Preventing the spread of fungal Candida auris infections as a global challenge

Grażyna Iwanowicz-Palus[1], Dorota Świst[2], Mariola Kicia[1], Magdalena Korżyńska-Piętas[1], Paulina Polska[1], Beata Żółkiewska[3], Anna Kwaśniewska[4], Michał Filip[4], Agnieszka Bień[1]

[1] Department of the Basics of Midwifery Faculty of Helath Science Medical Univeristy of Lublin, Poland

[2] Independent Public Health Care Center in Świdnik, Poland

[3] Independent Public Provincial Specialist Hospital in Chełm, Poland

[4] Department of Obstetrics and Pathology of Pregnancy, Medical University of Lublin, Lublin, Poland

European Journal of Medical Technologies
2019; 1(22): 66-72

www. medical-technologies.eu
Published online 15.02.2019

Corresponding address:
Grażyna Iwanowicz-Palus
Department of the Basics of Midwifery Faculty of Helath Science Medical Univeristy of Lublin, Poland Staszica 4-6, 20-081 Lublin, (Collegium Maximum), Poland
e-mail address: spupalus@gmail.com, tel. +48 603234560

Abstract

Nowadays preventing the spread of fungal infections is extremally important for the health of society. A new species of Candida species called Candida auris, which is the cause of many infections has been detected recently. Candida auris might be an etiological factor of invasive candidiasis in patients undergoing invasive procedures and / or long-term broad-spectrum antibiotic therapy. The species causes infection primarily in patients in hospitals, where the spread of infections takes place very quickly. Therapeutic difficulties related to this yeast result from the severe course of the disease and the resistance of the species to standard antifungal medicines. Moreover , Candida auris causes diagnostic difficulties since it is not correctly detected by yeast identification systems which are commonly used in laboratories. C. auris shows all the features of a pathogen which is a threat to public health. The species is a challenge for the health care system in Poland and in the world.

Key words:

fungal infection, prevention, candida auris

Introduction

There are various microorganisms in the human body that are human microbes. Fungis are part of the microbiome called mycobacteria. Currently, only about 5% of fungal species occurring in the human body are known [1,2,3]. Yeasts are one from three groups of fungi of medical importance in addition to filamentous fungiand dysmorphic forms [4,6]. Yeasts belong to the genus Candida and are widespread throughout the world. The most numerous species of yeast is Candida albicans, which occurs in 40-80% of healthy people and is part of the microorganisms of the physiological flora of the digestive system [4]. The species could cause yeast infection - candidiosis. In women, vulvovaginal candidiasis is common, especially during pregnancy. In the course of diabetes, candidiasis is manifested in the form of inflammation accompanied by acute pruritus and burning as well as white or yellow vaginal discharge [5,6].

Hospital infections are a serious problem in epidemiology and organization of health care system. Among hospital infections, fungal infections represent 9-10% of all infections. Infections caused by fungi from the genus Candida are, according to available data, around 89% [6,7]. Candidiasis are usually endogenous infections caused by the species C. albicans, C. tropicalis. C. parapsilosis, C. glabrata, C. krusei. They manifest themselves in fungemia, meningitis, lung, endocarditis, kidneys, joints, cerebral abscess and also inflammatory conditions in the gastrointestinal tract. Fungal infections are more common among oncological patients, especially those who have impaired cellular response, which is important in the elimination of fungi from an infected organism [7]. Fungal infections are more common in oncological patients, eg with leukemia, transplants, after chemotherapy, during and after the use of immunosuppressive drugs and broad spectrum antibiotics. Morover, low-birth weight infants, catheterized patients, parenteral nutrition, with artificial heart valves and long-term hospitalized patients are also exposed to this type of infection. Patients with AIDS with impaired cellular response are particularly exposed to fungal infections . Fungal infections are also a serious complication of surgical wounds and burn wounds. Studies show that 2 to 14% of cases of generalized candidiasis occur in burned patients [7,8].

