EVALUATION OF CURRENT BACTERIOLOGICAL PROFILE AND ANTIBIOTIC SENSITIVITY PATTERN IN CHRONIC SUPPURATIVE OTITIS MEDIA (CSOM)

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ABSTRAK

Objektif:

Untukmenilaiprofilmikroorganismapenyebabradangtelingatengahjeniskronik*(CSOM),*corakse nsitivitidankerintanganmerekakepadaantibiotiktempatan yang tersedia.

Kaedah: Kajianrentaskerataninimelibatkansejumlah91sampelcalitannanahdaritelingapesakit yang telahdiberi diagnosis secaraklinikalsebagai CSOM. Sampelcalitannanahinidihantarkemakmalmikrobiologidan proses kulturpembiakanmikroorganismadilakukandenganmenggunakanprosedurdiagnostik yang tersedia. Pemeriksaantahapkepekaanantibiotikdijalankandenganmenggunakankaedah*Modified Kirby-Bauer*. Data keputusantelahdiinterpretasikanberdasarkanpanduan CLSI 2017.

Keputusan: Pertumbuhanmikroorganismadilihatpada85 (93.4%) sampelmanakala 6 (6.6%) sampeltidakmempunyaipertumbuhan. Daripadajumlahpertumbuhan, 63 (69.2%) adalahmonomikrobial, 13 (14.3%) adalahpolimikrobialdan 9 (9.9%) menunjukkanpertumbuhancampuranmelebihitigamikroorganisma. Mikroorganismayang paling banyakdikesanadalah*Pseudomonas aeruginosa* (32.6%) diikutioleh*Staphylococcus aureus* (16.9%) dan*Klebsiella*spp(5.6%).Antibiotik yang berkesanterhadap*Pseudomonas aeruginosa*ialahceftazidime, meropenemdanpiperacillin-tazobactam. *Staphylococcus aureus*menunjukkansensitiviti paling tinggikepada rifampin, cefoxitindanasidfusidic.

Kesimpulan: Mikroorganisma yang paling banyakdikesanadalah*Pseudomonas aeruginosa*diikutioleh*Staphylococcus aureus*. Namunbegituterdapatperbezaancoraksensitivitidanrintanganantibiotikmereka. Pengetahuaniniadalahpentingsebagaipanduandalampemilihanantibiotik yang sesuaidanberkesankepadapesakit CSOM.

Kata kunci: Radangtelingatengahkronik; Profilmikroorganisma; Kepekaanantibiotik

ABSTRACT

Objectives: To determine the current bacteriological profile of CSOM, their antimicrobial sensitivity and resistance pattern towards local antibiotic used and the most sensitive antibiotic against isolated bacteria causing CSOM.

Methods: This was a cross-sectional study involving a total of 91 ear swabs obtained from patients clinically diagnosed of active CSOM. These swabs were cultured for microbial identification done according to the standard protocol. Microbiological laboratory diagnostic and antibiotic susceptibility testing was performed using Modified Kirby-Bauer's disc diffusion method. The diameter of inhibitory zone interpreted based on CLSI 2017.

Results: Microbial growth was seen in 85 (93.4%) samples while 6 (6.6%) of the samples had no growth. Out of total growth, 63(69.2%) were monomicrobial, 13(14.3%) were polymicrobial and 9 (9.9%) were mixed growth. The most common bacteria isolated was *Pseudomonas aeruginosa* (32.6%) followed by *Staphylococcus aureus*(16.9%) and *Klebsiella*spp(5.6%). *Pseudomonas aeruginosa*showed highest sensitivity towards ceftazidime, meropenem and piperacillin-tazobactam. *Staphylococcus aureus*showed highest sensitivity to rifampin, cefoxitin and fusidic acid.

