International Journal of Dental Hygiene

Official Journal of the International Federation of Dental Hygienists

ORIGINAL ARTICLE

Y Martínez-Beneyto
P López-Jornet
A Velandrino-Nicolás
V Jornet-García

Use of antifungal agents for oral candidiasis: results of a national survey

Authors' affiliations:
Y. Martínez-Beneyto, *P. López-Jornet*, *V. Jornet-García*, Department of Stomatology, University of Murcia, Murcia, Spain
A. Velandrino-Nicolás, Department of Psychology, University of Murcia, Murcia, Spain

Correspondence to:
Yolanda Martínez Beneyto
Clínica Odontológica Universitaria
Hospital Morales Meseguer
Avda. Marqués de los Vélez s/n
Murcia 30008
Spain
Tel.: +34 968 398588
Fax: +34 968 398576
E-mail: yolandam@um.es

Dates:
Accepted 18 November 2008

To cite this article:
Int J Dent Hygiene **8**, 2010; 47–52
DOI: 10.1111/j.1601-5037.2008.00357.x
Martínez-Beneyto Y, López-Jornet P, Velandrino-Nicolás A, Jornet-García V. Use of antifungal agents for oral candidiasis: results of a national survey.

Abstract: *Background: Candida albicans* is an opportunistic agent that colonizes the oral mucosa. *Objectives:* To determine the attitude of Spanish dentists toward the oral treatment of candidiasis. *Method:* Between May and November 2006, a questionnaire was circulated to a random selection of 1134 dentists obtained from the General Dental Council's main list. The survey consisted of a block of socio-demographic items followed by another block related to the diagnosis and treatment of oral candidiasis. Replies to the questionnaire were received from 840 (74%) dentists. *Results:* 50.4% of respondents were men, and 48.1% were female with a mean age of 38 and 12.2 years of professional experience. Miconazole was the most popular choice of antifungal agent prescribed (59.3%), followed by nystatin (57.7%) for topical use. Systemic antifungal agents were used by 30.20% of dentists, with a strong association between their use and the number of years in practice, gender and professional qualifications ($P < 0.005$). *Conclusion:* Most Spanish dentists make clinical diagnosis and treat oral infections by *C. albicans* themselves with topical drugs (miconazole and nystatin) as a first choice. Systemic treatments are more commonly chosen by male dentists with long professional experience, especially by stomatologists.

Key words: antifungal agent; candida; dentistry; Myconazole; Nystatine; oral disease

Introduction

Candida albicans is an opportunistic agent that colonizes the oral mucosa, requiring the presence of a series of factors before transforming itself into a pathogen and cause of disease. The

factors enabling this transformation may be microbiological in nature, environmental or related with the hosts themselves. Several factors may co-exist: for example, in the case of elderly persons, an immune system deficit may be one factor and removable prostheses/dentures another (1, 2).

The prevalence of oral candidal infections is increasing partly due to host-dependent factors (the use of antibiotics, immunosuppressives, etc.) and to the nature of the infection itself, with new pathogenic and anti-fungicide strains and species regularly appearing (3–7).

Such a scenario has led to a significant increase in the use of both topical and systemic antifungal agents, although errors were frequently observed in their prescription. This situation leads to numerous cases of resistance, particularly to the group of azole antifungals, the most common family of antifungals used (8, 9). Therapy has to be understood in the context of the individual's pathology, with attention paid to his/her physiological and pathological circumstances. To treat oral candidiasis in immunocompetent subjects, the first choice should be antifungals for topical use, while systemic treatment is used when topical treatment does not succeed in controlling the lesions, in mucocutaneous candidiasis, in the immunocompromised individuals and for prophylaxis in severely immunocompromised patients (10). Nystatin is the most commonly used antifungal agent for treating mucosa candidiasis (10). In many cases it is considered useful to combine systemic treatment with local medication, since in this way the systemic doses can be reduced or, at least, administered for shorter periods. In general, the prescription of antifungals by dentists reflects the type of infection and immune state of the patient (11).

The aim of this study was to analyse the behaviour of Spanish dentists faced with oral *C. albicans* infection in general, to detect differences in the therapeutic act and prescriptions, evaluating the possible influence of the years of professional experience, gender, practice (private or public) and professional qualification (odontologist or stomatological doctor) of dentists in General Dental Practice.

