

Current Antifungal Drug Recommendations to Treat Oral Thrush in Sulaimani City-Iraq

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ABSTRACT

Oral thrush or oral candidosis is one of the most widespread fungal infections of the mucous membranes in human. This study aims to evaluate the pattern of recommending three antifungal drugs as follows: Nystatin, amphotericin B, fluconazole, and miconazole by the pharmacists and assistant pharmacists, which are used to treat oral thrush. A questionnaire was circulated to a random selection of pharmacies in Sulaimani city of Iraq between March 2017 and June 2017, and responses to the questionnaire were received from 101 pharmacies. The results were analyzed and demonstrated as the absolute and relative frequencies using Statistical Package for the Social Sciences Program version 21. Among the participants, 65.3% were male, and 34.7% were female. The participant's age range was 21–70 years. The majority (52.3%) holds a postgraduate degree as their highest educational level, and they graduated after 2010. Miconazole and nystatin (70.3%) were the most popular choices of an antifungal agent that pharmacists would use, followed by fluconazole (31.7%) and amphotericin-B (11.9%).

Index Terms: Amphotericin B, Antifungal agents, Fluconazole, Nystatin

1. INTRODUCTION

In the past three decades, invasive life-threatening fungal infections have severely increased due to several reasons including broad-spectrum antibiotics, antagonistic surgery, and the use of immunosuppressive and antineoplastic agents [1]-[5]. Until the 1940s, comparatively few antifungal agents were available for the treatment of fungal infections. In addition, development in the growth of new antifungals agents was lagged behind the antibacterial investigation, from the year 2000 number of agents existing to treat fungal infections has increased by 30%. Nevertheless, still, only 15 agents are approved for clinical use at present [6], [7]. The

most common human fungal infection is oral candidiasis (also called oral thrush), which is characterized by an overgrowth of *Candida* species in the superficial epithelium of the oral mucosa [8], [9]. Treatment for oral thrush varies, polyenes, allylamines, and azoles are three classes of antifungal agents that used most frequently for treatments of oral thrush [10]. Nystatin and amphotericin-B both belong to the polyene' class of antifungals drug. These class of drugs act by binding to ergosterol in the cell membranes of the fungal; then, this causes in the membrane depolarization and pores formation which increases permeability to proteins and (mono and divalent) cations, disrupting metabolism, and eventually causing cell death [11]. Both antifungal agents are poorly absorbed by the gastrointestinal tract and are widely used for the topical treatment of oral candidal infections [12]. Intravenous forms of amphotericin-B are used in the treatment of systemic fungal infections. Similarly, nystatin has low oral bioavailability profile; therefore, it is generally used in inhibiting colonization with *Candida albicans* in the gut or as a topical treatment for thrush [13], [14]. Sweetened

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pastille has been developed to overcome the problem of the unpleasant taste of nystatin [15]. The azole antifungals (miconazole and fluconazole) work through inhibiting cytochrome P-450 enzyme in the fungal [16]. Miconazole was the first available azole; fluconazole is a more recently found systemic antifungal agent, which has a long half-life and as a result can be administered in a single daily dose [17]. Chlorhexidine is other antimicrobial agents that available for topical administration in oral candidiasis as mouthwash. It is effective against fungal yeasts, which can be used as an adjunctive therapy or as a primary treatment [18]. The aim of the present study was to examine the current practice of antifungal recommending pattern and attitude toward the treatment of oral candidiasis among pharmacists in Sulaimani City-Iraq during 2017. Hence, this project will commence with the treatment of oral thrush by using different types and form of antifungal agents.

2. MATERIALS AND METHODS

A hard copy questionnaire circulated to a random selection of 120 pharmacies. A complete data from 101 participants were returned and integrated into the analysis with 84.1% response rate. Data collection was carried out between March 2017 and June 2017, both males and females pharmacies were involved in the different street of the Sulaimani city. The pharmacies were visited and asked questions based on their interest to take part in the study; each of these pharmacists was given an explanatory letter of a questionnaire (Fig. 1). The questionnaire that was used for data collection in this study was specially created through a search of the relevant literature. The questionnaire was tested initially to estimate approximately the length of the questionnaire in minutes, verify the participant's interpretation of questions, and develop the questionnaire consequently. These questionnaires were tested in independent data sets; however, these candidate questionnaires were excluded from the concluding analysis. However, the final version of the survey was conducted in Sulaimani city. The final version of the questionnaire included eight questions and required approximately 2 min to complete. Approved by the ethics committee of University of Sulaimani (Sulaimani, Iraq) was obtained. The self-administered questionnaire was composed of two sections. The first section of the questionnaire was comprised of seven questions about sociodemographic data, such as gender, age, university degree and year of the last qualification, workplace (private sector vs. public sector), professional practice, and country of the first-degree qualification. Various antifungal drug options were integrated into the second section of