Conclusion: The commonest microorganism isolated in CSOM was aerobes which were *Pseudomonas aeruginosa* and *Staphylococcus aureus.* There is a difference in their antibiotic sensitivity and resistance pattern. This knowledge is important to guide a rational antibiotic use for an effective treatment of CSOM.

Keywords: Chronic suppurative otitis media; Bacterial profile; Antibiotic sensitivity

Chapter 1:

INTRODUCTION

1.1 INTRODUCTION

The World Health Organization (WHO) defines chronic suppurative otitis media (CSOM) as ear discharge through a perforated tympanic membrane present for at least 2 weeks (1). It is characterized by a permanent abnormality of the pars tensa or flaccida associated with production of pus discharge resulting from the chronic inflammation with varying degree of oedema, submucosal fibrosis, hypervascularity and infiltration with lymphocyte, plasma cell and histiocyte (2). In general, CSOM is considered if patients have perforated tympanic membrane with continuous ear discharge for periods of 6 weeks to 3 months. Patient can develop either recurrent bouts of otorrhea (active CSOM) or a dry but permanent tympanic perforation (inactive CSOM).

Global burden of illness from CSOM involves 65–330 million individuals with draining ears with 60 % of whom (39–200 million) suffer from significant hearing impairment. It accounts for 28000 deaths and a disease burden of over 2 million Disability Adjusted Life Years (DALYs) (1). National study conducted in the United Kingdom showed the prevalence of CSOM was about 16% of population (3). Our local study conducted in 1991 to evaluate the prevalence of CSOM among school children in Malaysia showed 5.3 over 1000 children diagnosed CSOM compared with 0.01-0.03 over 1000 children in the United States (4). Recent study done in 2010 by Khairi *et al.* showed prevalence of CSOM among the school children in a state in Malaysiawas about 2 % (5). The prevalence appears to be distributed equally between males and females but several studies showed gender predominance in females.

CSOM is an important cause of preventable hearing loss particularly in the developing world and inadequate treatment can lead to severe life threatening adverse effects like intra and

extra cranial complications. Since CSOM can cause significant morbidity, knowledge of the microorganisms responsible for CSOM can help in the selection of the most appropriate antibiotic regimen treatment regimen.

The aim of this study is to evaluate the current bacteriological profile of microorganisms causing CSOM and to study their antibiotic sensitivity pattern to our available antibiotics. This knowledge is very important for the clinician to decide the most appropriate antibiotic for the treatment in our local CSOM patients in order to prevent recurrent and further complications.

Chapter 2:

OBJECTIVES

OBJECTIVES OF STUDY

2.1 General objective

To describe current bacteriological profile of CSOM and their antibiotic sensitivity pattern

2.2 Specific objectives

1. To describe the microorganism causing CSOM

2. To determine the antibiotic sensitivity pattern toward isolated microorganism causing CSOM

3. To determine the most sensitive antibiotic against isolated microorganism causing CSOM

Chapter 3:

STUDY PROTOCOL

3.1 TITLE PAGE

JEPeM Code: USM /JEPeM/17120683

Study Title: Evaluation of Current Bacteriological Profile and Antibiotic Sensitivity Pattern in Chronic Suppurative Otitis Media (CSOM)

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Introduction

Chronic suppurative otitis media (CSOM) is defined as a chronic inflammation of the middle ear and mastoid cavity which presents with recurrent ear discharges or otorrhea through a tympanic perforation for more than 12 weeks(1). It is characterized by a permanent abnormality of the pars tensa or flaccida associated with production of pus discharge resulting from the chronic inflammation with varying degree of oedema, submucosal fibrosis, hypervascularity and infiltration with lymphocyte, plasma cell and histiocyte(2). The World Health Organization (WHO) defines CSOM as ear discharge through a perforated tympanic membrane present for at least 2 weeks. National study conducted in the United Kingdom showed the prevalence of CSOM was about 16% of population(3). Prevalence of CSOM among the school children in a state in Malaysia was about 2 %(5). CSOM is an important

cause of preventable hearing loss particularly in the developing world (1). It can cause severe adverse effects like intra and extracranial complications which can be life threatening.Since CSOM can cause siginificant morbidity,knowledge of the microorganisms responsible for CSOM can help in the selection of the most appropriate antibiotic regimen treatment regimen. The aim of this study is to evaluate the current bacteriological profile of microorganisms causing CSOM and their antibiotic sensitivity pattern to the locally available antibiotics in order to determine the most appropriate antibiotic therapy for CSOM patient in our local population.