Epidemiology of Candida auris infections

Candida auris was diagnosed for the first time in Japan in 2009, it was detected in a 70-year-old female patient with an external ear infection. From the place of detection, the name of species was taken , in Latin auris means an ear [9]. Later the species was identified in South Korea and India. In the following years it was detected many times: in 2014 in South Africa and Kuwait. In 2015 appeared the information about the occurrence of C. auris in the USA . In the same year, this type of infection was recorded in Colombia and Venezuela. In 2017, a report about the presence of dangerous yeast in a hospital in Panama was published. That was the first such information received from Central America. Scientist who were looking for C. auris infection pathways, noticed that the fungus's spread did not take place through travelling , but rather was related to the stay of infected people in hospitals. In Europe, the first cases of Candida auris were recorded in 2015 in the United Kingdom,. In the London hospital an epidemic outbreak which last 16 months , covered 50 cases related to Candida auris was created[10]. In the researchers opinion the species is a new pathogen that is a threat to public health on a global scale due to the rapid spread in the world [2,8]. In Europe, hospital epidemics caused by C. auris occurred in Great Britain and Spain. There are cases of patients with isolated C. auris in Germany, France, Austria and Norway [10,11,12]. In Switzerland the first case of the C. aulis was recorded in 2017.

The route infection of Candidia Auris

Candida auris exhibits all the features of a pathogen which is a threat to human health comparable with multi-drug resistant bacteria such as methicillin-resistant Staphylococcus ureus or

Carbapenemase-producing Enterobacteriaceae. These features include the ability to spread using horizontal transmission and causing epidemics, the ability to cause severe, even fatal disease and multidrug resistance [13]. To date it has been shown that C. auris, unlike other Candida species, most often causing endogenous infections, is easily acquired through contact with contaminated hospital surfaces and equipment as well as through contact between people. To break the route of spreading the species is necessary to identify the strain as soon as possible, by isolating infected or colonized patients and absolute compliance by medical personnel with the introduced principles of contact insulation [2]. Candida. auris could colonize the human skin for many months [13, 14, 15]. Studies which were conducted in 2012-2015 in a group of 54 patients infected with Candida auris yeast showed that the average time from contact with C. auris till the diagnosis of infection was 19 days in the interquartile range of 9-36 days [16].

The risk factors for C. auris infection

Candida auris yeasts are detected in patients with pre-existing diseases, usually after a few weeks of hospitalization. Most often, they attack patients who were treated for long periods in intensive care units, patients with respiratory diseases, patients after vascular surgeries and previously treated with antifungal therapy [17]. The infections usually spread in the genitourinary system. A study in a group of 54 patients diagnosed with Candida auris showed that 50% of patients had a surgery, 73% had a central catheter inserted and 61% had a bladder catheter inserted [16].

Mortality in the course of Candida auris infection

The first reported cases of C. Aulis infection were in patients with chronic otomycosis and were associated with healthcare. The infection occurred in the form of candidiasis or other invasive infections which lasti up to three weeks. The course of the disease was characterized by high mortality rate [11,12].

A study published in 2013 reported that mortality of C. auris blood infections was 33% for all patients and 57% for the subgroup of patients admitted to intensive care units [11]. Mortality in the studied group of 54 patients with Candida auris from 2012-2015 was 59%. Studies from 2018 indicate a 40-60% mortality rate in this group of respondents [13,16].

Laboratory diagnostic possibilities

Candida auris isolates were obtained from the lower respiratory tract, urine, bile, wounds and mucocutaneous swabs [17]. C. auris is characterized by thermo stability, i.e. the ability to develop at 37 ° C – 42 ° C, in contrast to C. haemuloniii and C. duobushaemulonii, which do not develop at 42 ° C [1,18]. C. auris could not be identified by microscopic examination or growth on chromogenic agar. Biochemical tests might incorrectly identify C. auris using Vitek-2, BD Phoenix, MicroScan or API strips. [11,12]. Molecular-based methods have been developed to detect and distinguish C.auris from other yeast [17]. In case of diagnostic doubts, it is indicated to send isolates to the reference mycological laboratory [11].

