

## Knowledge of Senior Dental Students Regarding the Antifungal Medication of Oral Candidiasis

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Management of oral candidiasis may become a challenge particularly in medically compromised individuals. Inappropriate prescription of antifungal agents promotes drug resistance. So, this study aimed to assess the students' knowledge of antifungal drug prescription. This cross-sectional, questionnaire based study was carried out in Tabriz school of dentistry, Iran. 90 multiple-choice questionnaires which included questions on the management of oral candida infections were distributed among the senior dental students. Descriptive statistics and frequency distributions were performed on the data. Nystatin was the most popular agent (62.2%) prescribed followed by amphotericin B (46.6%). Chlorhexidine was an alternative to medication in 25.5% while combination of chlorhexidine and antifungal medication was selected in 51.1%. More education is needed to improve knowledge of dental students regarding the treatment of oral candidiasis and proper antifungal therapy.

**Keywords:** Antifungal therapy, Candida, Prescription.

*Candida albicans* is common oral inhabitant of healthy population that becomes pathogenic in the presence of any predisposing risk factors<sup>1-3</sup>. Risk factors such as diabetes mellitus, broad spectrum antibiotic therapy, and immune deficits disrupt the balance between host and oral microbiology leading to candidiasis infection<sup>4-6</sup>.

Antifungal therapy should consider host and pathogen related factors<sup>1,2,5</sup>. Topical medication is selected as the treatment of choice for the healthy individuals infected with candidiasis, while systemic administration is indicated in recurrent or disseminated infection especially present in immune deficient patients<sup>1,2,4-6</sup>.

According to the guidelines of infectious diseases society of America, intensity

of the infection is considered in the treatment of oropharyngeal candidiasis. Topical agents such as nystatin suspension or clotrimazole troches are typically used in the treatment of mild infections. For moderate to severe infections, oral fluconazole, itraconazole solution, and posaconazole suspension are recommended. Intravenous echinocandin is limited to those patients with refractory diseases. Combinations of systemic and topical treatments are effective in reduction of dose and duration of treatment<sup>7</sup>.

Dentists often do not have the essential pharmacological knowledge and make errors in the prescription of antifungal drugs which leads to drug resistance. The current study aimed to assess the knowledge of antifungal prescription for the treatment of oral candidiasis among the senior dental students in Iran.

### MATERIALS AND METHODS

This questionnaire based cross sectional survey was conducted during a month period at

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the department of prosthodontics, Iran. The initial draft of the study questionnaire was prepared using previous studies and examined for item simplicity, responsiveness, and reading ease with the help from practitioners. Following the initial examination, questionnaire was revised and examined for its test-retest reliability in a 10-days period and Kappa statistics was calculated (0.89-0.91).

The final questionnaires contained multiple-choice questions about the desired antifungal therapy and their proper form of administrations. The questionnaires and introductory letters providing the information about the study objectives and an informed consent were prepared and distributed to 90 senior students.

Data were obtained and analyzed by using SPSS statistical package. Descriptive statistics and frequency distributions were performed on the data.

## RESULTS

The results of the study are shown in Table 1. 76.6% (n=69) of respondents indicated topical medication as their first choice, whereas 15.5% (n=14) preferred systemic therapy. Nystatin was the most common prescribed antifungal agent in mild candidiasis (62.2%, n=56) followed by Clotrimazole troches (15.5%, n=14). 46.6% (n=42) of respondents chose oral amphotericin and 21.1% (n=19) intravenous echinocandin as their first choice treatment of moderate to severe candidiasis. Chlorhexidine mouth rinse was chosen by 25.5% (n=23) of respondents which accompanied other antifungal agents in 51.1% (n=46). Considering the dosage and timing of drug administration, fluconazole, clotrimazole, and nystatin were prescribed correctly in 28.8% (n=26), 25.5% (n=23), and 37.7% (n=34) of responses respectively.

## DISCUSSION

In the current study, questionnaires were distributed among senior dental students and aimed to survey the antifungal prescribing knowledge of oral candidiasis treatment. Dentists often encounter with the cases of oral candidiasis in their practice and need to be expert in antifungal therapy on infections with different candida species;

however, it is reported that they are reluctant for the treatment of chronic oral candidiasis especially if accompanied by immunodeficiency virus infection (8). Oral candidiasis is managed by correct identification, rectification of the predisposing factors and the provision of a proper antifungal medication which eventually mandates sufficient knowledge of the clinicians on the diagnosis and antifungal treatment of the infections (1-3). In the current study, the preferred antifungal agents were nystatin, amphotericin B, intravenous echinocandin, and clotrimazole troches respectively. Nystatin was the most frequently prescribed medication for treating mild infections. Topical agents are the first line treatment for oral candidiasis and do not display the side effects of systemic therapy (5,6). They are often accompanied by systemic therapy in order to reduce the required dose and duration of treatment. Nystatin and amphotericin B have reduced gastrointestinal absorption following oral administration and are suitable for topical application<sup>1-6</sup>. However, rapid oral clearance of topical medication decreases the contact time of drug with oral mucosa and makes the therapy ineffective<sup>1,5</sup>. Additionally, frequent dosing regimens are problematic and require patient compliance<sup>5</sup>.

Amphotericin is as effective as fluconazole in the treatment of denture stomatitis, but is associated with a number of complications and is often poorly tolerated and unsatisfactory<sup>9,10</sup>. Miconazole is a fungicidal derivative, with simultaneous antifungal and antibacterial effect. A meta-analysis indicated that miconazole is an effective agent for the management of angular cheilitis and denture stomatitis and the recurrence rates of gel are lower than other formulations<sup>11</sup>; nonetheless, it is reported that miconazole affects warfarin activity causing severe bleeding<sup>12,13</sup>. When there is a risk of drug interaction, nystatin is a suitable alternative; although a recent study showed that nystatin suspension has strong effect on warfarin either<sup>12</sup>. So if miconazole is required for a patient receiving warfarin therapy, liaison with his haematologist is essential before any treatment<sup>14</sup>.