Literature review

Microbiological studies on causative agents of chronic otitis media show different result from region to region .The differences in the various studies could be due to differences in the patient populations studied and to geographical variation. These result also may be influenced by climate, patient population, techniques of specimen's collection and history of prior use of antibiotics (6) .

Verhoeff *et al*. reviewed 79 papers related to CSOM and they found that the most frequently isolated aerobic organisms were *Pseudomonas aeruginosa* (18-67%), *Staphylococcus aureus* (14-33%) and other Gram-negative organisms such as *Proteus* spp., *Klebsiella* spp., *Escherichia* spp. and *Haemophilus influenzae* while the most frequently isolated anaerobic organisms were *Bacteroides spp.* (1-91%) and *Fusobacterium spp*.(4-15%) (7).

Study done by Kazeem *et al.* in Nigeria also showed *Pseudomonas aeruginosa* (31.5%) was the highest prevalence of the isolated organism(8).This study also showed evidence of

isolated pathogens had gradual decline of sensitivity strength to a number of antibiotics probably due to indiscrimate use of antibiotics.

This is similar with study done by Nazir *et al.* in India which revealed *Pseudomonas aeruginosa* (38.23 %) as the commonest isolated organism followed by *Staphylococcus aureus* and *Proteus species.* This study also revealed that the strains of *Staphylococcus aureus* that previously were sensitive to streptomycin, tetracycline and chloramphenicol had no longer exhibit the old sensitivity pattern (9).

Other studies from Korea and Iran have reported that *Staphylococcus aureus* was the commonest isolates in CSOM patients(10, 11). This is similar with the study done by Lakshmi *et al.* in Chennai Hospital in 2013, that showed predominant organism isolated was *Staphylococcus aureus* (41.25 %) followed by *Pseudomonas aeruginosa* (37.5%). Among the *Staphylococcus aureus* , 18 % were *methicillin resistant Staphylococcus aureus* (MRSA)(12).

In the study by Patricia N.Ayson *et al.* conducted in Philippine in 2004 also found that the most common isolated bacteria was *Staphylococcus aureus* (50%) followed by *Pseudomonas aeruginosa* (33.3%) and *Proteus* spp (9.5%). Drug sensitivity pattern on *Staphylococcus aureus* showed that 61.9 % were resistant to penicillin while more than 90 % were sensitive to aminoglycoside, macrolides and quinolones. *Pseudomonas aeruginosa* was resistant to penicillin in 64.3 % of cases and was sensitive to ciprofloxacin in 85.7 %. The increasing trend of penicillin resistant *Staphylococcus aureus* has been a hindrance to empirical treatment, necessitating reassessment of antimicrobials of choice and awakening interest in microbiological monitoring (13).

In a study conducted in Malawi in 1998 showed *Proteus mirabilis* (74%) and *Enterococci* (60 %) as the most frequently isolated microbes(14). Adoga *et al*. found out that the predominant organisms cultured were coliform bacteria with *Klebsiella species* (41.3 %) followed by *Escherichia.coli* (29.3%),*Staphylococcus aureus* (9.3%) and *Pseudomonas aeruginosa* (8%)(15).A few study had revealed fungi particularly *Aspergillus species* and *Candida species* as the predominant fungi. However , Hazama *et al.* found that the majority of CSOM patient with persistent otorrhea was due to bacterial infection (93.5%) and the incidence of fungal infection was only 5.0 %(16).