Materials and methods

A questionnaire in plain envelopes was distributed by a representative of a nation-wide pharmaceutical laboratory to 1022 dentists in 52 Spanish provinces, the inclusion criterion being registration with the General Dental Council of Spain. The transversal, randomized stratified study excluded all professionals exclusively dedicated to a dental speciality. Thus, the questionnaire was targeted at general dentists practising in both the public and private domains. Initially, a mono stratified sampling procedure was planned, taking the professional in question as the primary sampling unity. The size of the sample was defined by adopting the random extraction method. Assuming a confidence interval or 95%. A maximum variance or $P = Q = 50$ and a sampling error of <3%. The number of questionnaires sent per province was in proportion to the number on the most recent professional census (22 100) provided by the Spanish General Dental Council. The study was previously approved by the Ethical Committee of the University of Murcia and carried out between May and November 2006.

The questionnaire was sent with an introductory letter describing in full detail the type of study involved, and the composition of the investigating team. One month later, the study subjects were reminded by the visiting representatives of the importance of participation and again their cooperation was requested. A third visit conveyed the same message to the non-respondents about 2 months after this second letter. Of the 1022 general dentists to whom the questionnaire was sent, 840 completed and returned the letter, a response rate (74%) that can be considered high.

The study questionnaire consisted of several blocks of items, of which two were central to the present study (Fig. 1). More specifically, the first block addressed socio-demographic and professional aspects (professional qualifications, years of professional activity and work setting), while the second explored attitudes towards oral mucosa lesions and treatment of oral candidal infections.

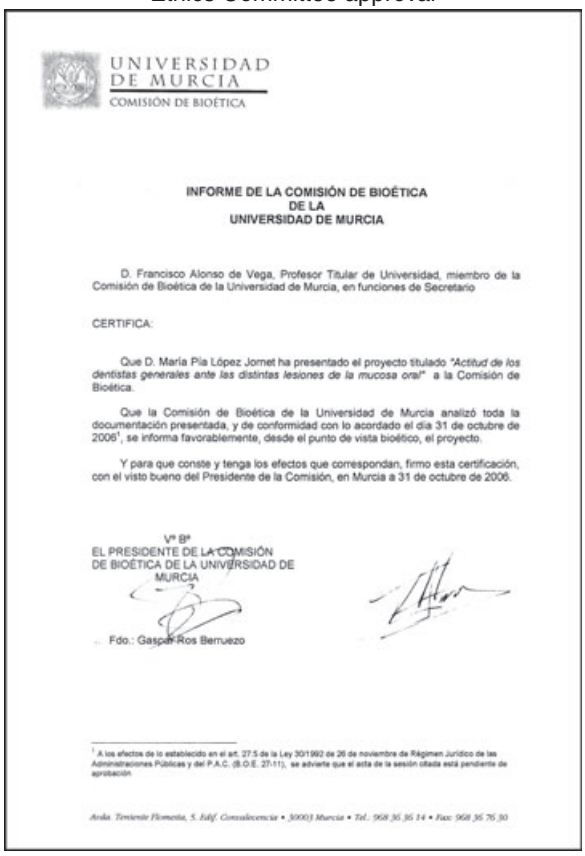
The questionnaire was previously evaluated by means of a cognitive pretest procedure to ensure that the questions were appropriate, understandable and acceptable to professionals. The study analysis focused on the differences and trends observed in relation to the variable 'years of professional experience, gender and professional speciality'.

The results were analysed using the SPSS (version 14.5, SPSS, Inc., Spain) statistical package. Hypothesis testing adapted to associations and variables of this kind was used. Parametric-type contrasts were not possible (12), since the variable 'years of professional experience' did not exhibit a normal distribution, as confirmed by the Kolmogorov-Smirnov test (KS = 0.18; $P < 0.001$).

Results

Of the questionnaires returned, none had to be discarded due to an insufficient number of answered questions (the criterion being <50%), although several did not answer all the questions adequately as a result of not understanding the questions or

Ethics Committee approval



UNIVERSIDAD DE MURCIA
COMISIÓN DE BIOÉTICA

INFORME DE LA COMISIÓN DE BIOÉTICA DE LA UNIVERSIDAD DE MURCIA

D. Francisco Alonso de Vega, Profesor Titular de Universidad, miembro de la Comisión de Bioética de la Universidad de Murcia, en funciones de Secretario

CERTIFICA:

Que D. María Pía López Jornet ha presentado el proyecto titulado *"Actitud de los dentistas generales ante las distintas lesiones de la mucosa oral"* a la Comisión de Bioética.

