

## Research Article



## Drug Utilization Study of Antifungal Agents Used in Department of Skin & V.D. of a Tertiary Care Teaching Hospital

Vegada BN<sup>1\*</sup>, Karelia BN<sup>2</sup>, Singh AP<sup>3</sup>

<sup>1\*</sup>Fourth year post graduate student, Department of Pharmacology, P.D.U. Govt. Medical College, Rajkot, Gujarat, India.

<sup>2</sup>Associate professor, Department of Pharmacology, P.D.U. Govt. Medical College, Rajkot, Gujarat, India.

<sup>3</sup>Professor & Head of the Department, Department of Pharmacology, P.D.U. Govt. Medical College, Rajkot, Gujarat, India.

\*Corresponding author's E-mail: [bhavishhavegada@gmail.com](mailto:bhavishhavegada@gmail.com)

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### ABSTRACT

The aim of the experiment is to assess the utilization pattern of antifungal agents used in department of skin and V.D. of tertiary care teaching hospital. This prospective, record based, observational study was carried out in department of skin and V.D. from December 2012 to April 2014. Patients diagnosed with fungal disorder by dermatologist were included in study as per inclusion criteria. Data were collected and analyzed for drug utilization pattern and prescribing indicators. Total 331 patients were included for the analysis. Combination therapy was most commonly prescribed than monotherapy. Most commonly prescribed oral antifungal agent was fluconazole (97.20%) and topical antifungal agent was clotrimazole (91.93%). Average number of drugs prescribed per encounter was 3.39. Percentage of drugs prescribed by generic name was 54.33%. Percentage of drugs prescribed from national list of essential medicine was 56.86%. Most common oral antifungal drug and topical antifungal drug were fluconazole and clotrimazole respectively. Combination antifungal therapy was more commonly used than monotherapy.

**Keywords:** Antifungal agents, Drug utilization study, prescribed daily dose.

### INTRODUCTION

Life expectancy has increased by at least ten years since the first use of antimicrobial agents for the treatment of microbial infections. Interestingly, this success has also increased the number of fungal infections.<sup>1</sup> Fungal infections are extremely common in the tropical region like India and some of them are serious and even fatal. These infections usually occur as a result of decrease in natural defences (immunocompromised state, critically ill, advanced age, use of immunosuppressive drugs) or opportunistic heavy exposure to the fungus. They produce diverse human infections ranging from superficial skin infection to internal organ invasion (systemic diseases).<sup>2</sup> Superficial fungal infections are not life threatening, but associated with a significant decrease in quality of life. They can be very uncomfortable and may have spread to other individuals or become invasive.<sup>2,3</sup> Most of the superficial and subcutaneous fungal infections are easily diagnosed and readily amenable to treatment.<sup>2</sup>

The antifungal drugs presently available fall into these categories – oral or parental for systemic infections, oral and topical drugs for mucocutaneous infections.<sup>4</sup> Amphotericin B was the only effective antifungal drug available for systemic use for a number of years, but because of toxicity and drug resistance; now its use is limited.<sup>5,6</sup> There has been a major increase in the prescription of antifungal agents after the introduction of fluconazole into the market in the late 1980s, and again in late 1990s.<sup>7</sup> So, pharmacotherapy of fungal disease has been revolutionized by the introduction of the relatively nontoxic oral drugs, combination therapy and new

formulations of older agents. Unfortunately, the appearance of azoles resistant organisms, as well as the rise in the number of patients at risk for mycotic infections, has created new challenges.<sup>4</sup>

Drug utilization research or studies are the powerful exploratory tools to ascertain the role of drugs in the society which refers to the marketing, distribution, prescription and use of drugs with special emphasis on the medical, social and economic consequences.<sup>8</sup> The Data regarding antifungal drug usage pattern in outpatient department of Dermatology in India are particularly lacking. Keeping these facts in consideration, the present study was planned to define the pattern of antifungal drug use for common fungal infections of skin.

### MATERIALS AND METHODS

This was a record based, observational, prospective study conducted from December 2012 to April 2014 at the Department of skin and V.D. of a tertiary care teaching hospital after approval from Institutional Ethics Committee of tertiary care teaching hospital.

Based on WHO (World Health Organization) recommendations for sample size in drug utilization studies, we used a sample consisting of 331 patients having 1252 encounters.

All newly diagnosed patients with cutaneous fungal disorders along with any other co-morbid conditions were included. After the diagnosis of fungal infection and treatment prescribed by dermatologist, all the details regarding personal details, past history, personal history, present complaints, investigations and given treatment were recorded.



Recorded data was analyzed using descriptive statistics to determine WHO drug use indicators, utilization pattern of drugs and drug utilization study metrics.

## RESULTS

A total of 1252 prescriptions were collected from 331 patients with fungal disorder out of which majority (35.35%) belonged to age group of 16-30 years.

Total number of males and females among all patients were 171 (51.66%), 160 (48.34%) respectively.

