



Otitis Media - A Review through its Continuum through Years and Various Treatment Options

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ABSTRACT

Otitis media or ear infection is one of the most common infections, especially in infants and children below 10 years of age. Due to the self-limiting nature of this infection, this is neglected from medical care in most of the case, as a result of which recurrences and complications arise. Complications may be mild like tinnitis or severe like otorrea. Otitis media may result from infection by many different species of bacteria, fungi and viruses. Among the bacterial agents, the biofilm forming ability combined with the rise of multiple drug resistance has made otitis media an issue to be considered seriously. Besides the conventional antibiotic therapy, there are many other alternative treatment options for this infection and a number of herbal remedies are also being used. However in spite of such vast number of treatment options, otitis media has not been curbed till now nor has its prevention been completely possible. Hence it is time to take this issue to the next level of focus and put in a little more effort to make complete prevention and cure of otitis media possible.

Keywords: Otitis media, bacteria, biofilm, multiple drug resistance, treatment.

INTRODUCTION

Otitis media (OM), commonly described as ear infection has been inflicting human population from ancient times and continues to do so despite the advancements achieved in the medical field. One of the main reasons behind this is ignorance. Since most cases of OM resolves on its own within 7-14 days, most of the patients consider it not worthy of medical supervision. Failure to seek medical assistance leads to recurrent episodes of the infection, which ultimately results in complications like Mastoiditis (a rare inflammation of a bone adjacent to the ear), hearing loss, perforation of the tympanic membrane, facial nerve paralysis and possibly Maniere's disease (disease affecting balance and hearing) in adults. This infection is especially predominant in infants, most of who tend to have recurrent episodes every year.

Commonly OM can be classified into four types namely, Chronic Supportive Otitis Media (CSOM), Acute Otitis Media (AOM), Otitis Media with effusion (OME) and Adhesive Otitis Media. AOM implies the rapid onset of the disease with symptoms such as Otagia, Otorhea, Headache, Fever, Loss of appetite, vomiting while OME has symptoms like hearing loss, Tinnitus, Vertigo and Otagia. Chronic Supportive OM is a persistent ear infection that results in tearing or perforation of the ear drum and adhesive OM occurs when a thin retracted ear drum becomes sucked into the middle ear space and gets stuck.

The common cause of OM is attributed to the dysfunction of the Eustachian tube, which in turn is due to the inflammation of the mucous membrane in the nasopharynx, which may be due to viral upper respiratory

tract infection, Strep throat etc. Due to this dysfunction, the gas volume in the middle ear is trapped and parts of it is slowly absorbed by the surrounding tissues, leading to negative pressure in the middle ear, causing fluid from surrounding tissues to get sucked into the middle ear cavity, which then gets infected by bacteria.

Microbiology of Om

Bacteria are the most common causative agents of otitis media even though many reports of viral ear infections have been reported. One of the major routes for the entry of microorganisms into the ear is from the nasopharynx. The microbial agents causing respiratory tract infections enter the Eustachian tube and leads to the infection. Otitis media can be caused by different bacteria and the incidences vary based on the geological locations. Out of these, mainly in India, majorly two pathogens has been found to be the major causative agents, one being *Staphylococcus aureus* and the other *Pseudomonas aeruginosa*. In many studies the ratios of these two pathogens were nearly the same with *Staphylococcus aureus* being predominant in some cases^{1, 2} and *Pseudomonas aeruginosa* being more dominating in others^{3, 4}. In other countries such as America and Australia, the predominant bacterial species are *Haemophilus influenza*, *Moraxella catarrhalis* and *Streptococcus pneumonia*^{5, 6}.

Viral otitis media is mainly the result of viruses infecting the upper respiratory tract and hence most of the viral otitis media are seen in those with recurrent respiratory infections, especially in infants⁷. Rhinoviruses are the major class of respiratory viruses responsible for otitis media and there are recent studies suggesting that along with rhinoviruses, entero viruses also acts as causative



agents⁸. Studies on viral otitis media also reveal that age is a major factor for the infection. Infants are the most susceptible population and the majority of infants infected had Upper Respiratory Tract Infections (URI) mainly caused by adenoviruses, RSV and influenza viruses. Also adenoviruses have been detected to be involved in the majority of cases as compared to others. Therefore, prevention of viral URI would be the best way to reduce OM⁹. However, as to the question regarding the connection of a particular virus to higher incidences of OM, there seems to be no conclusive result. This variation in the results may be due to the difference in the techniques followed. Those studies done using viral assay says that highest cases of Acute Otitis Media (AOM) is caused by adenoviruses, RSV and Influenza viruses while rhinoviruses have the lowest connection¹⁰. But those studies done using RT-PCR yielded results that says rhinoviruses are the most common causes of AOM with the rates of adenoviruses and corona viruses causing the infection, being significantly low¹¹. This was in accordance with the results obtained by PCR studies as well which points to rhinoviruses as being the major causative agent of AOM¹².

