

Study of the Effectiveness of Antibiotic Therapy for the Course of Chronic Purulent Otitis

Esamuratov A. I.¹, Mirzaeva M. A.², Shamsiev Zh. F.³

¹Dentistry and ENT Department, Urgench Branch of Tashkent Medical Academy, Urgench, Uzbekistan

²Department of Allergology, Immunology and Microbiology, Tashkent Pediatric Medical Institute, Uzbekistan

³ENT Department, Tashkent Institute of Dentistry, Tashkent, Uzbekistan

Abstract Acute otitis media (AOM) can progress to chronic purulent otitis media (CSOM) associated with perforation of the eardrum and purulent discharge. The effusion prevents the proper transmission of sound vibrations by the bones of the middle ear from the eardrum to the oval window of the inner ear, causing conductive hearing loss. In addition, inflammatory mediators formed in CSOM can penetrate the inner ear through a round window. This can cause loss of hair cells in the cochlea, which leads to sensorineural hearing loss. *Pseudomonas aeruginosa* and *Staphylococcus aureus* are the most common pathogens that cause CSOM. Although the pathogenesis of otitis media is well studied, there are very few studies on CSOM. It is very important to develop effective therapeutic strategies against CSOM due to the emergence of resistance to antibiotics, as well as the potential risk of ototoxicity of antibiotics and potential surgical risk.

Keywords Chronic purulent otitis media, Otorrhea, *Pseudomonas aeruginosa*, Antibiotics, Bacteriophages

1. Introduction

Chronic inflammation of the middle ear, despite significant progress in prevention, diagnosis and treatment, remains one of the most common and dangerous diseases of childhood. This is due to many medical and social causes, as well as to adverse consequences such as hearing loss and the risk of intracranial complications caused by exacerbations of the chronic process in the middle ear. The modern definition of chronic suppurative otitis media (CSOM), summarizing the main features of this disease, was given by V.T. Palchun et al. [1]. CSOM is a chronic suppurative inflammation of the middle ear, occurring with the presence of persistent perforation of the eardrum, constant or periodically recurring pus from the ear and hearing loss of varying degrees, gradually progressing with a prolonged course of the disease [1,2,3]. In addition, to date, CSOM is dangerous as a source of intracranial complications like/such as mastoiditis, meningitis, brain abscess, sinus thrombosis. Changes in the etiological structure and sensitivity of CSOM pathogens in the last decade have had an impact on the nature of inflammation in the middle ear, its severity and the duration of the course of the disease [4,5].

2. Materials and Methods

We examined 84 patients with chronic purulent otitis media who were on inpatient treatment in the ENT department, TMA clinic of the Urgench branch. Division by gender: men 58 (69%), women 26 (30.9%), division by localization of the inflammatory process: epitympanitis - 9 (10.7%), mesotympanitis - 53 (63%), epimesotympanitis - 22 (26.1%) patients. The duration of the disease ranged from 4 to 11 years. All patients underwent a standard examination of the ENT organs, otomicroscopy, endoscopy of the nasal cavity and nasopharynx, magnetic resonance imaging (MRI) of the temporal bones, audiological examination at the time of admission and after 1 month after the treatment. In all patients, upon admission, a microbiological study of purulent discharge from the middle ear was performed, and the contents of the antrum and the tympanic cavity were taken during sanitizing surgery on the ear. Microbiological methods included the study of the species composition of microflora from the ear on solid nutrient media; after species identification of the isolated microflora, its sensitivity to antibiotics of various groups was investigated by diffusion into agar with standard indicator discs. Microaerophilic conditions using 10% CO₂ were created for the cultivation of streptococci and *Haemophilus influenzae* cultures. Smears on the flora were also taken from the mucous membrane of the nasal cavity and nasopharynx to determine how its nature changes after treatment.

