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Original Research Article

A Study of Adverse Drug Reactions Due To Antifungal Drugs in the Dermatology Department of a Tertiary Care Teaching Hospital in Gujarat

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Abstract:

Background: In general, fungal infections are one of the contributors of disease burden in the community and Variation in drug response and day by day increasing burden of ADRs, this study emphasis on need of effective evaluation and need of reporting of ADRs.

Aim & Objectives: The present study was designed to analyze various clinical pattern of ADRs due to antifungal drugs in the dermatology department of a tertiary care teaching hospital.

Methods: After getting permission from the ethics committee, this prospective observational cross-sectional study was conducted for seven months in the dermatology outpatient department of a tertiary care teaching hospital in western India to evaluate various clinical patten of ADRs due to antifungal drugs.

Results: Total 24 ADRs were reported out of 900 patients. Most common ADRs noted wereepigastric pain in 11 patients, followed by hair fall in 9 patients. Itraconazole is most commonly responsible for hair fall and Fluconazole is most commonly responsible for epigastric pain.

Conclusions: For reduction of mortality and morbidity monitoring and reporting and assessment of ADRs were necessary. For better patient care, drug safety and rational use of medicines knowledge of various drugs responsible for ADRs are must for health care professionals.

Keywords: Adverse drug reactions, Anti-fungal Drugs.

Introduction

The WHO's definition of an adverse drug reaction is "a response to a drug that is noxious and unintended and occur at a doses normally used in man for prophylaxis, diagnosis and therapy of disease, or modification of physiological functions." [1] An adverse cutaneous reaction caused by a drug is any undesirable change in the structure or function of the skin, its appendages or mucous membranes and it encompass all adverse events related to drug eruption, regardless of the etiology. [2]

The systemic antifungals like griseofulvin, itraconazole, terbinafine, ketoconazole and fluconazole are widely used for superficial fungal infection. The most frequently encountered adverse events are gastrointestinal disturbance (nausea, constipation, abdominal pain) and drug reactions. [3] Over the last decade, new antifungal drugs have been introduced in clinical practice. Different antifungal drugs have different spectra of action, mechanisms of action, clinical efficacy, and tolerability, routes of administration, potential drug–drug interactions, safety profiles, and costs. Appropriate use of these novel agents has important implications for patient care and for health care–associated infection control.

Inappropriate use of antifungal agents may result in adverse events, unnecessary exposure, higher costs, and increased microbial resistance. [4]

Methods

After getting permission from the ethics committee, present hospital based prospective, observational, cross-sectional study was carried out in the dermatology outpatient department of Sir Sayajirao General Hospital, a tertiary care teaching hospital in western India.

The study was carried out for seven months from April 2021 to October 2021.

Aim & Objectives

Aim

The aim of the present study was to analyse various clinical pattern of ADRs due to antifungal drugs in dermatology department of a Tertiary care teaching hospital.

Objectives

- To document ADR, reported or experienced by the patient.
- To assess causality, severity and preventability of ADR.

Permission of Ethics Committee: This research was approved by the Institutional Ethics Committee for Biomedical and Health Research. [Approval Letter No. IECBHR/ 42- 2021]

Sampling and sample size:

Based on the data from the Dermatology department, we were likely to get 2-3 adverse drug reaction due to antifungal drugs per month.

So, considering duration based study of 7 months period we has estimated sample size of 20 participants who are likely to get ADR due to antifungal drugs.

Inclusion criteria:

1. Patients of any age and gender attending dermatology OPD for adverse drug reaction due to antifungal drugs.
2. Willing to give consent.

Exclusion criteria

1. Patient presenting with adverse reaction of a drug where drug taken is not known.

Ethical issues: Less than Minimal risk

Informed consent process:

Informed consent will be taken before obtaining the required information from the case history from patient.

Confidentiality issues and data safety:

Confidentiality and data safety will be maintained.

Data collection procedure: Data of Patients attending OPD of Dermatology Department for any adverse drug reaction due to antifungal drugs recorded in CRF as well as ADR form.