Resistance to antifungal medicines

C. auris infections are mainly observed in patients with previous exposure to antifungal drugs, which could have played a role in the emergence of a new pathogen [13]. Candida auris has the ability to maintain or develop multidrug resistance. Nowadays, there is no established limit value for Candida auris sensitivity [13]. There are three classes of systemic antifungal medicines which are used for treating invasive Candida infections: polyenes, triazoles and echinocandins. The studies have shown that 41% of Candida auris isolates were resistant to at least 2 classes and 4% were resistant to 3 classes of antifungal medicines. The majority of C. auris

isolates described worldwide are resistant to fluconazole [11,13,15]. Resistance to amphotericin B occurs in a maximum of 35% of isolates and resistance to echinocandin was reported in 2-8% of C. auris isolates. The resistance to all three major classes of antifungal drugs was described in 4% of isolates. An additional difficulty in the therapy is the ability of Candida auris to adhere to the surface of plastics and biofilm formation, which makes the effectiveness of medicines difficult [12,17].

Therapeutic possibilities

The optimal treatment scheme for Candida auris infections has not been defined. Studies conducted in the United States have demonstrated the sensitivity of C. auris to echinocandin, which is recommended for the treatment of fungal infections of this type [17].

For empiric treatment of C. auris in adults and children who are above two months of age, echinocandins are most frequently used. In the situation of failure of the treatment amphotericin B should be used. Due to the more frequent occurrences of resistance, treatment should be started with routine mycogram [1].

The spread of the patogen – methods of control

On June 24, 2016, the Centers for Disease Control and Prevention (CDC) issued an emergency alarm, recommending US healthcare facilities, conducting microbiological tests to early detect Candida auris in patients [19]. One of the most important pathogen transmission vectors is the hands of employees in contact with the patient and its surroundings, i.e. bed, table and other surfaces which the patient touches. It has been propen that the persistence of C. auris on moist and plastics sufraces is at least 14 days [15,17]. Despite the smaller predisposition to biofilm formation than C. albicans, C. auris has a greater ability to survive on dry or moist surfaces [13].

A special, separate staff should be provided for contact with patients with C. auris. It is necessary to constantly supervise the proper performance of procedures such as hand hygiene and disinfection of the surface. The minimum contact time for the acquisition of C. auris is only 4 hours. The colonization on human skin might last from several weeks to several months [10,11,15]. In the care of more patients with this pathogen, the use of isolation or cohorting principles plays a large role. In order to eliminate yeast from the skin, daily body washing with chlorhexidine should be used [20]. The documentation of patients who are transferred to other health care centres should include information about infection or colonization with C. Aulis. The patient's documentation should also include special recommedations. Before stopping the insulation principles, at least two control tests for the presence of C. Aulis should be carried out. The test should be conducted at least one week apart with negative results [12].

Recommendations for hand disinfection

All C. auris prevention procedures emphasize hand hygiene, however, they differ in the recommended methods. Centers for Diseases Control and Prevention, (CDC) at the Department of Health and Social Care in the USA recommends disinfection with alcohol-based products or washing with soap and water if hand are visually dirty. Public Health England (PHE) at the Department of Health and Welfare in the United Kingdom recommends washing hands with soap and water and then applying hands disinfectant to dry hands. Nowadays, in Poland and in the world there are no documented common arrangements for the effectiveness of disinfectant products against Candida auris in hand hygiene [15].

Recommended procedures for desinfection of surfaces in hospital

Formulations effective against C. difficile has shown effectiveness against C. auris present on hospital

surfaces Hydrogen peroxide and sodium hypochlorite formulations also have this property[11,15,21,22]. It was discovered that peracetic acid at 2000 ppm, shows activity against C. auris [15]. It was found that at least 20 minutes exposure to UV-C light could be effectively after disinfection of the surfa ces.Due to the possibility of C. auris biofilm formation, a longer contact time of the disinfectant with the surface should be taken into account in order to effectively penetrate the biofilm. The studies show the effectiveness of activities involving three times a day cleaning hospital surfaces with a solution of chlorine at a concentration of 1000 pppm and a final (general) cleaning at a concentration of 10,000 [11,15]. Hydrogen peroxide should be used in gaseous form (a spray) [20].

