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Short Communication

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A retrospective study on drug utilization pattern and cost utility analysis of antifungal drugs

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Abstract

Objectives Fungal infections in humans are superficial or systemic and are found to be life threatening. They are common among the middle age group and particularly in females and immunocompromised patients.

Methods This study was conducted to evaluate the prescription pattern of antifungal drugs and their economic burden on patients. The study was designed as a single centered, cross-sectional retrospective pharmacy database study of utilization of antifungal drug therapy and their cost analysis. Data for the period from 1 January 2019 to 31 December 2019 were retrieved from the inpatients and outpatient electronic pharmacy records along with the unit dose prices of antifungal drug in the study hospital.

Key findings Antifungals use was more among females (67.05%) compared with males (34.91%). The use was predominant among middle age group (31–45) with Clotrimazole being the most utilized lower cost topical drug and fluconazole the next preferred systemic drug with least toxicity. Variconazole is a novel drug utilized the least among all age groups due to its adverse effects and higher cost. Clotrimazole is the drug of choice topically due to low cost and lesser absorption orally. Fluconazole is the next preferred drug that can be given systemically and its use remain unchanged due to lower cost and least toxicity in immunocompromised patients.

Conclusions Variconazole although have adverse effects and used rarely it is the drug preferred in invasive treatments when benefit outweighs the risk. Variconazole is highly expensive drug used in invasive treatments and its adverse drug reactions, and cost need to be monitored.

Keywords: antifungal drugs; adverse drug reactions; cost analysis; retrospective study

Introduction

Fungal infections in humans are having a negative impact on the health and are found to be life threatening.[1] Some infections are just on skin, nail hair and mucosal surfaces called as superficial and the others are found to be systemic.[2, 3] Although systemic infections are life threatening, topical infections are considered important because of their epidemiology and widespread existence.[4] There is an increase in number of fungal infections in immunocompromised patients and the first line treatment for these infections is by antifungal agents that can be given by different routes.[2, 5, 6] As the number of infections and the mortalities rise in the past years there has been a rise in the development of novel antifungal agents.[1, 7]

Superficial infections are easily prone to drug resistance and the treatments for nail; hair lasts for a long duration of time that may

increase the financial burden on the patient.[8] In view of this, the aim of this study was to analyze the adherence of the prescribing patterns of antifungal drugs according to the standard guidelines and also to determine the economic impact of drug on the patient.

Methods

The study was designed as a single centered, cross-sectional retrospective pharmacy database study of utilization of antifungal drug therapy and their cost analysis. Data for the period from 1 January 2019 to 31 December 2019 were retrieved from the inpatients and outpatient electronic pharmacy records along with the unit dose prices of antifungal drug in Al-Mana General Hospital Al-Khobar, Saudi Arabia. The daily price of each drug was computed based on the World Health Organization (WHO) Defined Daily Dose (DDD) and Infectious Diseases Society of America (IDSA) and European Society of Clinical Microbiology and Infectious Diseases (ESCMID) guidelines. Patients who were not prescribed and dispensed any medications for antifungal drug therapy were excluded from the study.

The cost analysis of each studied drug was calculated in terms of the average price of each unit dose of each prescription. Lastly, the prescribing pattern was evaluated based on the adherence of guidelines and protocols of the Infectious Diseases Society of America (IDSA) and European Society of Clinical Microbiology and Infectious Diseases (ESCMID) guidelines.

Study place

A retrospective observational study was carried out in Al-Mana Group of Hospital (AGH), Saudi Arabia. AGH Al-Khobar is 250 bedded teaching private hospital with 74 out-patient clinic to provide health care facilities to the community of Saudi Arabia.

Statistical analysis

Demographic characteristics were demonstrated as frequencies and percentages (with Wilson 95% confidence intervals for proportions). The Chi-square (for *P*-value calculation) was used as appropriate to compare the utilization rates of antifungal drug for the treatment of various diseases. All statistical analyses were conducted using SPSS version 26 (SPSS Institute Inc., Cary, NC, USA) and Microsoft Excel 2013. *P*-value ≤ 0.05 considered as statistically significant.

Results

The study was conducted on 11,509 patients and the data were retrieved from the electronic records of Al-Mana General Hospital, Al Khobar, Saudi Arabia. As displayed in Table 1 there were significantly higher number of females (67.05%) receiving antifungal treatment than males (34.91%) with greater prevalence in middle age group 31–45 (33.64%).