Most of the patients were homemaker (38.27%) followed by unskilled labours (28.40).

Demographic characteristics of patients are summarized in Table 1.

**Table 1:** Demographic Characteristic of patients

Characteristics	No of Patients (n=331)
<b>Age (Years)</b>	
0-15	40 (12.09)
16-30	117 (35.35)
31-45	87 (26.28)
46-60	67 (20.24)
61-75	19 (5.74)
>75	1 (0.30)
Total	331(100)
<b>Sex</b>	
Male	171 (51.66)
Female	160 (48.34)
Total	331(100)
<b>Occupation</b>	
Unskilled labours	92 (28.40)
Skilled labours	19 (05.86)
Service	13 (04.01)
Business	19 (05.86)
Homemaker	124 (38.27)
Student	57 (17.60)
Total	324(100)*

\*- Patients less than 5years of age were excluded from analysis.

Regarding treatment pattern, as shown in Table-2, majority of the patients (95.92%) were prescribed a combination of a topical with an oral antifungal drug followed by solely topical (2.00%) or oral antifungal drug (2.08%).

The most commonly prescribed antifungal drug classes were imidazole (99.84%) followed by triazole (97.20%), allylamine (1.92%), antibiotics (0.64%). Most commonly prescribed oral antifungal agent was fluconazole (97.20%) and topical antifungal agent was clotrimazole (91.93%).

Combination therapy of oral fluconazole and topical clotrimazole was prescribed in highest number of encounters.

**Table 2:** Treatment pattern during entire study period

Treatment Modalities	Number of encounters (n=1252)
<b>Combination therapy</b> (Oral + Topical)	<b>1201 (95.92)</b>
<b>Monotherapy</b>	<b>51 (4.08)</b>
Oral therapy	25 (2.00)
Topical therapy	26 (2.08)
<b>Topical Antifungal Agents*</b>	<b>Number of encounters (n=1252)</b>
A. Single topical agent	
Clotrimazole	1151 (91.93)
Miconazole	16 (1.28)
Ketoconazole	19 (1.52)
Terbinafine	17 (1.36)
Butenafine	6 (0.48)
B. Fixed drug combinations	
Clotrimazole + Betamethasone	64 (5.11)
Whitfield's ointment	106 (8.47)
<b>Oral Antifungal Agents*</b>	<b>Number of encounters (n=1252)</b>
Fluconazole	1217 (97.20)
Griseofulvin	8 (0.64)
Terbinafine	1 (0.08)

**Note:** \*The sum of the variables exceeds 100.0 due to combined prescriptions of more than one agent or pharmaceutical form.

**Table 3:** Details on prescribing indicators

Indicators	Number
Average number of drugs prescribed per encounter	3.39
Average number of antifungal prescribed per encounter	2.08
Average number of systemic antifungal drugs prescribed per encounter	0.98
Average number of topical antifungal drugs prescribed per encounter	1.10
Average number of antihistaminic prescribed per encounter	0.97
percentage of encounter with injections	1 (0.08)
Percentage of encounters with fixed dose combinations	171 (13.66)
Percentage of drugs prescribed by generic drugs	2308/4248 (54.33)
Percentage of drugs prescribed from WHO EML*	22/51 (43.14)
Percentage of drugs prescribed from NLEM**	29/51 (56.86)

\* WHO model list of essential medicines, 18<sup>th</sup> edition, 2013

\*\* National list of essential medicines, India, 3<sup>rd</sup> edition 2011

Regarding WHO specified drug use indicators as shown in Table-3, the 1252 prescriptions contained 4248 drugs. Out of these, 2605 drugs were antifungal drugs. The other commonly co-prescribed drugs were antihistaminic,



topical steroids and vitamins. The average number of drugs per encounter was 3.39. In majority of encounters (71.80%), three drugs were prescribed. Percentage of drugs prescribed by generic name was 54.33%. Percentage of drugs prescribed from national list of essential medicine was 56.86%.

The ATC coding, PDD and PDD to DDD ratios are also summarized in Table 4. DDDs mentioned in the table are for the oral route and obtained from the WHO ATC/DDD website. Ratio of prescribed daily dose and defined daily dose of fluconazole was 1.35.