Data analysis: The recorded data will be entered in excel sheet and will be analyzed for percentage and frequency with the help of appropriate statistical software. For all the ADR collected, causality assessment, severity assessment and preventability assessment done using appropriate scale. (Causality-WHO causality assessment scale and Naranjo Algorithm, severity- modified Hartwig and Siegel scale preventability- Schumock and Thornton scale)

Results: During this study, out of 900 patients, 24 patients developed some ADR. Most common ADRs noted wereepigastric pain in 11 patients, followed by hair fall in 9 patients. Other ADRs recorded were folliculitis, nausea and headache which were observed in 4 patients. [Figure 1] During this study out of 900 patients, 24 (2.67%) patients developed some ADR, out of 524 male patients included in this study, 16 (3.05%) developed ADR while out of 376 female patients, 8 (2.12%) developed ADR.

Table 1: Number and Percentage of ADR Developed According to Drug

ADR	Drug Responsible	Number of ADR	Number of prescriptions	Percentage of ADR developed
Hair Fall	Itraconazole	9	114	7.89%
Headache	Griseofulvin	1	14	7.14%
Nausea	Terbinafine	1	26	3.85%
Epigastric Pain	Fluconazole	7	805	0.87%
	Itraconazole	3	114	2.63%
	Terbinafine	1	26	3.85%
Folliculitis	Fluconazole	2	805	0.25%

Causality Assessment: Assessment of ADRs using WHO-UMC criteria showed that 79.17% of ADRs were possible and 20.83% were classified as probable. [Table 2]

Table 2: Causality Assessment Using WHO-UMC algorithm

Category	Number of ADRs	Percentage
Certain	0	**0.00%**
Probable	5	**20.83%**
Possible	19	**79.17%**
Unlikely	0	**0.00%**
Total	**24**	**100.00%**

Assessment of ADRs using Naranjo's causality assessment scale showed that91.67% of ADRs were possible and 8.33% were classified as probable. [Table 3]

Table 3: Causality Assessment Using Naranjo Algorithm

Causality	Number of ADRS	Percentage
Definite	0	**0 %**
Probable	2	**8.33 %**
Possible	22	**91.67 %**
Doubtful	0	**0 %**
Total	**24**	**100.00%**

Severity Assessment: According to modified Hartwig and Siegel scale, Level 1 ADRs requires no change in treatment with the suspected drug. Level 2 ADRs requires the suspected drugs be withheld, discontinued or otherwise changed, No antidote or other treatment is required. This are collectively known as mild ADR. In the present study 91.67% of ADRs were mild ADR (3 ADR in level 1 and 19 ADR in level 2). Level 3 ADRs requires the suspected drugs be withheld, discontinued or otherwise changed, and/or antidote or other treatment required and they are labelled as moderate ADR. 8.33% of ADRs in the present study were moderate ADR (2 ADR in level 3) [Table 4]

Table 4: Severity Assessment Using Modified Hartwig and Siegel Scale

Category	Number of ADRs	Percentage
Mild (level 1,2)	22	**91.67%**
Moderate (level 3,4)	2	**8.33%**
Severe (level 5,6,7)	0	**0.00%**
Total	**24**	**100.00%**