According to WHO guidelines, CSOM patients will receive a wide spectrum of antibiotic based on an empiric basis. In cases of unresolved ear discharge, possibility of bacterial resistance must be suspected and ear swab for bacterial culture will be performed (1). Previous studies have provided evidence for the resolution of CSOM using topical ear drops alone as the first line of treatment (17). Other studies, however showed an increasing numbers of treatment failures. The widespread use of antibiotics has precipitate the emergence of multiple resistant strains of bacteria which can lead to persistent infections. With the emergence of antibiotic resistance as well as the ototoxicity side effect of certain antibiotics and the potential risk of surgery, there is an urgent need to develop effective therapeutic strategies against CSOM by determining their current antibiotic sensitivity. Treatment of the cases based on antimicrobial sensitivity pattern will help in preventing the further emergence of resistant strains in the community.

In conclusion, various difference of bacteria causing CSOM in different region worldwide emphasize the need to re-evaluate our current bacteriological profile of CSOM and their

sensitivity pattern to locally available antibiotics. This knowledge is essential to guide cost-effective treatment, avoid further recurrent and complications and to provide local data for future references.

Problem Statement and Rationale of Study

In the literature reviews, many studies have been conducted on microbiology of CSOM worldwide and different region showed different result of predominant pathogens. The most common organism involved in CSOM is bacteria either Gram positive or Gram negative bacteria. Generally, *Pseudomonas aeruginosa* is the most common microorganism cultured from ear discharge worldwide (9, 13, 18, 19). On the contrary, other studies found that *Staphylococcus aureus* was the commonest isolated organism which has different sensitivity strains (10, 11, 13). A few studies had revealed rare pathogens such as *Proteus* spp and *Klebsiella* spp as the predominant organisms cultured (14, 15).

Even though , our local study data conducted by Hazama *et al*. in 2012 confirmed bacteria was the predominant organisms cultured from ear discharge compared to fungi but further evaluation on the type of bacterial species commonly isolated was not performed (16). Therefore, it is important to carry out this study in order to determine the possibility of significant changes or differences in bacteriological trend of CSOM in our population. Furthermore, this study can provide our own local data for future reference.

Recently, an irrational use of antibiotic and poor patient's compliance resulting in organism's resistance to the commonly used drug which lead to the failure of treatment. Most of these

bacteria show multidrug resistance and there is a gradual decline in their sensitivity pattern to a number of antibiotics.

Kazeem *et al.* showed that the commonly available antibiotics such as cotrimoxazole and tetracycline were generally ineffective against *Pseudomonas aeruginosa* .The emergence of resistant strains may be due to indiscriminate use of antibiotics. This study also showed that the sensitivity of ofloxacin, gentamicin and ceftazidime towards *Pseudomonas aeruginosa* is gradually dropping comparing the similar study conducted in the same institution about a decade ago, probably because of the widespread self-medication or inappropriate antibiotic treatment (8).

The doubt regarding the possibility of the emergence of bacterial resistance following prolonged use of ototopical medications was also raised in persistent otorrhea supported the need to evaluate back the sensitivity and resistance of the isolated bacteria towards our local available antibiotic. By determining the sensitivity strength of different antibiotic toward the commonest isolated organisms, we can revise our antibiotic regime for CSOM.

Based on result of isolated culture, we could suggest the choices for the narrowest spectrum antibiotic applicable in our setting, significantly assuring the most efficient and cost-effective protocol of treatment.

Therefore, the aims of our study is to identify the common microorganism isolated from patients diagnosed CSOM and to determine the sensitivity and resistance pattern of these isolated microorganism toward commonly used antibiotics. So that, the occurrence of

recurrent and further complications of CSOM can be prevented by initiating an appropriate antibiotic treatment.

Research objectives

General objectives

To describe current bacteriological profile of CSOM and their antibiotic sensitivity pattern.