3. Results and Discussion

Treatment was carried out in accordance with the standards of specialized medical care: antibiotic therapy, catheterization of the auditory tubes (in the case of preperforative otitis media), transtympanic injection of antibacterial drugs (in case of perforation of the eardrum or after paracentesis), vascular therapy (in the case of concomitant sensorineural hearing loss). In 20% of cases, bypass surgery of the tympanic cavity was performed on one or two sides. The first step studied the effectiveness of ototope antibiotics, caplions with an antibiotic in combination with ear hygiene procedures are the basis of CSOM therapy and, as shown in randomized controlled trials, are the most effective. Quinolones are the most commonly used topical antibiotics in Uzbekistan due to their established effectiveness. Topical quinolones have a low side effect profile and are superior to aminoglycosides. Quinolones are especially effective against *P. aeruginosa* and do not have the potential side effects of cochleotoxicity and vestibulotoxicity, which are attributed to aminoglycosides. Couzens *et al.*, 2003 showed that ciprofloxacin is more effective than aminoglycosides, and also showed the effectiveness of the topical antibiotic ofloxacin compared to oral administration of amoxicillin and clavulanic acid in the treatment of otorrhea [6].

Corticosteroids are sometimes used in combination with quinolones for CSOM, but they are not well understood. Combined ear drops can be prescribed for inflammation of the mucous membrane of the external auditory canal or middle ear, as well as in the presence of granulation tissue. Dexamethasone is often used in combination with ciprofloxacin in these conditions. There are several alternative solutions for topical use that can be used in conditions where antibiotic drops are not available. They are used in clinics but are much more common in resource-limited settings due to their low cost and availability. Some of these include acetic acid, aluminium acetate (Barrow solution) or combinations thereof (Domboro solution) and iodine-based antiseptic solutions. Several studies are comparing these solutions with orthotopic quinolones. However, one retrospective study found that aluminium acetate solution was as effective as gentamicin in treating otorrhea [7]. In addition, 57% of patients in another study resolved otorrhea after washing the affected ear with acetic acid three times a week for 3 weeks in the absence of any other therapy [8]. Aluminium acetate could potentially be even more effective than acetic acid due to its increased activity against many pathogens *in vitro* [9,10]. An antiseptic solution based on povidone-iodine has a wide spectrum of action against many microorganisms that can colonize the middle ear - bacteria, viruses, fungi and protozoa. One randomized controlled trial found that povidone-iodine has the same efficacy as ciprofloxacin droplets in treating otorrhea. In addition, it was shown that the resistance of bacteria to iodine solution was much lower than to ciprofloxacin [11]. Further large-scale studies are needed to

confirm the safety and efficacy of these topical agents in CSOM. The next stage was the study of the effectiveness of systemic antibiotics and the analysis of the literature on this topic. If the main treatment of otorrhea is ineffective after 3 weeks of therapy, alternative measures should be considered. Oral antibiotics are the second-line therapy for CSOM. Systemic therapy was not as effective as direct local delivery of antibiotics due to the impossibility of achieving effective concentrations in infected middle ear tissues. The effectiveness of the drug is influenced by many factors, including bioavailability, body resistance, scarring of middle ear tissues and reduced vascularization of the mucous membrane of the middle ear in chronic diseases. Topical medications, such as quinolones, are the drugs of choice for second-line therapy. However, they should be used with caution in children because of possible growth problems associated with tendons and joints and should be used for organisms that are otherwise resistant to other treatments, or when there is no safe alternative. Amoxicillin/clavulanic acid (Augmentin) or erythromycin/sulfafurazole are other antibiotics that are recommended for children. Intravenous antibiotics have been shown to be effective against CSOM but are not a first-line treatment option for several reasons. Because of the risk of systemic side effects and the increased likelihood of developing antibiotic resistance, intravenous antibiotics should be used as the last line of treatment for patients with CSOM. When possible, antibiotics should be directed to seeding, and you should seek the advice of an infectious disease specialist. Since the most common microorganisms are *P. aeruginosa* and methicillin-resistant *S. aureus* (MRSA), penicillin-based antibiotics and macrolides have very limited efficacy because microorganism resistance rates are high. The most effective antibiotics for *P. aeruginosa* and MRSA are quinolones, such as ciprofloxacin, and a combination of vancomycin and trimethoprim-sulfamethoxazole (Bactrim), respectively. Other common antibiotics that can be used against *Pseudomonas* spp. include imipenem and aztreonam. In one study, *P. aeruginosa* isolates resistant to ciprofloxacin also demonstrated high resistance to aminoglycosides, piperacillin-tazobactam, and ceftazidime (Jang & Park, 2004), making these drugs less than ideal candidates for intravenous therapy. Despite being active against the most common infectious agents, intravenous antibiotics are certainly not a panacea for CSOM. The cure rate of patients receiving intravenous vancomycin culture-directed action in MRSA CSOM was similar to that of patients receiving an ear toilet and topical solutions of acetic acid and aluminium acetate [12,13]. This further demonstrates the concept that ototoxic treatment in combination with aggressive ear sanitation is the preferred primary therapeutic method for CSOM. Systemic antibiotics should be used for varying degrees of the ineffectiveness of primary treatment or for the development of intracranial complications [1-18].

