Infection Control against *Candidaauris* in Healthcare Facilities

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Candida auris is an emerging multidrug-resistant yeast with high mortality rate, especially in patients with underlying co-morbidities. It has been known to contaminate the environment and colonize human skin for prolonged periods in healthcare settings leading to difficult-to-control outbreaks. However, there is limited literature on the efficacy of different disinfectants/antiseptics, which can effectively decontaminate the environment and decolonize patients to prevent the spread of *C. auris.*

Candida auris | outbreak | infection control | disinfection | decolonization | decontamination

1. Introduction

Members of the genus *Candida* can be part of microbiome on human skin, mucous membranes, female genital tract, and gastrointestinal tract. Of the 150 *Candida* species described in the literature only 10% are known to cause infections (candidiasis), which could be localized and or invasive leading to candidemia [1][2]. *Candida* infections are among the most common fungal nosocomial infections and are emerging as a serious threat in the hospital-associated outbreaks [3]. Although infections can occur in patients of all ages, extremes of age are more often affected [4]. Invasive candidiasis is emerging in critically ill patients with several risk factors, which include older age, comorbidities, long-term hospitalization, diabetes, recent extensive surgical procedures, broad-spectrum antibiotics, immunosuppression, and presence of medical devices such as endotracheal tubes, feeding tubes, and central venous catheters [3][4][5]. *C. albicans* has been known to be the most common species causing invasive candidiasis in hospitalized patients. However, in the past decade a wide range of non-albicans species, especially *C. glabrata*, *C. parapsilosis*, *C. tropicalis,* and *C. krusei* (now *Pichia kudriavzevii*) have emerged as progressive pathogens [2][3]. The plausible explanation for this switch is an increasing use of fluconazole for prophylaxis or therapy leading to selection of azole-less susceptible/resistant species.

In 2009, *C. auris* emerged as a novel *Candida* species isolated from patients with candidemia, wound infections, and otitis. Since then, this multidrug-resistant *Candida* species is being increasingly identified worldwide and reported to cause outbreaks of invasive infections in healthcare facilities around the world. It is, therefore, imperative to implement robust infection control measures to control *C. auris* outbreaks, especially in view of the organism having the ability to cause difficult-to-treat life-threatening infections [6]. Transmission-based precautions are required to prevent further spread leading to outbreaks, especially in high dependency units in the healthcare

setting. Since the *C. auris*-colonized/infected patients and the contaminated environment/equipment play an important role in the transmission, it is of utmost importance to decolonize patients and clean the environment and equipment using effective antiseptic and disinfectant, respectively [7]. An update on best practices for control of *C. auris* transmission in healthcare facilities, based on available information, was recently published by the Infection Prevention and Control working group of the International Society for Antimicrobial Chemotherapy [8].

2. Infection Control

Candida species are considered commensal organisms, and generally infection occurs because of autoinoculation or translocation as opposed to patient-to-patient transmission. However, *C. auris* is highly transmissible among patients, perhaps due to its proclivity for persistence on skin and environment and has emerged as a formidable pathogen considering its virulence factors, high resistance to multiple anti-fungal agents, the ability to colonize patients, as well as contaminate environmental surfaces and produce outbreaks with increased mortality rate [9].

Hence, implementation of infection control measures plays a crucial role in controlling *C. auris* outbreaks and reduce mortality rate in healthcare settings [8][10]. It is therefore imperative to select appropriate agents with antifungal activity (**Table 1**) for disinfections and decontaminations of the healthcare environment, hand hygiene of HCWs, and decolonization of patients as part of a robust and effective infection control measures against *C. auris* (**Table 2**).

2.1. Contact Precautions and Hand Hygiene

Patients, in healthcare facilities and long-term care infirmary, who are infected or colonized with *C. auris* should be isolated in a single room and placed on contact precautions. In the event of non-availability of a single room, patients colonized or infected with *C. auris* could also be cohorted in a room with other *C. auris* patients [11][12][13][14]. Cohorting may prove difficult or impractical if *C. auris* patients are found to be co-colonized with other MDR organisms [15]. Transmission-based precautions are continued as long as a patient remains colonized or infected with *C. auris.* Generally, colonization appears to be protracted among patients in the healthcare setting especially because of non-availability of methods for decolonization. Since the typical duration of *C. auris* colonization remains unknown, the most conservative strategy to prevent spread of infection would be to continue transmission-based precautions for the duration of present or future hospital stay [15]. Enhanced barrier precautions such as use of personal protective equipment (PPE) have been recommended by the Centers for Disease Control and Prevention (CDC) for patients from whom body fluid exposure is anticipated or high contact activities such as performing invasive procedure, dressing, device care etc., are performed [16]. However, use of PPE is not required if the patient does not have uncontained secretions or excretions.