Que la Comisión de Bioética de la Universidad de Murcia analizó toda la documentación presentada, y de conformidad con lo acordado el día 31 de octubre de 2006[1], se informa favorablemente, desde el punto de vista bioético, el proyecto.

Y para que conste y tenga los efectos que correspondan, firmo esta certificación, con el visto bueno del Presidente de la Comisión, en Murcia a 31 de octubre de 2006.

Vº Bº
EL PRESIDENTE DE LA COMISIÓN DE BIOÉTICA DE LA UNIVERSIDAD DE MURCIA

Fdo.: Gaspar Ros Berruezo

[1] A los efectos de lo establecido en el art. 27.5 de la Ley 30/1992 de 26 de noviembre de Régimen Jurídico de las Administraciones Públicas y del P.A.C. (B.O.E. 27-11), se advierte que el acta de la sesión citada está pendiente de aprobación

Avda. Teniente Flomesta, 5. Edif. Convalecencia • 30003 Murcia • Tel.: 968 36 36 14 • Fax: 968 36 76 30

through a lack of precision (there were no rectifications or modifications in the returned questionnaires).

50.4% of respondents were male and 48.1% female, while this information was not provided in the rest of the returned questionnaires. The mean age of the global series was 38 years, with SD = 9.967. As to the variable 'years of professional experience', the mean was found to be 12.2 (SD = 8.432). Lastly, in relation to the work setting, 97.3% of the interviewed professionals worked in private practice, 8.8% in public practice. 67.1% of the dentists questioned had studied dentistry at dental schools (odontologists) and 32.9% had a degree from a medical school with stomatology as their speciality (stomatologists).

The monthly frequency with which oral candidal infections were diagnosed in dental practice was put at 0–1 cases for 64.6% of dentists, 2–3 for 26.2% and more than three for the remaining 7.9%, with stomatologists diagnosing a statistically significant greater number of cases than odontologists (Fisher's exact test $P < 0.05$). There was a statistically significant relationship (ANOVA, $P = 0.022$; $P < 0.05$), between the years of experience and the number of cases diagnosed: those with most experience (13.7 years) diagnosing 2–3 cases per month, followed by the group with 13.1 years experience (three cases) and then the group with 11.5 years experience, which identified the least number of cases (see Fig. 2, Table 1).

1. Socio professional questions

- Years of birth…. • GENDER: Male □ Female □
- Years of professional activity:.....…
- Work setting:
  - □ Private:
  - □ Public:
  - □ Both of them:
- Professional qualifications
  - □ Odontologist
  - □ Estomatologist .....
  - □ Especialist (especficar): .....

2. Attitudes towards oral mucosa lesions

- Clinical Frecuency cases/month: □ 0-1 □2-3 □ >4
- Is Denture Estomatitis Cases the most frecuent oral clinical candidiasis observed)? □ Yes □ No
- Do you treat oral candidosis after been diagnsoted? □ Yes □ No

In case you treat oral candidosis	**Yes**	**No**
Do you use topical drugs as first option?		
Do you use systemical treatment?		
Do you use Clorhexidine?		
Do you use Nystatin (topical)?		
Do you use Miconazol (topical)?		
Do you use Clotrimazole (topical)?		
Do you use Ketoconazole (systemical)?		
Do you use Itraconazole (systemical)?		
Do you use Fluconazole (systemical)?		
Other treatments		

Fig. 1. Questionnaire.

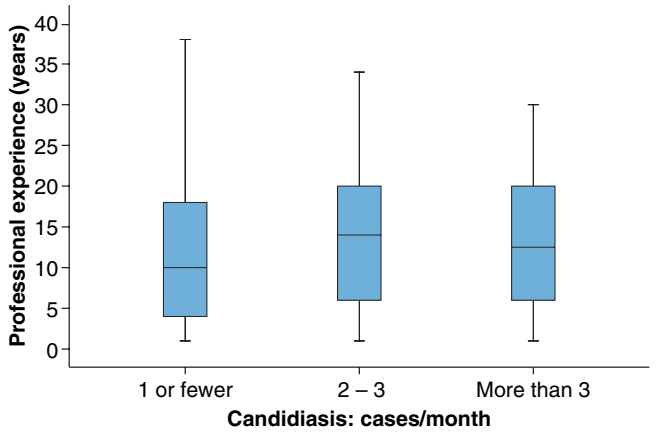


Fig. 2. Relation between monthly detection rates of oral candidiasis and years of professional experience.