Surgical treatment should be considered as a last resort after maximum drug therapy has been exhausted in cases of HHSO (expand), especially persistent or recurrent ones.

Surgical intervention in the form of tympanomastoidectomy is also indicated in cases of CSOM in which there are complications, some of which can be potentially life-threatening, such as significant hearing loss, facial nerve paralysis, subperiosteal abscess, petrositis, dural venous sinus thrombosis, meningitis, cerebral abscess and labyrinth fistula, among others. Chronic cholesteatoma CO requires surgery, usually in the form of a tympanomastoidectomy, to eliminate cholesteatoma, which is usually the main cause of chronic infection.

Tympanoplasty can be performed 6-12 months after the infection is eliminated. A large percentage of perforations heal on their own after the infection resolves, but in cases where this does not occur, tympanoplasty is indicated to improve hearing and prevent recurrence of the infection by closing the middle ear space. In addition, patients should take precautions for the dry ear to reduce the incidence of recurrent infections and otorrhea.

4. Conclusions

Bacteriophages may be a viable treatment option for bacterial infections due to the emergence of multi-resistant strains. Bacteriophages are viruses that specifically and uniquely destroy bacteria. Bacteriophages are considered safe, economical, self-replicating and effective bactericidal agents. In addition, research is needed to characterize the interaction of the middle and inner ear during the pathogenesis of CSOM. This is especially true of the role of inflammatory mediators, which appear to be able to cross the membrane of a round window and cause potentially irreversible hearing loss due to damage to auditory hair cells. The identification of genetic and prognostic markers will help in predicting individuals susceptible to CSOM and possibly even in new therapeutic strategies. Understanding the molecular mechanisms leading to CSOM will provide opportunities to develop new treatments for the disease and subsequent hearing loss.