Recommendations for eradication of the pathogen from patients' skin

Unlike other species of Candida, C. auris has a high propensity to be transferred through a contact from a colonized patient and through contact with colonized equipment [11].

Since it has been recognized that colonization of patients is one of the ways of transmitting a pathogen in the hospital environment, effective methods of eradication of the fungus from the body of patients, especially intensive care and surgical wards, are tested. The most studied formulation is chlorhexidine gluconate. The studies have shown efficacy in the eradication of C. auris with 2% chlorphexidine gluconate with a 2 minute contact time. It was also noticed that 2% chlorhexidine digluconate was even more effective in 70% isopropyl alcohol also in a two-minute contact time. In the combating of C. aris, local use of nystatin and terbinafine is recommended at most important body parts , such as the area where an intravenous cannula was established [15]. In eradication of the pathogen from the patients' skin, it was suggested to use iodine based formulas and these which are based on chlorhexidine. Nowadays, decolonization scheme and the effectiveness of the technique in the eradication of C. Aulis from the skin is not described in detail [11].

Recommendations for eradication of the pathogen from the patients'skin

Unlike other species of Candida, C. auris has a high propensity to be transferred through a contact from a colonized patient and through contact with contaminated equipment [11]. Since it has been recognized that colonization of patients is one of the ways of transmitting a pathogen in the hospital environment, effective methods of eradication of the fungus from the body of patients, especially from intensive care and surgicalunits , are tested. The most studied formulation is chlorhexidine gluconate. Studies have shown efficacy in the eradication of C. auris with 2% chlorphexidine gluconate with a 2 minute contact time. It was noticed that 2% chlorhexidine digluconate was even more effective in 70% isopropyl alcohol in a two-minute contact time. In the treatment of C. aris, local use of nystatin and terbinafine is recommended at key areas , such as the area where an intravenous cannula was established [15]. In eradication of the pathogen from the patients' skin, it was suggested to use iodine based preparations and preparations based on chlorhexidine. Nowadays, there are no approved decolonization regimens and their effectiveness in the eradication of C. auris from the skin [11].

The rules of home care for patient dealing with C. auris infection-information for family

In the prevention of the C. auris outbreak, it is very important that patients and their family members receive reliable information about the proper conduct of contact with an infected or colonized person. It is important to explain that colonization means the possibility of transmitting a pathogen susceptible

to a person and that colonization in the situation of a decrease in immunity might turn into an active infection. Healthcare workers should explain to family members the need to thoroughly wash and disinfect hands before and after the contact with the patient or his/her environment (a bed, a cupboard, a drip stand), especially before leaving the patient's room. Although for healthy people, the risk of C. auris infection is low, patients and their family members should continue the practice of hand hygiene after returning home. If family members care of patients with C. auris, they should consider wearing disposable gloves while performing certain nursing activities such as changing the dressing on the wound or assisting the patient in the bath. Patients with colonization of the pathogen should strictly abide hand hygiene, moreover all wounds should be covered with a special dressing [11,23].

Summary

Due to difficulties with laboratory identification, there is unsatisfactory reports on the spread of Candida auris in different regions of the world. It is commonly known that the pathogen has been detected on five continents in Europe, Asia, North America, and South America and Africa. C. auris isolates which were studied in the United Kingdom have different geographical origins, which suggests multiple introductions into the country. American research indicates clonal pathogen spread in several countries. European research based on the data from 2018 showed that C. auris was repeatedly placed in hospitals in Europe, which poses a serious threat to public health around the world [11,23].