Apart from viruses, fungal agents have also been found to be responsible for ear infections. *Candida albicans* and *Aspergillus niger* were found to be the most common species with the latter being found mostly in adults¹³. The fungal ear infections are attributed to the use of steroid medications for bacterial otitis media treatment¹⁴ and another reason may be the increased use and overuse of antibacterial medications¹⁵. In case of those patients who have undergone antibiotic treatment, the most commonly found fungus were *Aspergillus niger* and *Penicillium* sp while the former has been found to be the major causative agent of otomycosis¹⁶.

Biofilm Formation

Biofilms are an aggregation of bacteria encased within an extracellular polysaccharide matrix, which provides them better protection against adverse external conditions and also help them better defend themselves against antibacterial agents. The formation of biofilms by the otitis media bacteria is the reason for the recurrence of such infections¹⁷ and this also yields such infection highly resistant to antibiotic treatments. *Staphylococcus aureus* and *Pseudomonas aeruginosa* are the most common pathogens which produce biofilms in the middle ear mucosa in the case of Chronic Supportive Otitis Media (CSOM).

The detection of biofilm formation is mainly done by three methods: Congo red agar (CRA) method, Tube method (TM) and Tissue culture plate (TCP) method. In Congo red plate method, the biofilm forming bacteria produce black colored colonies while others give pink colonies. However, the credibility of the technique has been questioned by various researchers over time¹⁸. Especially in the case of *Staphylococcus sp.*, the recent finding that PIA/PNAG has little part in its biofilm

formation shows that this method may not be much effective in detecting all biofilm forming *Staphylococcus sps.*¹⁹ In tube method, the biofilm formation is checked by growing the isolated bacteria in medium such as Trypticase Soy broth or Brain Heart Infusion broth supplemented with glucose or sucrose. After incubation for 24- 48 hours, these tubes are stained for checking the strength of biofilm formed, which is seen as a thin film covering the bottom and inner walls of the tube. This method detects biofilm formers much effectively than CRA method and is considered more reliable.

The Tissue Culture Plate method uses microtitre plates to detect biofilm formers by a methodology similar to the Tube method. However, after staining, the biofilm formation is read using microtitreplate reader, by measuring the OD value, which is the reason why out of these three methods, TCP is regarded as the most reliable. This method detects biofilm producers more effectively and with more accuracy as here, a strength of biofilm can be estimated based on OD values that by manual observation alone²⁰.

Multiple Drug Resistance

As is the case of various other infections, in otitis media as well, multiple drug resistant organisms are now being observed. The ability to resist multiple drugs makes the pathogen even more effective in causing infections and makes the treatment less effective. There have been many cases of antibiotic resistance arising against otitis media patients, especially since the recent decade. *Pseudomonas aeruginosa*, which is one of the most common pathogens causing otitis media, has been showing resistance against ciprofloxacin, which is one of the most effective drugs used²¹. Another major causative agent of otitis media, especially in India is *Staphylococcus aureus* and the resistance shown by this organism to major antibiotics, leading to its evolution to Methicillin Resistant *Staphylococcus aureus* (MRSA) has been a major threat to the health care industry for the last two decades²². MRSA has been a major cause of various skin and wound infections since and the same applies to those causing otitis media as well. Some otitis media isolates has been found to be resistant to major antibiotics like amoxicillin sodium–clavulanate potassium, cefpodoxime proxetil, levofloxacin, erythromycin and cefprozil and to fluoroquinolone ear drops (ofloxacin, ciprofloxacin) as well²³. There has been a drastic increase in the percentage of MRSA in otitis media in the last decade²⁴.

Anti biogram

Antibiotic therapy is the treatment of choice for otitis media, once diagnosed but even then the chances of recurrence is not ignorable. Antibiotic therapy is decided based on the bacterial species isolated and its sensitivity to the commercial antibiotics tested against it by Kirby Bauer method²⁵. This treatment option highlights the necessity for antibiogram to be done for the otitis media isolates.



Pseudomonas aeruginosa was found to be sensitive to Amikacin followed by imipenem and piperacillin plus tazobactam, while *Staphylococcus aureus* showed maximum sensitivity to vancomycin²⁶. Another study has found that *Pseudomonas aeruginosa* was highly sensitive to cefotaxime, azithromycin and gentamicin and *Staphylococcus aureus* to Cefotaxime, Azithromycin, Amoxicillin, Clavulanic Acid and Gentamicin²⁷. Yet again, another study, *Pseudomonas aeruginosa* showed high sensitivity to Meronem, Piperacillin-Tazobactam and Ceftazidim and *Staphylococcus aureus* was highly resisted by Vancomycin, Piperacillin- Tazobactam and Amikacin²⁸. Cefoperazone, cefpirome and once again, Piperacillin-Tazobactam were the most effective drugs against *Pseudomonas aeruginosa* and against *Staphylococcus aureus*, again Vancomycin was the lead drug of choice followed by Linezolid and Teicoplanin as per another study²⁹.