the questionnaire about pharmacists' recommendation to treat oral candidal infections. Data from the completed questionnaires were entered into a computer database and analyzed using Statistical Package for the Social Sciences Program version 21. Following the statistical evaluation of data and the summarization of frequencies and percentages were produced.

3. RESULTS

With the use of the hard copies of the questionnaires, different pharmacies have been participated in Sulaimani city, and 101 questionnaires were returned completed (84.1% response rate), 65.3% were male, and 34.7% were female pharmacist as shown in Table 1. The majority of participants (70.3%) graduated after 2010, while 19.8% graduated between 2000 and 2009. Moreover, the participants, who graduated between 1990 and 1999 recorded 6.9%, with a lower proportion (2%) graduating between 1980 and 1989. Only 1% graduated between 1970 and 1979. There were no respondents from earlier than 1970. The range of the participant's age was 21–70 years; more than 70% were aged between 21 and 30 years. The majority (47.5%) holds

TABLE 1
Sociodemographic data of the participated pharmacists

Sociodemographic data	Frequency (%)
Gender	
Male	66 (65.3)
Female	35 (34.7)
Age	
21–30	73 (72)
31–40	21 (21)
41–50	3 (3)
51–60	3 (3)
61–70	1 (1)
First-degree graduation year	
After 2010	71 (70.3)
2000–2009	20 (19.8)
1990–1999	7 (6.9)
1980–1989	2 (2)
1970–1979	1 (1)
Educational level	
Diploma	48 (47.5)
Undergraduate	30 (29.5)
Postgraduate (Msc, PhD)	23 (22.8)
Workplace	
Private sector	60 (59.4)
Public sector	3 (3)
Both (private and public)	38 (37.6)
Professional practice	
Pharmacist	54 (53.5)
Assistant Pharmacist	47 (46.5)

popular form with 73% of those recommending nystatin considering this formulation. About 24% of those suggesting nystatin would consider recommending it in the form of an ointment. Only 3% was observed for Pastille form of nystatin suggestion. However, capsules were the most common form of fluconazole considered for recommendation (91%). A lozenge form of amphotericin drug was recommended by the participants more than oral suspension form (as shown in Fig. 2). Only 6% of respondents cited other treatment options, which included clotrimazole, terbinafine, econazole triamcinolone, and anginovag spray.

4. DISCUSSION

The present study investigated the currently antifungal drugs recommendation at pharmacies in Sulaimani city, Iraq, in relation to the sociodemographic details as illustrated in a study by Martínez-Beneyto *et al.* [19]. The previous studies similar to this kind in the United Kingdom and Jordan were conducted; however, they were conducted among the general

dental practitioners instead of pharmacists. The first study was undertaken in the UK in 1987 and reported in 1989 [20]. The second study that conducted in the UK reported in 2004 [21]. Furthermore, another study was undertaken in Jordan in 2015 [22]. In accordance with those studies like the present study, nystatin was the most popular antifungal agent recommended (70.3%). In addition, nystatin oral suspension was selected by 73% of the respondents who suggested nystatin. However, in this study, miconazole was recorded as one of the most frequently recommended antifungal agents also (70.3%). There has also been a visible increase in the proportion of participants recommending miconazole in the present survey compared to the previous studies, and it has now become more popular than amphotericin.

In addition, miconazole and nystatin were also the commonly employed antifungals in studies that have been done by other researchers [19], [21], [22]. This is because these drugs may cause less intestinal irritation and other side effects. However, one of the limitations of using topical formulations of nystatin is high sucrose content, which may reduce the amount of practice in diabetes, steroid use, or an immunocompromised state [9].