**Table 4:** ATC/DDD classification system with calculated prescribed daily dose

Drug	ATC Code	DDD (mg)	PDD (mg)	PDD/DDD
Fluconazole	J02AC01	200/7	270/7	1.35
Griseofulvin	D01BA01	500	300	0.6
Terbinafine	D01BA02	250	250	1

## DISCUSSION

As per Table 1, out of total enrolled patients with fungal infections of skin, most common age group (35.35%) was 16 – 30 years. Mean age of patients was 34.35 ± 16.21 (mean ±SD) years. Rajathilagam T. conducted a study in Tamilnadu showed that the average age of all patients was 31.96 years.<sup>5</sup> Total number of males and females among all patients were 171 (51.66%), 160 (48.34%) respectively. Rajathilagam T. conducted a study showed that 61% of the patients were men and 39% were women. Most of the patients of fungal infections were homemakers (housewife and retired person) followed by unskilled labours. The least affected ones who are in service or business. Andrea carried out a study also showed that most of the patients were homemaker.<sup>9</sup>

Most of the fungal infections can be managed with topical therapy alone; however, in an attempt to increase the cure rate, topical and systemic (oral) medications are often combined. In our study, 95.92% of patients received combination of topical and systemic therapy during entire study period. (Table – 2) Rajathilagam and Minocha conducted studies showed that most of the patients were also mostly treated with a combination of oral as well as topical antifungal agents.<sup>5, 10</sup>

Our study showed that fluconazole (97.20%) was the most commonly prescribed oral antifungal drug. (Table – 2) Rajathilagam conducted a study also demonstrated that fluconazole (63%) was most commonly used oral antifungal agent.<sup>5</sup> Sarkar conducted a study in Nepal showed that fluconazole was the most commonly prescribed oral antifungal agent because its once a week dose schedule results in cost-effective treatment and a lower propensity for adverse effects.<sup>11</sup> Minocha and Narwane conducted studies also showed that most common oral antifungal agent was fluconazole due to availability in hospital pharmacy.<sup>10,12</sup> Andrea carried out in Brazil also showed that fluconazole was most widely

systemic antifungal agent for dermatophytosis.<sup>9</sup> Its other advantages include fewer drug interactions and better gastrointestinal tolerance.

In our study, most commonly prescribed topical antifungal agent was clotrimazole (91.93%) followed by ketoconazole (1.52%) and miconazole (1.28%). (Table – 2) In our hospital pharmacy, only clotrimazole was available from azole group and other topical antifungal agent from allylamine group was not available. Topical therapy with the fungicidal allylamine antifungal is associated with slightly higher cure rates and shorter courses of treatment than therapy with the fungistatic azoles.<sup>9</sup> However; this therapeutic advantage is offset by their significantly higher cost. Rajathilagam T. Conducted a study showed that eberconazole (45%) and clotrimazole (31%) followed by terbinafine (18%) were noted to be the frequently prescribed topical antifungal drugs.<sup>5</sup> Minocha conducted a study in Ludhiana showed that clotrimazole was most commonly prescribed antifungal agent.<sup>10</sup>

As per Table 3 average 3.39 drugs per encounter were prescribed. Rajathilagam conducted a study showed that average 2.32 drugs per encounter were prescribed.<sup>5</sup> Polypharmacy can lead to poor compliance, drug interactions, and adverse drug reactions, under use of effective treatments, medication errors and increased cost of therapy. Drug interactions due to polypharmacy may lead to unnecessary hospitalization, increasing the cost of treatment again.<sup>12,13</sup>

Standard prescription writing includes prescription of drug by its generic name to avoid dispensing errors and to lessen influence of pharmaceutical companies on prescribers. Prescription of drug by its brand name may also increase the cost of the treatment.<sup>14</sup> Total 54.33% of drugs was prescribed by generic names. The proprietary names were used for the drugs prescribed from outside the hospital. WHO model list of essential medicines represents list of minimum medicine needs for a basic health-care system, listing the most efficacious, safe and cost-effective medicines for priority conditions.<sup>15</sup> Here, during the study period, 51 different drugs were prescribed on outpatient basis in enrolled patients by Dermatologist (Table 3). Twenty two out of fifty one drugs (43.14%) were listed in WHO model list of essential medicines, 18<sup>th</sup> edition. In contrast to this, National List of essential medicines, India, 3<sup>rd</sup> list, 2011 contains twenty nine out of fifty one drugs (56.86%).<sup>15,16</sup>

The defined daily dose is the assumed average maintenance dose per day for a drug used for its main indication in adults. The DDD is a unit of measurement and does not necessarily agree with the recommended or prescribed daily dose. The prescribed daily dose is defined as the average dose prescribed according to representative sample of prescriptions.<sup>17,18</sup> The DDD for fluconazole is 200/7 mg/day and PDD of fluconazole in our study is 270/7 mg/day, so PDD/DDD ratio of fluconazole was more than one. (Table – 4) When the PDD/DDD ratio is either less than or greater than one, it



may indicate either under or over utilization of drugs. But it is important to note that the PDD can vary according to 'patient' and 'disease' related factors.<sup>19</sup> A limitation of all prospective observational studies is the Hawthornes bias, that is, the prescriber's behaviour might be influenced by the fact that they are being observed.<sup>20</sup> A retrospective study can overcome this problem.

### CONCLUSION

Our study shows that most common antifungal drug class was imidazole group and most common oral antifungal drug and topical antifungal drug were fluconazole and clotrimazole respectively.

Combination antifungal therapy was more commonly used than monotherapy. Fluconazole was overused in our study.

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