Herbal Remedies

Herbs have been a part of our traditional medicine and have been utilized for the treatment of all types of ailments from time immemorial. In earlier days, herbal medicine was the only treatment option available and especially with respect to otitis media, herbal remedies had gone a long way in curing this ailment. Mango leaves has been used for the treatment. Of ear infections since olden times and current research has proven that mango (*Mangifera indica*) leaves does possess antibacterial activity against various pathogens³⁰.

Garlic and garlic oil were used at homes for treating ear infections and this has been scientifically studied and results confirmed their antibacterial activity against gram positive bacteria such as *S. aureus*, *B. cereus* and *S. pneumoniae* and gram negative bacteria like *P. aeruginosa*, *E. coli* and *K. pneumoniae*^{31, 32}. The latter study also proves that garlic possesses anti biofilm activity as well against the six pathogens tested. The antifungal activity of garlic against *Aspergillus* sp. and *Candida* sp.³³ has been investigated and found effective. Another study highlights the activity of *Sempervivum tectorum* against otitis media caused by *Pseudomonas aeruginosa*³⁴. Other herbal remedies used were tea tree oil, onion etc.

However as compared to herbal studies against various other infections, it can be noted that research on finding herbal medications against otitis media pathogens has received only very little attention and this may be due to the self limiting nature of the disease and due to the lack of understanding of its serious complications.

Complementary Medicines

The name complementary medicine refers to those treatments not listed under the conventional medicines and which may or may not include oral medications as such. Homeopathy, acupuncture, hypnosis and spiritual healing are some of the treatment options that come under this category. Complementary medicine has been present parallel to the allopathic medicines and continues

to do so, even replacing allopathic medicines in case of certain serious ailments. The lack of evidence as to their complete effectiveness prevents them from being scientifically accepted as a real method of treatment. Of the various alternative medicines, Homeopathy ranks first in acceptance. It has been taken as a major field of medicine due to its effectiveness and lack of side effects, by majority of the people. Homeopathy uses herbal extracts and certain chemical compounds mixed in various proportions for the treatment. Belladonna, Aconite, Pulsatilla, Ferrum phosphaticum, Chamomilla, Capsicum, Mercurius etc. are the major constituents used as otitis media remedy. However the number of studies on otitis media treatment is very small as there are, as such no pinpoint medications for the infection. The medications given are based on the symptoms of the disease in the patients. Besides, the use of some of the constituents in homeopathic treatments may not be completely accepted which keeps this field out of being a conventional treatment.

Probiotics are mainly bacteria like *Lactobacillus plantarum*, *Streptococcus salivarius* which are generally provided as dietary supplements, which boost the immunity of the patients, thereby improving the ability to resist infections. There are a fair number of reports which says that probiotic bacteria possess the ability to prevent otitis media. *Streptococcus salivarius* has been found to prevent otitis media caused by *Streptococcus pyogenes*³⁵. Also regular oral administrations of *Streptococcus salivarius* may contribute in reducing the incidences of the infection³⁶. However the effectiveness of using probiotics is limited and there are researches which says that probiotics does not decrease the incidences of otitis media³⁷ and some other studies, although has obtained positive results in the regard, fail to conclude a positive result due to the lack of confirmative studies³⁸.

Xylitol is a 5-carbon sugar alcohol, which is naturally found in low concentrations in the fibers of fruits and vegetables. There have been many studies in the past mainly, which says that xylitol has the ability to cure as well as prevent the recurrence of otitis media in children. The use of xylitol syrups or even xylitol chewing gums was found to help prevent acute otitis media^{39, 40}. On the other hand, there are some researchers who does not accept this and their work has proved that xylitol administration does not significantly reduce occurrence of otitis media in children⁴¹.

Acupuncture is one of the alternative treatment options, where needles are inserted into the body, at certain pressure points. This is a part of the Chinese traditional medicine and has spread now to various other countries. Basically used for pain relief, this is now being used to treat various other ailments as well. For the treatment of otitis media using acupuncture, needles are inserted into four pressure points on the ear surface, which is said to clear the built up of fluid⁴². However articles describing



the use of acupuncture for otitis media is rare, which makes it difficult to be confident about this form of alternative medicine.

CONCLUSION

A glance through the various aspects of otitis media shows us that the main reason for its continuum through years is due to our ignorance coupled with the modern evolution of the pathogens in resisting drugs and successfully forming biofilms. Besides the antibiotic treatment, a variety of other alternative and complimentary therapies are available, which should be taken into account so that this ailment may be curbed once and for all.

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