The triazoles constitute fluconazole being suggested by 31.7% of the participants. Fluconazole in the form of suspension and with different dosages has been used for the treatment of oropharyngeal candidiasis. The theoretical benefit of using topical fluconazole is that a higher concentration of the active drug is delivered to the oral mucosa without the untoward systemic side effects [23], [24]. However, most of the participants recommended capsule form of fluconazole 91% whereas only 9% of the respondents suggested oral suspension form of the drug. Fluconazole oral suspension is

TABLE 2
Choice of antifungal agents. Numbers (%) of pharmacists choosing each antifungal (N=101)

Antifungal agents ^a	Responses	% of cases
	N (%)	
Nystatin	71 (31.4)	70.3
Amphotericin	12 (5.3)	11.9
Fluconazole	32 (14.2)	31.7
Chlorhexidine	32 (14.2)	31.7
Miconazole oral gel	71 (31.4)	70.3
Miconazole and hydrocortisone cream	8 (3.5)	7.9
Total	226 (100)	223.8

^aDichotomy group tabulated at value 1

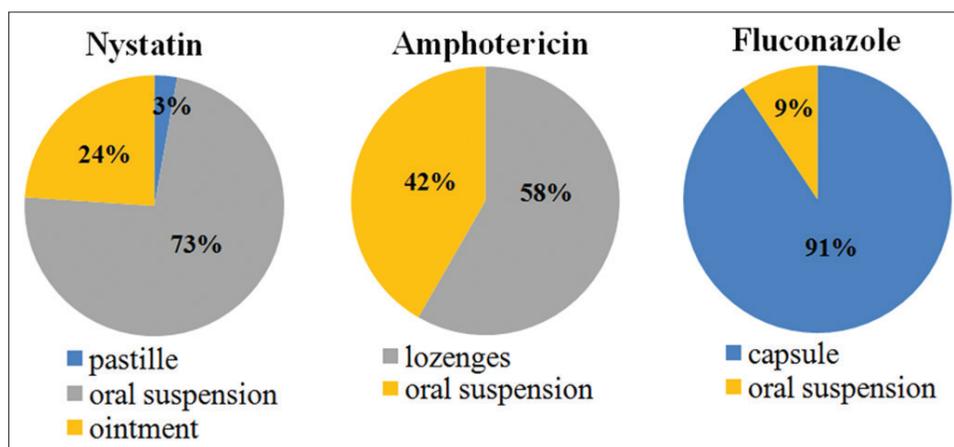


Fig. 2. Different form of antifungal recommended by participants.

administered in a dosage of 10 mg/ml aqueous suspension. Various studies show that fluconazole is a very effective drug, and it has a rapid symptomatic response [25].

Chlorhexidine mouth rinse formulations are widely used for decreasing the microbial burden in the oral cavity. For example, chlorhexidine gluconate with 0.2% concentration is used as an antiseptic oral rinse because of its activity against a broad range of oral microbial species including *Candida* [26]. Chlorhexidine should not be used simultaneously with nystatin as they interact and render each other ineffective, even though it is suggested as a practical addition to the antifungal agents [27]. In this study also, chlorhexidine was recommended by pharmacists and assistant pharmacist (31.7%) along with other antifungal agents as an adjunctive therapeutic agent.

In this study, the result of amphotericin was less frequently recommended (11.9%), and 58% of the participants suggested lozenges form of the drug. This recommendation was very similar to the previous study which demonstrated by Anand *et al.* [28]. Miconazole in combination with hydrocortisone was recommended by 7.9% of the respondents. However, in general, the diagnosis of oral candidiasis is based on clinical features and symptoms in conjunction with a detailed medical history [29].

Despite the above-mentioned results, this study has several limitations. The small sample size was the main limitation of this questionnaire. Therefore, the future studies with larger sample size covering a wider data may provide better. Furthermore, the possible improvement in the methodology could be the insertion of doctors' recommendation and compare both results. Differentiation between respondents recommending antifungals based on their knowledge or recommending it based on doctor's prescription.

5. CONCLUSION AND RECOMMENDATION

In summary, nystatin and miconazole are the most popular antifungal agents prescribed in Sulaimani city, Iraq. There appears to be a trend toward the use of miconazole, particularly among more recent graduates. The majority of the participant suggested nystatin as a type of oral suspension and miconazole as an oral gel. We suggest that collecting more data in different cities concerning the use of antifungal drugs could turn into a strong motivation in the near future for the implementation of policies for prevention and treatment of oral thrush fungal infections.

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