescribed. Similarly, a study in the American population also reported nocturnal leg pain, neurological pain and fibromyalgia to be the most common indications likely to be treated in an off-label manner. [6] In a done in Colombia, tension headache and insomnia were the most frequent indications for off-label use of psychotropic drugs. [11] There is a similarity in the findings of these studies concerning the conditions for which off-label use is resorted to despite the diverse geographical locations.

Such studies may be used as useful tools to guide research on labeled indications and indications that are contraindicated and also the appropriateness of these new indications. [15] It is also needed that guidelines be laid down regarding the off-label prescribing of drugs. The British Association for Psychopharmacology had proposed certain recommendations for off-label use of medicines in children and adolescents for maximum benefit to the patients. [16] The same is already legal in the US and is governed by the Federal Food, Drug, and Cosmetic Act of 1938 (FDCA) wherein the legal framework for off-label prescribing has been laid down. In a large country like ours where off-label prescribing is prevalent, certain guidelines may be laid down for off-label prescribing in the interest of benefit to the patients. Limitations: Our study was not without limitations, the foremost one being a small sample size. It could be attributed to the inclusion of prescriptions of only new patients and not the follow-up ones.[17] Secondly, no comparison was made with the package inserts or existing drug formularies for ensuring off-label use. The results mainly depict the prevalence of the use of psychotropics in non-psychiatry settings.

Conclusion

There is a substantial prevalence of off-label prescribing of psychotropic medicines in medicine OPD in our setup. Inadequate symptom relief or limited availability of drugs in these conditions prompts the physicians to explore newer options, despite lack of evidence. More extensive research is warranted in this domain to generate a robust evidence base regarding off-label uses to help in rational decision-making. It is imperative that the regulatory authorities also take the initiative to reassess and review the status of these drugs in this regard.

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Conflicts of Interest

There are no conflicts of interest.

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