Table 1. **Clinical diagnosis of cases of candidiasis according to professional experience**

Cases of oral candidiasis	*N*	Mean	SD	Error	95% CI Lower limit	95% CI Upper limit	Minimum	Maximum
1 or fewer	525	11.5	8.539	.373	10.8	12.2	1	–*
2–3	210	13.7	8.058	.556	12.6	14.8	1	–*
More than 3	66	13.1	7.497	.923	11.2	14.9	1	–*
Total	801	12.2	8.381	.296	11.6	12.8	1	–*

*Statistically significant at $P < 0.05$.

With regards to the action taken following oral candidal infections diagnosis (treat or refer to oral medicine specialists), statistical significant differences ($P = 0.010$) were observed between the professional qualification, OR = 0.462. For every stomatologist that treated the infection, 0.462 odontologists did so: OR = 0.462; 95% CI: 0.257–0.828. However, no significant differences ($P = 0.799$) were found between genders (OR = 1.063, OR = 1.063; 95% CI: 0.666–1.697). As regards private or public practice, no significant differences ($P = 0.113$) were found (OR = 0.385), so that for every professional working in public or public + private practice who treated oral candidal infections, 0.385 in private practice did so. Although this difference may seem great, it was probable due to the imbalance between the categories 'public' o 'public + private' ($n = 71$), on the one hand, and private ($n = 729$), on the other. OR = 0.385; 95% CI: 0.118–1.253; $P = 0.113$.

The most common clinical form of oral candidosis reported (84.4% of cases) was significantly related to prostheses (denture stomatitis) (ANOVA, $F = 19.29$ and $P = 0.000$; $P < 0.05$). Following diagnosis, 89.7% of dentists said they treated it themselves, while 10.3% referred the patients to a specialist.

Table 2. **Oral candidiasis**

Treatment oral candidiasis	Experience	Gender	Work setting	Professional qualifications
Topical treatment	$T = 0.607$ $P = 0.544$	$\chi^2 = 1.331$ $P = 0.249$	$\chi^2 = 0.358$ $P = 0.836$	$\chi^2 = 0.040$ $P = 0.842$
Systemic treatment	$T = -7.532$ $P = 0.000$	$\chi^2 = 12.194$ $P = 0.000$	$\chi^2 = 3.527$ $P = 0.171$	$\chi^2 = 46.16$ $P = 0.000$
Nystatin	$T = -0.775$ $P = 0.438$	$\chi^2 = 0.127$ $P = 0.722$	$\chi^2 = 0.609$ $P = 0.737$	$\chi^2 = 0.745$ $P = 0.388$
Miconazole	$T = -1.185$ $P = 0.236$	$\chi^2 = 0.419$ $P = 0.517$	$\chi^2 = 0.810$ $P = 0.667$	$\chi^2 = 1.489$ $P = 0.222$
Clotrimazole	$T = -1.930$ $P = 0.054$	$\chi^2 = 5.282$ $P = 0.022$	$\chi^2 = 0.206$ $P = 0.902$	$\chi^2 = 19.318$ $P = 0.000$
Ketaconazole	$T = -3.890$ $P = 0.000$	$\chi^2 = 9.363$ $P = 0.002$	$\chi^2 = 2.038$ $P = 0.361$	$\chi^2 = 12.706$ $P = 0.000$
Itraconazole	$T = -3.509$ $P = 0.000$	$\chi^2 = 4.401$ $P = 0.036$	$\chi^2 = 0.614$ $P = 0.736$	$\chi^2 = 6.124$ $P = 0.013$
Fluconazole	$T = -0.948$ $P = 0.343$	$\chi^2 = 5.035$ $P = 0.025$	$\chi^2 = 2.356$ $P = 0.308$	$\chi^2 = 4.323$ $P = 0.038$
Other	$T = -1.312$ $P = 0.190$	$\chi^2 = 0.52$ $P = 0.616$	$\chi^2 = 0.226$ $P = 0.893$	$\chi^2 = 0.424$ $P = 0.515$
Clorhexidine	$T = -0.599$ $P = 0.549$	$\chi^2 = 1.034$ $P = 0.309$	$\chi^2 = 0.066$ $P = 0.968$	$\chi^2 = 3.321$ $P = 0.068$

Experience (years of professional experience), gender (males and females), work setting (public, private and mixed) and professional qualifications (odontologist and stomatologist).
Student *T*-test and test of independence χ^2.

