

Literature Review**Efficacy of topical povidone iodine ear drops 5%
in chronic suppurative otitis media****Bambang Suprayogi Resi Utomo, Dyah Sari Kusumawati,
Egon Ilman Saputra, Hervina Restianty Hanny**Department of Otorhinolaryngology-Head and Neck Surgery, Faculty of Medicine,
Universitas Kristen Indonesia, Jakarta**ABSTRACT**

Background: Povidone iodine (PVP-I) is a well-known antiseptic and chemical compound to kill and inhibit the growth of microorganisms. PVP-I 5% antiseptics are expected to have similar or better clinical efficacy compared with topical antibiotics in Chronic Suppurative Otitis Media (CSOM) patients but this is not fully clear. Topical antibiotics in the form of ear drops are often used in CSOM therapy. As there was a raising concern of microbial susceptibility towards antibiotics, and also the price of antibiotic ear drops are fairly expensive, it was essential to find the effectiveness of PVP-I 5% compared with antibiotic ear drops. **Purpose:** To find out the clinical efficacy of povidone iodine 5% in CSOM patients. **Literature review:** Conducted in accordance with the Cochrane Handbook for Systematic Review and Intervention, in adherence with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses. Several databases including Google Scholar, PubMed, Springer Link, and Cochrane were employed. The collected data were then analyzed. **Result:** A total of 407 research articles were included in this analysis obtaining 24 literatures. Final result, only 2 literatures met the inclusion criteria. **Conclusion:** Our analysis revealed that PVP-I 5% had similar efficacy with topical antibiotics, and there were no side effects of treatment. More evidence-based research is needed to determine the effectiveness of topical PVP-I 5% in the treatment of CSOM.

Keywords: chronic suppurative otitis media, povidone iodine, ear drops, efficacy

ABSTRAK

Latar belakang: Povidone iodine (PVP-I) adalah antiseptik yang diketahui dapat membunuh atau menghambat pertumbuhan mikroorganism. Dalam beberapa penelitian PVP-I 5% dinyatakan sebanding atau lebih baik dari antibiotik topikal, namun sebagai obat tetes telinga, untuk tatalaksana otitis media supuratif kronik (OMSK) manfaatnya belum sepenuhnya jelas. Antibiotik topikal dalam bentuk tetes telinga sering digunakan dalam pengobatan OMSK. Adanya masalah perubahan pola kepekaan kuman terhadap antibiotik, serta harga yang cukup mahal, dirasa perlu dilakukan penelitian untuk membandingkan efektivitas tetes telinga PVP-I 5% dengan tetes telinga antibiotik. **Tujuan:** Mengetahui efektivitas PVP-I 5% dalam tatalaksana OMSK. **Tinjauan pustaka:** Dilakukan telaah sistematis dan meta analisis literatur mengenai penggunaan tetes telinga PVP-I 5% dibandingkan dengan antibiotik tetes telinga untuk tatalaksana OMSK memakai database PubMed, Springer Link, Cochrane dan Google Scholar. Data kemudian dianalisis. **Hasil:** Didapatkan 407 artikel penelitian, dan setelah penyaringan tersisa 24 literatur. Hasil akhir penyaringan diperoleh 2 literatur yang memenuhi kriteria inklusi. **Kesimpulan:** Pada kedua literatur tersebut, pemberian topikal PVP-I 5% memberi hasil pengobatan sama baiknya dengan penggunaan tetes telinga antibiotik, serta tidak ditemukan adanya efek samping pengobatan. Dibutuhkan penelitian lebih lanjut untuk mengetahui efektivitas pemberian PVP-I 5% topikal pada pengobatan OMSK.

Kata kunci: otitis media supuratif kronis, povidone iodine, tetes telinga, efektivitas

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INTRODUCTION

Chronic suppurative otitis media (CSOM) is a chronic inflammatory disease of the middle ear with specific symptom of otorrhea with perforated tympanic membrane for more than eight weeks, which could be categorized into continuous or intermittent.^{1,2} The cause of otitis media (OM) is generally viruses or bacteria, and bacteria frequently cause CSOM in children. Methicillin-Resistant Staphylococcus Aureus (MRSA) is the most common microorganism that causes CSOM, and there are also other bacteria like *Pseudomonas aeruginosa*, *Proteus* spp, *Klebsiella* spp, *Bacteroides* spp, and *Fusobacterium*. CSOM caused by microorganisms can be inhibited by topical antiseptics. The use of topical antiseptics could be given alone, or together with other medications such as antibiotic or ear canal cleaner (aural toilet).¹

Intracranial and mastoid infections are common complication of CSOM, especially in developing countries and widely cause hearing loss and disability.² Prevalence of CSOM in developing countries is ranged about 36-200 million people or 60% of the CSOM population in the world, and could decrease hearing function. Based on national health survey *Indra Penglihatan dan Pendengaran* in eight provinces in Indonesia, CSOM morbidity rate was 67%. It could have an impact on the ability to speak, psychosocial and cognitive development in children, including academic ability.^{3,4}