Invasive and refractory mucocutaneous candidiasis infection is managed by systemic medication. Contrary to previous studies<sup>15,16</sup>, the

**Table 1.** Survey questions and the frequency distribution of responses (n=90)

No	Question	Response options	(%)
1	In patient with oral candidiasis, you would usually prescribe:	Antifungal agent	23.3
		Chlorhexidine alone	25.5
		Antifungal plus chlorhexidine	51.1
2	In patient with oral candidiasis, which antifungal would be your first choice before knowing the species of Candida:	Topical	76.6
		Systemic	15.5
		Combination	7.7
3	In the treatment of mild candidiasis which antifungal would be your first choice:	Clotrimazole troches	15.5
		Miconazole gel	10
		Nystatin suspension or pastille	62.2
		Oral fluconazole	12.2
4	In the treatment of moderate to severe candidiasis, which antifungal would be your first choice?	Nystatin pastille	13.3
		Oral fluconazole	18.8
		Oral amphotericin	46.6
		Intravenous echinocandin	21.1
		Itraconazole solution	42.2
5	In the treatment of candidiasis by a fluconazole-refractory infection, which antifungal would be your first choice?	Intravenous echinocandin	14.4
		Clotrimazole troches	26.6
		Miconazole tablet	17.7
		Nystatin suspension	32.2
6	In your opinion, the best preventive prophylaxis of oropharyngeal candidiasis in HIV and cancer patients is:	Oral fluconazole	20
		Oral voriconazole	12.2
		Oral amphotericin	35.5
		Fluconazole 100mg 3 times weekly	34.4
7	In the chronic suppressive treatment of candidiasis for patients who have recurrent infections, you would usually prescribe:	Fluconazole 100-200 daily, for 7-14 days	25.5
		Amphotericin oral suspension, 100 mg/mL 4 times daily	18.8
		Amphotericin oral suspension, 200 mg/mL 4 times daily	21.1
		Fluconazole 100mg 3 times weekly	13.3
8	In the treatment of candidiasis by a fluconazole susceptible infection, which dosage is correct?	Fluconazole 200mg 3 times weekly	82.1
		Fluconazole 100-200mg daily, for 7-14 days	28.8
		Fluconazole 200-400mg daily, for 7-14 days	32.2
		Clotrimazole troches 10mg 5 times daily	25.5
9	In the treatment of candidiasis with clotrimazole which dosage is correct?	Clotrimazole troches 20mg 5 times daily	16.6
		Clotrimazole troches 10mg 3 times daily	37.7
		Clotrimazole troches 20mg 3 times daily	21.1
		Nystatin suspension 100000 U/mL 4 times daily	37.7
10	In the treatment of candidiasis with nystatin, which dosage is correct?	Nystatin suspension 200000 U/mL 4 times daily	31.1
		Nystatin pastilles 100000 U 4 times daily	31.1
		Nystatin pastilles 200000 U 2 times daily	12.2
		Candida glabrata can become resistant to fluconazole.	14.4
11	Choose the right answer among the following statements:	Candida Krusei is always resistant to fluconazole.	18.8
		Candida albicans is usually susceptible to fluconazole.	21.1
		All of the above are true.	45.5

majority of survey respondents chose oral amphotericin as the first choice of systemic therapy followed by intravenous echinocandin and fluconazole. Fluconazole has excellent safety and clinical efficacy in the management of denture stomatitis. It is well absorbed by gastrointestinal tract and reaches the salivary levels similar to the plasma concentration of the drug<sup>1,2</sup>. However high rates of partial relapse has been recorded after long term medication<sup>9,17,18</sup>. Also, non-albicans species of candida isolated from HIV-infected patients are less sensitive to fluconazole<sup>2,9,10,17</sup>. Itraconazole is a broader spectrum antifungal agent that shows better efficacy and appears to be better tolerated than miconazole and ketoconazole<sup>8,19</sup>. Some studies have reported that none of these agents are active against *C. glabrata*, *C. Krusei* and *Fusarium* species<sup>13,17</sup>.

Majority of the study participants prescribed chlorhexidine as an adjunct to other antifungal therapies. Chlorhexidine possesses a broad spectrum antimicrobial activity against *Candida albicans* and other common non-*albicans* species and is used as antiseptic mouth rinse and denture disinfectant<sup>20</sup>. Some investigators applied it as an alternative to antifungal drugs and achieved an acceptable results in reducing the risk of oral candidiasis<sup>21-24</sup>. In other studies, chlorhexidine rinse is reported as a promising therapy supplementing the effect of antifungal medication<sup>2,20-22</sup>.

In summary, the results demonstrated that the pharmacological knowledge of dental students needs to be strengthened. Also, additional attention should be devoted to the appropriate drug dosage and timing alteration in training programs to guarantee the competent prescribing. Pharmacology which is one of the key preclinical courses in the schools of dentistry is offered to the third year students and constitutes a very small part of the curriculum. Students should acquire the basic knowledge of pharmacology, clinical applications and drug administration skills in a relatively short period of time. This prompts the need to review the curriculum for any possible changes and highlights the importance of problem-based learning method in dental education to enables dental practitioner to improve the clinical skills of dental students.

## CONCLUSION

The pharmacological knowledge of dental students needs to be strengthened with a special focus on prescribing medications and providing the opportunity to practice more.

### Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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