Topical drugs were the first-line antifungal agents chosen by 82.5% ($n = 668$) of respondents, and significantly more so among the least experienced (mean 11.6 years) ($P = 0.005$).

The most experienced dentists ($P < 0.001$) opted for systemic treatment in 30.20% ($n = 245$) of cases, with a statistically significant association with the sex and professional qualifications, male stomatologists being the principal prescribers of these ($P = 0.000$) (Table 2). A similar picture was seen as regards the prescription of Ketaconazole (systemic) ($P < 0.05$) and Clotrimazole (topical) ($P < 0.05$). In general, males tend to prescribe systemic antifungal agents more than females (Table 2).

As the experience of the dentists increased, the more likely they were to use miconazole oral gel ($P = 0.236$) and the above-mentioned systemic drugs ($P < 0.001$) (Table 2). A high percentage of dentists (44.5%) administered chlorhexidine in cases of oral candidal infections of the oral mucosa.

A statistically significant relation ($P < 0.05$) was observed between the use of the Clotrimaloze with the gender and professional qualifications of the dentist, male dentists and stomatologists once again standing out in this respect (Table 1). However, the most prescribed antifungal agent was miconazole oral gel (59.3%) followed by nystatin for topical use (57.7%). Clotrimazole in its topical form was only used by 8.3 of dentists (Table 3). As regards systemic antifungals, itraconazole

Table 3. **Choice of antifungal agents (topical or systemic use)**

Antifungal agents	Use (*n*, %)	Not use (*n*, %)
Miconazole (topical)	481 (59.30)	330 (40.70)
Nystatin (topical)	468 (57.70)	343 (42.30)
Clotrimazole (topical)	67 (8.26)	744 (91.74)
Ketoconazole (systemic)	116 (14.30)	744 (85.70)
Itraconazole (systemic)	117 (14.42)	695 (85.57)
Fluconazole (systemic)	106 (13.07)	705 (86.93)
Other antifungal agents	12 (1.47)	799 (98.53)

and ketoconazole were prescribed by 14.4% and 14.3% of dentists, respectively, while fluconazole was used by 13.1%.

Discussion

A review of the literature has revealed no studies similar to our own exploring professional attitudes among Spanish general dentists towards oral candidosis.

The innovation of using pharmaceutical company representatives to distribute the questionnaires helped us to obtain a very high response rate, although it must be admitted that such a system might cause a degree of bias in the results. When similar questionnaires have been used to ascertain professional attitudes towards different pathologies, telephonically or by sending letters through the post, the response rate has usually been much lower (13), which makes it difficult to extrapolate replies to the whole population of the professionals concerned.

Treatment of oral candidoses depends on its early diagnosis, the correction of facilitating factors or underlying diseases, the clinical type (pseudomembranous, atrophic, hyperplasic, etc.) and the use of suitable antifungal agents, evaluating the ratio between efficacy and toxicity in each individual case. In our study, a substantial proportion of dentists did not treat the disease but preferred to refer the patients to specialist centres, such as university hospitals. This situation may be related with the fact that there are comparatively few specialists in oral medicine in Spain. The most common clinical form of oral candidoses reported was significantly related to prostheses (denture stomatitis). However, one of the limitations of the present study was that the questionnaire did not specify which treatment was assigned to each form of oral candidiasis, an ambiguity pointed out by several respondents. The main aim of the study was to ascertain which antifungal agents Spanish dentists use to treat oral candidal infections.

In general, the longer the experience of the responding dentists, the greater the tendency to treat oral candidoses. Since 1986, Spain has trained odontologists in odontology faculties as a degree course separate from medicine. This situation implies that the most experienced dentists tend to be stomatological doctors trained in medical faculties. Many such doctors have worked in the public health system in public hospitals, which might make it easier for them to diagnose oral infections by candida more easily.