Table 2 describes the prescribing patterns of antifungal drugs according to Infectious Diseases Society of America (IDSA) and European Society of Clinical Microbiology and Infectious Diseases (ESCMID) guidelines. All the drugs have *P* ≤0.05. Clotrimazole which is available in drops, suppository contributed to the highest percentage 18.31%. Mometasone Furoate, Miconazole combination contributed to the next preferable drug. They all are utilized majorly among age group 31–45. Fluconazole and miconazole nitrate are the antifungal drugs utilized to similar extent (10.77%) and both can be used orally, with fluconazole being available also as an infusion. Variconazole given systemically is utilized the least 0.32%. Furthermore, there are no data of its prescription in age group above 60. Miconazole nitrate (3%) Mometasone Furoate, Miconazole (3.61%) are the antifungal drugs prescribed the most among children (below 15) and Variconazole and Itraconazole the least prescribed among children (below 15) and older (above 60). Miconazole, miconazole nitrate are prescribed most among age group 61–75 and miconazole nitrate is utilized the most in age group above 75.

Table 1 Baseline demographic characteristics of the studied patient's

Characteristics	Total 11,509% (95% CI) (*n*)
Gender	
Male	34.91% (33.65–35.38) (3972)
Female	67.05% (66.19–67.90) (7717)
Age (Years)	
0–15	12.78% (12.18–13.4) (1471)
16–30	24.98% (24.21–25.79) (2876)
31–45	33.64% (32.78–34.51) (3872)
46–60	17.87% (17.18–18.58) (2057)
61–75	7.22% (6.77–7.72) (832)
>75	3.84% (3.16–3.83) (401)
Nationality	
Saudi	51.77% (51.33–53.15) (6012)
Non-Saudi	48.23% (47.74–49.56) (5599)

Table 3 shows cost-utility analysis prescription wise in SR (USD). Variconazole is found to be the most expensive drug 374.72 (99.90), Miconazolenitrate, clotrimazole, itraconazole, miconazole, Econazole nitrate are among the least expensive drugs. Duration of therapy (days) was highest for ketoconazole (37.29) and least for Econazole Nitrate (3.28).

Discussion

In our study, the most commonly used antifungal drug is found to be Clotrimazole. Clotrimazole is one of the oldest drugs. It has low absorption orally and used in oral and vaginal candidosis. It is found to be the most prescribed topical antifungal.[9, 10] In contrast many other studies have reported fluconazole to be the drug of choice for systemic use and its preference for treatment in immunocompromised patients remains unchanged with introduction of newer antifungals. It has lower cost and least toxicity.[10–14] Variconazole is found to be the least prescribed medication. This may be due to the fact that although effectively used for prophylactic and treatment of fungal infections of lungs and bone transplants it has serious side effects on skin.[15] This is in contrast to a study that states that with the development of Variconazole it has replaced older antifungals and is been the drug of choice in systemic infections with shortest time of therapy.[13]

Conclusion

The pattern of drug utilized for fungal infections was in parallel to the results of studies in other countries. Clotrimazole is found to be the most prescribed drug topically. Variconazole although effective in invasive treatments its benefit risk ratio and cost should be monitored. As the utilization of antifungals is greater among females, ADR (adverse drug reactions) should be monitored when prescribed in pregnant and lactating females. This is study shall form

Table 2 Prescribing patterns of antifungal drugs according to Infectious Diseases Society of America (IDSA) and European Society of Clinical Microbiology and Infectious Diseases (ESCMID) guidelines (n = 11,509)