Specific objectives

1. To describe the microorganism causing CSOM

2. To determine the antibiotic sensitivity pattern toward isolated microorganismcausing CSOM

3. To determine the most sensitive antibiotic against isolated microorganismcausing CSOM

Research questions

1) What is the microorganism causing chronic suppurative otitis media?

2) What is the list of antibiotic that sensitive and resistant towards isolated microorganism?

3) What is the most sensitive antibiotic against isolated microorganism causing CSOM?

Research Study Design

This cross sectional study will be conducted in Otorhinolaryngology Department at Hospital Raja Perempuan Zainab II (HRPZ II) and Hospital Universiti Sains Malaysia (HUSM) Kubang Kerian.

Place of Study

Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan (HUSM) and Hospital Raja Perempuan Zainab II,Kota Bharu,Kelantan (HRPZ II). Both of these are the tertiary hospital in Kelantan.

The Study Population

CSOM patients attending ORL clinic in Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan (HUSM) and Hospital Raja Perempuan Zainab II,Kota Bharu,Kelantan (HRPZ II) will be taken as participant following inclusion and exclusion criteria.

Inclusion and Exclusion Criteria

Inclusion criteria:

All patients diagnosed with CSOM with active ear discharge

Exclusion criteria:

1) Patients with otomycosis

2) Patient with acute otitis externa

3) Patients with ear discharge due to cholesteatoma

4) Patients on antibiotic or antifungal treatment (topical or systemic) within the previous 2 weeks *(Patient must be free of antibiotic or antifungal therapy for duration 14 days to be included in this study. This is to avoid false negative or sterile sample due to antibiotic usage)*

Sample frame

The sample will be obtained from the list of patients who werediagnosed to have CSOM in HRPZ II and HUSM who met the inclusion and exclusion criteria.Patient will be selected by using simple random sampling.

Sampling time frame

Study will be conducted for 10 months duration from 1st June 2018 until 31st March 2019

Sample size estimation

Objective 1

To describe the bacteria causing chronic suppurative otitis media

$$\mathbf{N = \left(\frac{Z\,\alpha}{\Delta}\right)^2 P\,(1\text{-}P)}$$

$Z\alpha = 1.96$

P = 31.5 % (percentage of prevalence *Pseudomonas aeruginosa* as bacteria causing chronic suppurative otitis media) (Kazeem *et al* 2016)

Δ = precision =10%

N = 83

Considering 10% non-response rate= **91 ears of CSOM**

Objective 2

To determine the antibiotic sensitivity pattern toward isolated bacteria causing CSOM

$$\mathbf{N = \left(\frac{Z\,\alpha}{\Delta}\right)^2 P\,(1\text{-}P)}$$

$Z\alpha = 1.96$

P = 78.6 % (Percentage of ofloxacin sensitivity against *Pseudomonas aeruginosa*) (Kazeem *et al*, 2016)

Δ = precision=10%

N = 64.6

Considering 10% non-response rate= **71 ears of CSOM**

Objective 3

To determine the most sensitive antibiotic against isolated bacteria causing CSOM

$$\mathbf{N = \left(\frac{Z\,\alpha}{\Delta}\right)^2 P\,(1-P)}$$

$Z\alpha = 1.96$

P = 93.2% (Percentage of levofloxacin sensitivity as the most effective antibiotic against *Pseudomonas aeruginosa*) (Kazeem *et al*, 2016)

Δ = precision=10%

N = 21.3

Considering 10% non-response rate= **24 ears of CSOM**

Therefore, the selected sample size for this study are 91 ear swabs which is based on objective no 1

Sampling method and subject recruitment

Convenience sampling method will be used. All CSOM patients attending ORL clinic HUSM and HRPZ II will be screened for inclusion and exclusion criteria. Patient with perforated tympanic membrane for duration 3 months and continuous ear discharge within duration of 2