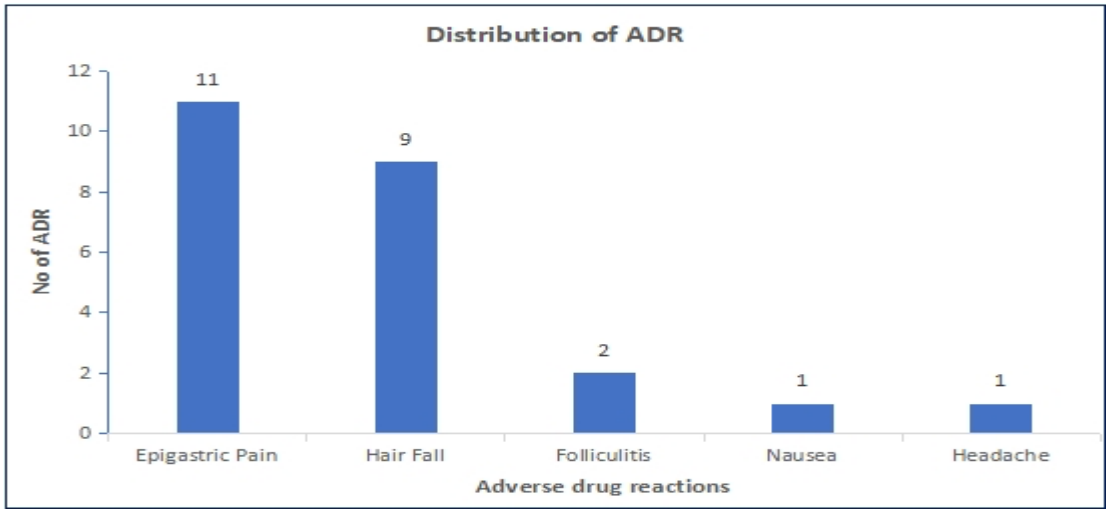

Figure 1: Distribution of ADR among Patients

Preventability Assessment

Preventability was assessed based on Schumock and Thornton scale. ADRs were categorized into definitely preventable, probably preventable or not preventable. All reported ADRs were not preventable ADRs. None was preventable ADR.

Discussion

Assessment of ADR based on causal relationship, severity and predictability and classifying them by reaction type and drug class is useful in identifying opportunities to reduce adverse drug reactions.

In the present study, among 900 patients, 24 ADRS were reported. Highest number of ADRs observed in the present study was with itraconazole followed by fluconazole. Most common adverse drug reaction recorded in present study was epigastric pain in 11 patients which was due to fluconazole, itraconazole and terbinafine. Second most common ADR recorded in present study was hair fall, which was most commonly seen with itraconazole.

Davis et al. in 2018 studied tolerability of long-term fluconazole therapy (60 to 400 days) in which they reported alopecia, xerosis, fatigue, nausea, vomiting, Anorexia, headache and other ADR due to fluconazole. [5]

Thakare V et al, in 2015 studied safety and efficacy of oral itraconazole in dermatophytosis in 524 patients. in their study they reported ADRs Like gastrointestinal upset (nausea, abdominal pain, constipation), headache, dizziness, thrombocytopenia, and metabolic side effects like hypokalaemia, and hypertriglyceridemia. It is reported that the level of hepatic transaminases

increases in about 1%-5% of patients who have received continuous therapy with systemic itraconazole. [3] In present study, ADR reported due to terbinafine were nausea and epigastric pain in one patient. Verma N et al, observed terbinafine induced hot flushes in two patients. They had also assessed biochemical parameters like liver function test and renal function test. All the lab parameters were within range and showed insignificant difference in all the groups. Hence, they concluded that terbinafine is safe when given for higher doses or for longer duration. [6]

Other ADR reported in present study were headache and folliculitis. In the present study, assessment of ADRs using WHO-UMC criteria showed that 79.17% of ADRs were possible while 20.83% were classified as probable. [7] Assessment of ADRs using Naranjo's causality assessment scale showed that 91.67% of ADRs were possible and 8.33% were classified as probable. [8]

Moderate ADRs require that treatment with the suspected drug to be held, discontinued or changed. In this study, 22 ADRs were mild ADR and only 2 were moderate ADR according to Modified Hartwig and Siegel scale. In both ADR of moderate category, the suspected drug was changed. No additional treatment was required in either case. [9]

ADR can be grouped as preventable and non-preventable ADR according to Schumock and Thornton scale. In case of preventable ADR, proper history taking, lab investigation and regular monitoring can help in preventing development of such ADR. In present study, no reported ADR was of preventable category which reflects good clinical practice in our set up. [9]

However, this study has following limitations.

Findings of prescription pattern of this study might not be generalizable to other parts of the country and It was not possible to include each and every patient who was prescribed antifungal drug.

Conclusions

For reduction of mortality and morbidity monitoring and reporting and assessment of ADRs were necessary.

For better patient care, drug safety and rational use of medicines knowledge of various drugs responsible for ADRs are must for health care professionals.

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Declarations

Ethical approval: Approved by Institutional Ethics Committee for Biomedical and Health Research of Medical College [Approval Letter No.IECBHR/ 42- 2021]

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