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REFERENCES

- [1] Gydé, M.C., 1981. A double-blind comparative study of trimethoprim-polymyxin B versus trimethoprim-sulfacetamide-polymyxin B otic solutions in the treatment of otorrhea. *The Journal of Laryngology & Otology*, 95(3), pp.251-259.
- [2] Gyde, M.C., 1981, January. Double-blind comparative trial of trimethoprim-polymyxin B and trimethoprim-sulphacetamide-polymyxin B ear drops in the treatment of otorrhea (author's transl). In *Annales D'oto-laryngologie et de Chirurgie Cervico Faciale: Bulletin de la Societe D'oto-laryngologie des Hopitaux de Paris* (Vol. 98, No. 1-2, pp. 37-40).
- [3] Milo, M., Brodsky, A., Ben-David, J., Srugo, I., Larboni, J. and Podoshin, L., 1997. Chronic otitis media treated topically with ciprofloxacin or tobramycin. *Archives of Otolaryngology-Head & Neck Surgery*, 123(10), pp.1057-1060.
- [4] Tong, M.C., Yue, V., Ku, P.K. and van Hasselt, C.A., 2002. Preoperative topical ofloxacin solution for tympanoplasty: a randomized, controlled study. *Otology & neurotology*, 23(1), pp.18-20.
- [5] Tong, M.C., Yue, V., Ku, P.K. and van Hasselt, C.A., 2002. Preoperative topical ofloxacin solution for tympanoplasty: a randomized, controlled study. *Otology & neurotology*, 23(1), pp.18-20.
- [6] Marais, J. and Rutka, J.A., 1998. Ototoxicity and topical eardrops. *Clinical Otolaryngology & Allied Sciences*, 23(4), pp.360-367.
- [7] Acuin, J., 2007. Chronic suppurative otitis media. *BMJ clinical evidence*, 2007. 553-555.
- [8] Aminifarshidmehr, N., 1996. The management of chronic suppurative otitis media with acid media solution. *The American journal of otology*, 17(1), pp.24-25.
- [9] Longridge, N.S., 1994. Topical gentamicin vestibular toxicity. *The Journal of Otolaryngology*, 23(6), pp.444-446.
- [10] Matz, G., Rybak, L., Roland, P.S., Hannley, M., Friedman, R., Manolidis, S., Stewart, M.G., Weber, P. and Owens, F., 2004. Ototoxicity of ototopical antibiotic drops in humans. *Otolaryngology-Head and Neck Surgery*, 130(3_suppl), pp.S79-S82.
- [11] Jaya, C., Job, A., Mathai, E. and Antonisamy, B., 2003. Evaluation of topical povidone-iodine in chronic suppurative otitis media. *Archives of Otolaryngology-Head & Neck Surgery*, 129(10), pp.1098-1100.
- [12] Choi, H.G., Park, K.H., Park, S.N., Jun, B.C., Lee, D.H. and Yeo, S.W., 2010. The appropriate medical management of methicillin-resistant *Staphylococcus aureus* in chronic suppurative otitis media. *Acta oto-laryngologica*, 130(1), pp.42-46.
- [13] Bhat, K.V., Naseeruddin, K., Nagalotimath, U.S., Kumar, P.R. and Hegde, J.S., 2009. Cortical mastoidectomy in quiescent, tubotympanic, chronic otitis media: is it routinely necessary?. *The Journal of Laryngology & Otology*, 123(4), pp.383-390.
- [14] Colletti, V., Fiorino, F.G. and Indelicato, T., 1991. Surgery vs. natural course of chronic otitis media: long-term hearing evaluation. *Acta oto-laryngologica*, 111(4), pp.762-768.
- [15] Brennan-Jones, C.G., Head, K., Chong, L.Y., Burton, M.J., Schilder, A.G. and Bhutta, M.F., 2020. Topical antibiotics for chronic suppurative otitis media. *Cochrane database of systematic reviews*, (1).
- [16] Shashikala, B.S., Deepthi, P. and Viswanatha, B., 2018. Fungal Flora in Chronic Suppurative Otitis Media: A Prospective Study in a Tertiary Care Hospital. *Research in*

Otolaryngology, 7(1), pp.5-8.

[17] Balan, S. and Viswanatha, B., 2017. Microbiology of chronic suppurative otitis media: a prospective study in a tertiary care hospital. *J Otolaryngol ENT Res*, 9(1), p.00277.

[18] Khomtchouk, K.M., Kouhi, A., Xia, A., Bekale, L.A., Massa, S.M., Sweere, J.M., Pletzer, D., Hancock, R.E., Bollyky, P.L. and Santa Maria, P.L., 2020. A novel mouse model of chronic suppurative otitis media and its use in preclinical antibiotic evaluation. *Science advances*, 6(33), p.eabc1828.

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