Drug	Dosages form	Route of administration	Total 11,509% % (95% CI) (n)	0–15 years % (95% CI) (n)	16–30 years % (95% CI) (n)	31–45 years % (95% CI) (n)	46–60 years % (95% CI) (n)	61–75 years % (95% CI) (n)	>75 years % (95% CI) (n)	P-value
Clotrimazole	Drop, Suppository	Rectal, Vaginal, Ophthalmic	18.31% (17.62–19.04) (2108)	1.69% (1.47–1.69) (195)	4.73% (4.37–4.74) (545)	6.46% (6.03–6.46) (744)	3.77% (3.44–4.13) (434)	1.25% (1.07–1.48) (145)	0.39% (0.29–0.52) (45)	≤0.05
Econazole Nitrate	Vaginal Pessary	Vaginal	4	13	0	4	0	0	0	–
Fluconazole	Capsule, Intravenous	Oral, Infusion Vial	10.77% (10.22–10.77) (1240)	0.46% (0.35–0.60) (53)	2.67% (2.40–2.99) (308)	4.16% (0.56–0.9) (479)	2.31% (3.81–4.54) (267)	0.71% (0.57–0.71) (82)	0.44% (0.33–0.58) (51)	≤0.05
Itraconazole	Capsule	Oral	4.13% (3.79–4.52) (476)	0.09% (0.06–0.18) (11)	1.13% (0.96–1.35) (131)	1.78% (1.55–2.04) (205)	0.85% (0.70–1.03) (98)	0.23% (0.16–0.834) (27)	0.03% (0.01–0.08) (4)	≤0.05
Ketoconazole	Cream	Topical	8.99% (8.48–9.53) (1035)	1.69% (8.48–9.53) (195)	2.85% (2.03–2.58) (263)	2.58% (2.32–2.92) (298)	1.56% (1.35–1.80) (180)	0.57% (0.45–0872) (66)	0.28% (0.21–0.41) (33)	≤0.05
Miconazole	Oral liquid, Cream, Vaginal Pessary	External, Vaginal	13.20% (12.60–0.18) (1520)	0.10% (0.06–5.12) (12)	5.09% (4.70–5.51) (586)	6.18%% (5.76–6.65) (712)	6.46% (6.03–6.92) (744)	1.52% (1.31–1.76) (175)	0.21% (0.15–0.32) (25)	0
Miconazole Nitrate	Gel, Powder, Cream	Oral, External	10.77% (10.22–11.35) (1240)	3% (2.71–3.34) (346)	1.46% (1.27–1.71) (169)	1.72% (1.51–1.98) (199)	2% (1.77–2.28) (231)	1.41% (1.22–1.65) (163)	6.46% (6.03–6.92) (744)	≤0.05
Miconazole Nitrate, Hydrocortisone	Cream	External	6.69% (6.25–7.16) (770)	1.25% (1.07–1.48) (145)	1.59% (1.39–1.85) (184)	2.13% (1.89–2.42) (246)	1.21% (1.04–1.44) (140)	0.39% (0.30–0.53) (46)	0.07% (0.04–0.15) (9)	≤0.05
Mometasone Furoate, Miconazole	Cream	External	16.71% (16.05–17.42) (1924)	3.61% (3.28–3.97) (416)	3.24% (2.94–2.59) (374)	4.71% (4.35–5.12) (543)	2.96% (2.67–3.29) (341)	1.38% (1.18–1.61) (159)	0.79% (0.64–0.97) (91)	≤0.05
Terbinafine	Spray, Cream, Tablet	External, Oral	9.88% (9.36–10.45) (1138)	0.85% (0.07–1.30) (98)	2.65% (2.38–2.97) (306)	3.65% (3.33–4.02) (421)	1.53% (1.33–1.78) (177)	0.95% (0.8–1.16) (110)	0.22% (0.16–0.34) (26)	≤0.05
Voriconazole	Tablet, Intravenous	Oral, Parenteral	0.32% (0.23–0.44) (37)	0.05% (0.25–0.49) (6)	0.10% (1.76–2.34) (12)	0.08% (2.01–2.61) (10)	0.07% (7.76–8.87) (9)	–	–	–

Table 3 Antifungal drugs approved by SFDA for marketing in Saudi Arabia and their cost-utility analysis prescription wise

Drug (ATC code)	WHO (DDD)	Average therapy of duration in days	Average cost in unit dose prescription wise in SR (USD)
Clotrimazole	0.1 g	13.44	10.37 (2.76)
Econazole Nitrate	0.1 g	3.28	7.92 (2.11)
Fluconazole	0.1 g	15.66	34.56 (9.21)
Itraconazole	0.2 g	9.31	9.90 (2.64)
Ketoconazole	0.2–0.4 g	37.29	16.32 (4.34)
Miconazole	0.1–1 g	5.33	9.48 (2.53)
Miconazole Nitrate	0.1 g	11.77	12.89 (3.44)
Miconazole Nitrate, Hydrocortisone	–	8.55	13.64 (3.64)
Mometasone Furoate, Miconazole	–	9.95	25.55 (6.81)
Terbinafine	0.25 g	21.32	28.52 (7.60)
Voriconazole	0.4 g	4.91	374.72 (99.90)

DDD, Daily Defined Dose; SFDA, Saudi Food and Drugs Administration Authority; WHO, World Health Organization; 1USD = 3.76 SR.

a basis for future drug utilization studies in Saudi Arabia based on the indication.

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Author contributions

M.D.A. designed the study, analysed data, and drafted the study. A.Y. and M.P. also analysed data and proofread the study. N.B. and Y.A.H reviewed and edited the drafted study. All Authors state that they had complete access to the study data that support the publication.

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Conflict of Interest

None declared.

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