Topical antiseptics are often used in the treatment of CSOM, with the ear washing method to remove earwax. Topical antiseptics kill or stop the growth of the microorganisms that may be responsible for the infection. PVP-I is a very active oxidizing agent

damaging the cellular activity of protein and membranes resulting in the death of bacteria.⁴ Antiseptics could make outer ear skin irritation, discomfort, itching, pain, and can even cause ototoxicity in the inner ear.^{4,5} A case study reported PVP-I 10% generated ototoxicity in the inner ear.⁶ However, several studies with lower concentrations (PVP-I 5%) provided safety in the inner ear and had no toxic effects or other complications.^{7,8}

The main antimicrobial treatment for CSOM is antibiotic ear drops. Topical quinolone (ciprofloxacin) had been proven to be more effective than oral or systemic antibiotics.⁴ The raising problem of changed pattern of microbial susceptibility to antibiotic and high cost of CSOM treatment, had made antiseptic ear drops especially antiseptic PVP-I 5%, provide a good solution to overcome high costs and bacterial resistances.

There had not been many reviews regarding the effectiveness of topical antiseptic, especially PVP-I 5% for CSOM treatment. Therefore, the authors were interested in analyzing the efficacy of PVP-I 5% in CSOM patients.

METHOD

A systematic review was used to assess the efficacy of PVP-I 5% ear drops as a treatment for CSOM, compared with topical antibiotic. Reference for data collection was using Patients, Interventions, Comparison, and Outcome (PICO), which could be seen in Table 1.

Data collection was using electronic media like PubMed, Google Scholar, Cochrane, and Springer Link, using keywords “povidone iodine”, “topical antibiotic”, and “chronic suppurative otitis media”.

There were also inclusion and exclusion criteria. Inclusion criteria: journal efficacy of PVP-I 5% in CSOM treatment; there was a comparison with antibiotic ear drops; and the literature research was a Randomized Controlled Trials (RCT). Exclusion criteria: review article; literature did not have full text and comparison group; did not put patient data

before and after CSOM therapy; and research with animal subjects.

Journal quality review performed using Jadad's criteria for randomized double-blind design (RCTs). Journals with a Jadad's score of 3-5 are categorized as high-quality data. Jadad's criteria are presented in Table. 2

Table 1. PICO study

<i>Patients</i>	:	CSOM patients
<i>Interventions</i>	:	PVI-5% ear drops
<i>Comparison</i>	:	Topical antibiotic (ear drops)
<i>Outcomes</i>	:	Clinical sign and symptom.

Table 2. Jadad's criteria

Journal	Score	
	Yes	No
Randomization	1	0
Double-blind	1	0
Withdrawal and drop-out	1	0
The randomization method is done correctly	1	-1
The blinding method is done correctly	1	-1

Characteristic of study

Table 3. Summary of study characteristics

Journal	Year	Jadad score	<i>n</i>	Improvement	Improvement (%)	Doses
Al.-Abbasi ⁷	2006	4				
PVP-I 5%			16	13	81.2	3 x 3 drops/day for 2 weeks
Neomycin+ dexamethasone			16	11	68.75	
Normal saline			16	4	25	
Jaya <i>et.al</i> ⁸	2003	4				
PVP-I 5%			18	16	88.9	3 x 3 drops/day for 2 weeks
ciprofloxacin 0.3%			21	19	90.4	

RESULT

Study Selection

Study selection used Preferred Reporting Item for Systemic Review and Meta-analyses (PRISMA) guidelines. Literature search engine run by PubMed, Cochrane, Google Scholar, Springer Link databases using the terms of MeSH: “Povidone Iodine” and “Chronic Suppurative Otitis Media”, also known as identifying data. The identification results were followed by screening literature pertaining to the title and removing it in case there was duplication, then followed by reviewing abstract. After the title and abstract had been reviewed, a complete text assessment was then carried out. A complete review of the whole text of literature was undertaken by two persons. Excluded literatures were: that was not written in English, animal research, a chapter in a book, review article and research methods which were not RCTs.

The results of the literature search were 407 articles, 384 were excluded after being reviewed including 26 literature that had a duplication, and based on a review of the titles of 357 irrelevant journals, remained 24 journals. On subsequent review, 19 literatures were excluded because they were not RCT, and animal studies, and 3 literatures were not fully accessible. Screening resulted in 2 literatures and then a review of the entire text was carried out to test eligibility. Literature eligibility test used Jadad Score on both literatures; Al-Abbasi et.al and Jaya et.al were declared feasible with each total score of 4.

Table 3 showed Al-Abbasi⁷ found the percentage of improvement in CSOM patients, using PVP-I 5% after two weeks of treatment was 13/16 (81.2%), slightly higher than combination of Neomycin with Dexamethasone shown 11/16 (68.7%), while normal saline only 4/16 (25%). Jaya et.al,⁸ reported the percentage of improvement in CSOM patients, using PVP-I 5% after two weeks of treatment was 16/18 (88.9%), using

ciprofloxacin 0.3% was 19/21 (90.4%). In both studies, no side effects were found using PVP-I 5%.