One of the important steps in controlling the spread of infection in the hospital setting is proper hand hygiene by the HCWs. Hand hygiene may be practiced with the use of alcohol-based hand sanitizer (ABHS), soap and water, or alcohol and chlorhexidine hand rubs [15][17][18][19]. It is imperative for HCWs to practice frequent hand hygiene as it remains one of the most basic components of infection control practices. While all the available guidelines

emphasize strict adherence to hand hygiene, the recommended methods, however, differ. CDC recommends use of ABHS or washing with soap and water if the hands are visibly soiled. The Public Health England (PHE) and the South African Center for Opportunistic, Tropical, and Hospital Infections (COTHI) recommend washing hands with soap and water followed by the use of ABHS on dry hands before donning gloves. There are no specific guidelines for hand hygiene by the European Center for Disease Prevention and Control (ECDC), Pan American Health Organization/World Health Organization (PAHO/WHO). There may be additional benefit of ABHS when combined with chlorhexidine [20].

Table 1. Different disinfectants and antiseptic agents found effective against *C. auris*.

Disinfectants (Concentration)	Level of Evidence	References	Antiseptic (Concentration)	Level of Evidence	References
Chlorine (1000 ppm)	Good	[18][19][21][22][23]	**Chlorohexidine gluconate (2%)**	Good	[13][17]
Hydrogen peroxide (1.4%) (8 g/m^3)	Moderate	[18][22][24][25]	**Povidine Iodine (10%)**	Moderate	[26][27]
Phenolics (5%)	Low	[25]	**Isopropanol alcohol (70%)**	Low	[28]
Peracetic acid (2000 ppm)	Low	[26][29]			
Benzalkonium bromide (2000 ppm)	Low	[26]			
[a] UV-C light (253.7 nm)	**?**	[27]			
Ozone (≥300 mg/m^3)	**?**	[30]			

Table 2. Recommendation of infection control of *C. auris*.
? Limited studies and comment on the level of evidence. [a] ultraviolet—C light.

Identification of Colonized/Infected Patients	Transmission—Based Precautions	Environmental Disinfection (Health Organization [c])	Hand Hygiene Procedures (Health Organization [c])	Decolonization Procedures
Determination of *Candida* species isolated from sterile site	Contact precaution apply for colonized/infected patients in acute care settings	Daily and terminal cleaning with registered hospital grade disinfectant effective against *C. difficile* spores (CDC)	Use of alcohol-based hand sanitizer or hand washing with soap and water before and after donning of gloves (CDC)	No recommendations by any health organization

Identification of Colonized/Infected Patients	Transmission—Based Precautions	Environmental Disinfection (Health Organization [c])	Hand Hygiene Procedures (Health Organization [c])	Decolonization Procedures
Identify *Candida* species isolated from non-sterile site when patient resides at a location where *C. auris* has been identified	Isolation of all patients infected or colonized in a single room, side room or cohorted	Terminal cleaning by using hypochlorite at 1000 ppm. Shared medical equipment should be cleaned and disinfected (PHE)	Hand washing with soap and water followed by alcohol-based sanitizer on dried hands before and after donning of gloves (PHE, COTHI)	
Screen patients who are admitted to wards where *C. auris* cases has been identified	Equipment should not be shared	Terminal cleaning using a disinfectant with antifungal activity (ECDC)	No recommendations (ECDC, PAHO, WHO)	
same infection control interventions apply for patient colonized or infected with *C. auris*	PPE [a] in the form of gloves and gowns for HCWs [b]	Regular and terminal cleaning with chlorine—releasing agent at 1000 ppm, use of hydrogen peroxide vapor in terminal cleaning where feasible (COTHI)		
	Strict adherence of HCEs to standard infection control precautions including hand hygiene	Daily and terminal cleaning with soap and water followed by 0.1% bleach. Clean disinfectant and sterilize medical equipment. machine wash linens and clothes (PAHO, WHO)		
	Visitors encouraged to use PPE			

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contaminated with *C. auris* [21]. One of the studies showed that 1% of chlorine as NaOCl was effective against all *Candida* species tested, in both planktonic and biofilm forms [29]. The CDC recommends daily and terminal cleaning using the United States Environmental Protection Agency (EPA)-registered hospital-grade disinfectant effective against *C. difficile* [26] whereas COTHI and PHE recommend use of hypochlorite as chlorine-based disinfectant at 1000 ppm (parts per million). Several in vitro studies have confirmed the efficacy of chlorine-based disinfectants on different surfaces such as stainless steel, ceramic, plastic and glass. Different concentrations of

[a] PPE—Personnel protection equipment, [b] HCWs—healthcare workers, [c] CDC Centre for Disease Control, PHE—Public Health of England, ECDC—European Center for Disease and Control, COTHI—Center for Opportunistic,

NaOCl and tested their effectiveness against *C. auris* [27].