The most commonly observed form of oral candidal infections in our study was denture stomatitis. The literature describes many treatments for this clinical situation, some providing good results, such as the use of topical nystatina (14) and miconazole gel (15), fluconazole systemical (16). However, studies using Itraconazole in the form of a mouthwash or in capsular form have not been very promising (17). In our study, Miconazole was the most popular antifungical prescribed followed by nystatin, which differs substantially from findings in other European countries, such as the UK (18, 19), where nystatin is prescribed by 81% of dentists, followed by miconazole (45%). Miconazole was the first azole to be marketed but, despite its effectiveness, interactions with other drugs and hepatic alterations have been observed (19). The literature suggests that Resistance of *C. albicans* to the polyene antifungals is rare and the contraindications to be used are lower rather than for azoles (20). However, their disagreeable taste means that other polyene antifungals are sometimes prescribed, such as amphotericin B (21), which is particularly effective in the treatment of denture stomatitis (22–25).

The systemic fluconazole is used equally both in the UK (26) and, according to our results, in Spain. Numerous cases of resistance to the triazoles has been reported recently (27) and also interactions with other drugs (3).

We also found that the prescription of systemic drugs is closely associated with the years of experience of the dentists questioned, most of those who do so being male and with degrees in stomatological medicine.

Many dentists prescribe chlorhexidine mouthwashes along with antifungal agents, although interactions with nystatin have been noted (28). Our study revealed that a substantial number of dentists questioned use chlorhexidine in the form of mouthwash. It has been described that a possible cause for drug concentrations to fall to sub-therapeutic levels is the flushing effect of saliva and the cleansing action of the oral musculature. For these and other reasons chlorhexidine is widely prescribe in dentistry both as an antiseptic mouthwash and a denture disinfectant (28). Chlorhexidine has a broad spectrum of antimicrobial activity including *C. albicans* but chlorhexidine has to be used always as an adjunct to conventional antimycotic therapy, obteniendo buenos resultados (29). At present, other antimicrobial agents, such as cetylpyridinium chloride and essential oils, are being incorporated in antifungal therapies (26).

Careful planning and prioritization in the use of medicines are necessary if resistance is to be reduced and so it may be

interesting to issue protocols or guides concerning treatments for the different forms of oral candidoses (30). Finally, emphasis must be placed on the importance of postgraduate training in handling oral candidal infections.

Conclusion

In general, Spanish dentists treat oral infections caused by *C. albicans* properly. The most widely used topical antifungal in oral candidal infections in Spain is miconazole. Topical antifungals are the fist-line agents chosen and systemic antimycotics are significantly more used among the least experienced male stomatologists.

Acknowledgements

The authors express their gratitude to Isdin® Laboratory for financial support of the present study.