DISCUSSION

Chronic Suppurative Otitis Media (CSOM) is an inflammation of the middle ear characterized by persistent or recurrent discharge from the ear with a perforation of the tympanic membrane, for more than two months.^{1,2} CSOM is a multifactorial disease. There are several factors that play a role in the pathogenesis of CSOM such as microbes, immunology, genetic and characteristic of the Eustachian tube.⁹ Persistent suppurative otitis media could lead to damage of the ossicles in the middle ear and resulting conductive hearing loss. The chance of developing a permanent sensory neural hearing loss rises when the inflammatory mediators penetrate the inner ear through the round window.⁴ Particularly in developing country, CSOM is a major contributor to hearing loss. The long-term consequences of this hearing loss, particularly in children, could disrupt the development of speech, language, and social interaction abilities, as well as cognitive development and educational attainment progress.¹⁰ Based on the Indonesian Ministry of Health's National Survey of Sight and Hearing Sense Health, the high prevalence of CSOM, which was 2.1-5.2% in 1994-1996, had attracted special attention of doctors specializing in Ear, Nose, Throat, Head, and Neck Surgery (ORL-HNS).^{11,12} The limited number of available medications, as well as the high cost of treating CSOM in regions with insufficient health services, can potentially undermine Indonesia's goal of reducing hearing loss by 90% by 2030.

Topical quinolone antibiotic is the gold standard for active CSOM treatment. The quinolone group is clinically effective against CSOM and does not cause ototoxicity.^{13,14} However, fluoro-quinolones

such as ciprofloxacin use could lead to bacterial resistance and fungal superinfection. The increasing prevalence of quinolone-resistant bacteria had been reported.^{8,15} The sensitivity of quinolones to germ isolated from CSOM was not high, as reported in a study at a hospital in Jakarta, the sensitivity of quinolone (ciprofloxacin) was only 42%, while the intermediate value was 23.5% and resistant 35.3%.¹⁶ To overcome this situation, it was considered that a solution in dealing with CSOM is necessary. Treatment using povidone iodine has been reported to improve clinical outcomes in patients with CSOM. Povidone iodine is also commonly used as an antiseptic in ENT practice to clean the ear canal in cases of ear infections. PVP levels in ear cases are set at 5%, while levels in other organs vary. Povidone iodine is available throughout Indonesia. The bacterial activity of povidone iodine was still good despite increasing the dilution.⁷ The benefits of povidone iodine to overcome problems in CSOM cases are quite favorable because apart from being an antimicrobial, PVP-I is widely available and relatively inexpensive when compared to quinolone ear drops.

The current literature search is looking for studies by using RCT methods to compare PVP-I cure rates to antibiotics in CSOM treatment procedures. This literature search revealed two studies that matched the search criteria: Al-Abbasi⁷ and Jaya et al.⁸ According to Al-Abbasi⁷, there was an 81.2% good clinical improvement in CSOM by using PVP-I 5% than by using neomycin + dexamethasone by 68.75. There was no laboratory data on bacteria resistance to antibiotics or 5% PVP-I. Jaya et al.⁸ reported that the administration of 5% PVP-I contributed 88.9% clinical improvement in CSOM, which was nearly as good as ciprofloxacin, namely 90.4%. They also presented bacterial resistance to ciprofloxacin but not to PVP-I 5%. The founding of

ciprofloxacin resistance data in Jaya et al.⁸ study raised a problem because it showed an increase in prevalence of quinolone-resistant bacteria, and ciprofloxacin is less effective against anaerobic bacteria. Both studies used audiometric assessment to look for ototoxic effects, and there were none.

Topical antiseptic works to inhibit the growth of microorganisms that causes CSOM. The main mechanism of topical antiseptics is to inhibit the formation of bacterial cell walls which make it able to penetrate directly inside. Antiseptics provide the possibility of low impact resistance.^{14,17} Povidone iodine is a broad-spectrum antiseptic, actively against bacteria, viruses, and protozoa. Povidone iodine works by inhibiting metabolism of bacterial enzymes thereby interfering with the multiplication of bacteria so that they become weak.^{18,19}

There is no adverse effect of PVP-I 5% on hearing function.^{7,8} Reports of ototoxic, such as the finding of Piromichai⁶ who reported the use PVP-I 10% in cases of ear injury are very concerning. Topical antibiotics reach inner ear in several ways, may cross to round window membrane, annular ligament of the stapes, congenital micro or acquired fractures, and may originate from systemic uptake by the middle ear mucosa.^{9,20} In the case reported by Piromchai⁶, it was possible that there was a fracture that was not detected by radiological investigation. Bone damage can be caused by cholesteatoma or malignant type of CSOM, so more evidence is needed regarding the management of all types of CSOM with PVP-I 5%.

In conclusion, the result of PVP-I 5% treatment in CSOM was as good as the use of topical antibiotics, and there were no side effects of treatment. More evidence is needed to determine the effectiveness of topical PVP-I 5% in the treatment of CSOM.

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