Hydrogen peroxide vapor at a concentration of (8 g peroxide/m^3) used in conjunction with 10,000 ppm chlorine-based disinfectant has shown to effectively decontaminate the environment [31]. In vitro studies have confirmed the killing efficacy of hydrogen peroxide and found it being comparable to that of chlorine-based disinfectants against *C. auris* showing 96.6–100% killing [22]. Another study demonstrated that hydrogen peroxide solutions in a concentration of 0.5 and 1.4% was found to be effective in killing *C. auris* with comparable results to that of chlorine-based disinfectants. A formulation of 11% hydrogen peroxide with 0.01% silver nitrate has also been found to be effective but requires 60 min contact time for complete eradication of *C. auris* [15]. Disinfection of healthcare equipment such as ECG monitor leads and blood pressure monitor and cuffs with hydrogen peroxide vapor has been used [22].

Although quaternary ammonium compounds are widely used as disinfectants for their fungicidal, bacterial, and virucidal (against lipophilic viruses) activity, a recent study demonstrated them to be ineffective against *Candida* species including *C. auris* [26]. Among other disinfectants, alcohol, peracetic acid, acetic acid, phenol, and glutaraldehyde have also been evaluated against *C. auris.* It was reported that 2% glutaraldehyde and 5% phenol were found to be effective on multiple surfaces with contact times of 20 and 60 min, respectively [15]. While ethyl alcohol 29.4% has been shown to have some killing activity it is not to the same degree as chlorine-based disinfectant or hydrogen peroxide. As with NaOCl, complete eradication of *C. auris* was achieved by peracetic acid at 2000 ppm. Furthermore, peracetic acid at 1200 ppm in combination with hydrogen peroxide and acetic acid was found to have killing activity similar to chlorine-based disinfectants [22].

Among other measures, efficiency of ultraviolet light was also evaluated against *C. auris.* Exposure of *C. auris* to ultraviolet-C (UV-C) light at 254 nm for 20 min at optimal distance produced significant killing of *C. auris* [32]. UV-C killing can be augmented by increasing the length of exposure and combining it with standard cleaning methods can eliminate *C. auris* from the environment.

The LK/CXD bed unit ozone disinfection machine, which produces an ozone concentration of ≥300 mg/m^3, has been used for disinfecting inpatient bed unit. Two cycles of routine disinfection reportedly completely eradicated *C. auris* on bed sheets [33].

2.3. Decolonization

Currently, only limited data on the efficacy of skin-antiseptic compounds against *C. auris* colonization in patients are available. Furthermore, the recommendations of major health organizations regarding hand hygiene procedures for control of *C. auris* infection are different or lacking [33]. There are no established guidelines for decolonization of patients found to be colonized with *C. auris* on screening. While no decolonization methods have been offered by CDC, COTHI and ECDC, PHE recommends body washes and mouth gargles with chlorhexidine. However, specific details such as concentration of chlorhexidine, frequency of application etc., are not provided

and it is not clear if it is efficacious in clearing colonization with *C. auris.* Since no specific decolonization protocol is established to date, it is imperative to evaluate other antiseptics. Among compounds which have generated some interests are very dilute NaOCl and povidone iodine which according to some studies appear to support their use for antiseptic skin preparation against *C. auris* [34][35].

In a recent report from Saudi Arabia, an outbreak due to *C. auris* in a tertiary-care facility was successfully controlled by employing a combination of infection control measures mentioned in the text above. Briefly, patients with laboratory-confirmed diagnosis of *C. auris* infection were placed on contact isolation. The positive cases and HCWs were cohorted in the same unit with a strict implementation of hand hygiene, proper use of PPE and limiting the use of shared medical equipment. In addition, the positive patients were subjected to daily bathing using 2% chlorhexidine wipes and daily environmental cleaning was performed using sodium NaOCl 1000 ppm. For terminal cleaning hydrogen peroxide fumigation was included with use of NaOCl 10,000 ppm [23].

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