References

1 Cannon RD, Holmes AR, Masson AB, Monk BC. Oral candida: clearance, colonization, or candidiasis? *J Dent Res* 1995; **74:** 1152–1161.
2 Grimoud AM, Lodter JP, Marty N *et al*. Improved oral hygiene and *Candida* species colonization level in geriatric patients. *Oral Dis* 2005; **11:** 163–169.
3 Kuriyama T, Williams DW, Bagg J, Coulter WA, Ready D, Lewis MAO. *In vitro* susceptibility of oral candida to seven antifungal agents. *Oral Microbiol Immunol* 2005; **20:** 349–353.
4 Epstein JB. Oropharyngeal candidiasis in the immunocompetent host. *J Mycol Med* 1996; **6:** 31–41.
5 Abu-Elteen KH, Abu-Alteen RM. The prevalence of *Candida albicans* populations in the mouths of complete denture wearers. *New Microbiol* 1998; **21:** 41–48.
6 Zaremba ML, Dniluk T, Roxkiewicz D *et al*. Incidence rate of *Candida* species in the oral cavity of middle-aged and elderly subjects. *Advanced Med Sci* 2006; **51:** 233–236.
7 Lyon JP, da CostaSC, Totti VM, Munhoz MF, De Resende MA. Predisposing conditions for *Candida* spp. Carriage in the oral cavity of denture wearers and individuals with natural teeth. *Can J Microbiol* 2006; **52:** 462–467.
8 Rex JH, Rinaldi MG, Pfaller MA. Resistance of *Candida* species to fluconazole. *Antimicrob Agents Chemother* 1995; **39:** 1–8.
9 Goldman M, Cloud GA, Smedema M *et al*. Does long-term itraconazole prophylaxis result *in vitro* azole resistance in mucosal *Candida albicans* isolates from persons with advanced human immunodeficiency virus infection? The National Institute of Allergy and Infectious Diseases Mycoses Study Group. *Antimicrob Agents Chemother* 2000; **44:** 1585–1587.
10 Hoppe J. Treatment of oropharyngeal candidiasis in immunocompetent infants: a randomized multicenter study of miconazol gel vs. nystatin suspension. The Antifungal Study Group. *Pediatr Infect Dis J* 1997; **16:** 288–293.
11 Viudes A, Peman J, Canton E, Lopez-Ribot J, Gobernado M. The activity of combinations of systemic antimycotic drugs. *Rev Esp Quimioter* 2004; **4:** 30–39.
12 Martín-Andrés A, Luna Del Castillo J. *Bioestadística Para las Ciencias de la Salud*. Madrid, Capitel Ediciones, S.L., 2004.
13 Lopez-Jornet P, Camacho-Alonso F, Molina-Miñarro F. Knowledge and attitude towards risk factors in oral cancer held by dental hygienists in the Autonomous Community of Murcia (Spain): a pilot study. *Oral Oncol* 2007; **43:** 602–606.
14 Geerts GA, Stuhlinger ME, Basson NJ. Effect of an antifungal denture liner on the saliva yeast count in patients with denture stomatitis: a pilot study. *J Oral Rehabil* 2008; **35:** 664–669.
15 Santos VR, Gomes RT, Mesquita RA *et al*. Efficacy of Brazilian propolis gel fro the management of denture stomatitis: a pilot study. *Phytoher Res* 2008; **11:** 1544–1547 (Epub ahead of print).
16 Cross LJ, Bagg J, Wray D, Aitchison T. A comparison of fluconazole and itraconazole in the management of denture stomatitis: a pilot study. *J Dent* 1998; **26:** 657–664.
17 Cross LJ, Williams DW, Sweeney CP, Jackson MS, Lewis MA, Bagg J. Evaluation of the recurrence of denture stomatitis and candida colonization in a small group of patients who received itraconazole. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2004; **97:** 351–358.
18 Lewis MA, Meechan C, MacFarlane TW, Lamey PJ, Kay E. Presentation and antimicrobial treatment of acute orofacial infections in general dental practice. *Br Dent J* 1989; **166:** 41–45.
19 Oliver RJ, Dhaliwal HS, Theaker ED, Pemberton MN. Patterns of antifungal prescribing in general dental practice. *Br Dent J* 2004; **196:** 701–703.
20 White TC, Marr KA, Bowden RA. Clinical, cellular and molecular factors that contribute to antifungal resistance. *Clin Microbiol Rev* 1998; **11:** 382–402.
21 Budtz-Jörgensen E, Lombardi T. Antifungal therapy in the oral cavity. *Periodontology* 2000 1996; **10:** 89–106.
22 Bissel V, Feliz DH, Wray D. Comparative trial of fluconazole and amphotericin in the treatment of denture stomatitis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1993; **76:** 35–39.
23 Albougy HA, Naidoo SA. Systematic review of the management of oral candidiasis associated with HIF/AIDS. *SADJ* 2002; **57:** 457–466.
24 Patton LL, Bonito AJ, Shugars DA. A systematic review of the effectiveness of antifungal drugs for the prevention and treatment of oropharyngeal candidiasis in HIV-positive patients. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2001; **92:** 170–179.
25 Pienaar ED, Young T, Holmes H. Interventions for the prevention and management of oropharyngeal candidiasis associated with HIV infection in adults and children. *Cochrane Database Syst Rev* 2006; **19:** CD003940.
26 Giuliana G, Pizzo G, Milici ME, Giuangreco R. *In vitro* activities of antimicrobial agents against *Candida* species. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1999; **87:** 44–49.
27 Ellepola AN, Samaranayake LP. Oral candidal infections and antimycotics. *Crit Rev Oral Biol Med* 2000; **11:** 172–198.
28 Ellepola AN, Samaranayake LP. Adjunctive use of chlorhexidine in oral candidiasis: a review. *Oral Dis* 2001; **7:** 11–17.
29 Anil S, Ellepola AN, Samaranayake LP. The impact of Chlorhexidine gluconate on the relative cell surface hydrophobicity of oral *Candida albicans*. *Oral Dis* 2001; **7:** 119–121.
30 Alou-Cervera L, Maestre-Vera JR, Moreno-Ubeda R. Consumo de antifúngicos de uso tópico en España. *Rev Esp Quimioter* 2001; **14:** 340–344.