References

1. Mikołajczyk A. Candida auris – nowe zagrożenie ze strony drobnoustrojów. Aktualności Narodowego Programu Ochrony Antybiotyków 2018; 2: 1-5.
2. Wróblewska M, Sulik-Tyszka B. Candida auris-epidemiologia i diagnostyka laboratoryjna zakażeń. Diag Lab. 2017; 53 (4): 235-240.
3. Malinowska M, Tokarz-Deptuła B, Deptuła W. Mikrobiom człowieka. Post. Mikrobiol. 2017; 56 (1): 33-34.
4. Salvo AD. Grzybice oportunistyczne W: Virella G. (red.): Wyd. I polskie Heczko. P. Mikrobiologia i choroby zakaźne. Wyd. Medyczne Urban & Partner, Wrocław 2000.
5. Kabir MA, Hussain MA, Ahmmmmad Z. Candida albicans: A Model Organism for Studying Fungal Pathogens. ISRN Microbiol 2012, doi: 10.5402/2012/538694 [data dostępu: 30.01.2019].
6. Magdzik W, Naruszewicz-Lesiuk D, W: Zieliński A. (red.): Choroby zakaźne i pasożytnicze-epidemiologia i profilaktyka. Bielsko –Biała: Wydawnictwo. á-medica press. Wyd VI; 2007: 11-12.
7. Garczewska B. Szpitalne zakażenia grzybicze W: Dzierżanowska D. (red.): Postaci kliniczne zakażeń szpitalnych. Bielsko-Biała: Wyd. á-medica press; 2007: 7-9.
8. Grondalska D, Kmieciak W. Candida auris - nowy patogen grzybiczy. Post. Mikrobiol. 2017; 56 (3): 282-288.
9. Satoh K, Makimura, K, Hasumi Y. Candida auris sp. nov., a novel ascomycetous yeast isolated from the external ear canal of an inpatient in a Japanese hospital. Microbiol Immunol 2009 ;53 (1): 41-44.
10. Schelenz S, Hagen F, Rhodes JL. First hospital outbreak of the globally emerging Candida auris in a European hospital. Antimicrob Resist Infect Control 2016; 5 (1): 35-42.
11. European Centre for Disease Prevention and Control. Candida auris in healthcare settings – Europe – first update, Stockholm: ECDC; 2018.
12. Schwartz IS, Hammond GW. First reported case of multidrag-resistany Candida auris in Canada. Can Commun Dis Rep. 2017; 43 (7/8): 150-153.
13. Lamoth F, Kontoyiannis DP. The Candida auris Alert: Facts and Perspectives. J Infect Dis. 2018; 217 (4): 516-520.
14. Heat CH, Dyer JR, Pang S, Coombs GW. Candida auris Sternal Osteomyelitis in a Man from Kenya Visiting Australia, 2015. EID Journal 2019; 25 (1): 192-194.
15. Ku TSN, Walraven CJ, Lee SA. Candida auris: Desinfectants and Implication for Infection Control. Frontiers in Microbiology 2018; 9 (726): 1-12.
16. Lockhart SR, Etienne KA, Vallabhaneni S. Simultaneous Emergence of Multidrug-Resistant Candida

auris on 3 Continents Confirmed by Whole-Genome Sequencing and Epidemiological Analyses. Clin Infect Dis 2017; 64 (2): 134-140.

17. Spivak CS, Hanson KH. Candida auris: an Emerging Fungal Pathogen. Journal of Clinical Microbiology 2018; 56 (2): 1-10.
18. Ben-Ami R, Berman J, Novikov A, Bash E. Multidrug-Resistant Candida haemulonii and C. auris, Tel Aviv, Israel. Emerg Infect Dis 2017; 23 (1): 195-203.
19. Clancy CJ, Nguyen MH. Emergence of Candida auris : An International Call to Arms. Clin Infect Dis 2017; 64 (2): 141-143.
20. Riat A, Neofytos D, Coste A, Harbarth S. First case of Candida auris in Switzerland: discussion about preventive strategies. Swiss Med Wkly. 2018; 148: 1-4.
21. Belkin A, Belkin A, Gazit Z, Keller N, Ben-Ami R. Candida auris Infection Leading to Nosocomial Transmission, Emerg Infect Dis. 2018; 24 (4): 801-804.
22. Cadnum JL, Shaikh AA, Piedrahita CT. Effectiveness of disinfectants against Candida auris and other Candida species. Infect Control Hosp Epidemiol 2017; 38: 1240 -1243.
23. Centers for Disease Control and Prevention: Recommen -dations for Infection Prevention and Control for Candida auris. https://www.cdc.gov/fungal/candida-auris/index.html [data dostępu: 06.02.2019].