Editorial

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Fight Against Pneumococcal Pneumonia: An Overview

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Editorial

Community acquired pneumonia (CAP) is a major public health problem worldwide. Pneumonia is an acute respiratory infection of lungs affecting people of all ages, especially the young children, immunocompromised individuals and elderly. In pneumonia, the alveoli become inflamed and fluid filled resulting in chest pain and limited oxygen intake. Pneumonia spread from person to person through contact with respiratory secretions like saliva and mucus. According to a WHO report, pneumonia is the single biggest cause of children's death worldwide. In 2015 it killed 920136 children less than 5 years of age which accounts to 16% of total deaths of children under 5 years old [http://www.who.int/mediacentre/factsheets/fs331/en/]. Pneumonia is widespread in South Asia and sub-Saharan Arica though it affects children and families worldwide. Pneumonia can be caused by a number of pathogens like bacteria, viruses and fungi.

The most common cause of bacterial pneumonia is *Streptococcus pneumoniae* (Pneumococcus). Besides pneumonia, it causes bronchitis, sinusitis, otitis media, septicemia and meningitis. It is a gram positive non-motile bacterium with more than 90 known serotypes, and each produces a unique polysaccharide capsule that protects the bacterium against host immune effectors [1]. It is an opportunistic pathogen usually inhabiting the human respiratory tract and causing serious infections in people with weak immunity. Pneumococcal pneumonia is the most common pneumococcal infection in adults. An estimated 900,000 adults in USA get pneumococcal pneumonia every year and approximately 5-7% succumbs to it [2].

Antimicrobial resistance among *Streptococcus pneumoniae* has soared dramatically over the past three decades owing to overuse or misuse of antibiotics and dissemination of few clones carrying resistance-determining genes [3]. Ever since the discovery of penicillin in 1940, it has been the drug of choice for treating pneumococcal infections. The first report of penicillin resistant clinical strain of *S. pneumoniae* was described in 1967 from a patient in Papua New Guinea [4]. Since then resistance against other antibiotic classes like macrolides, tetracyclines, fluoroquinolones, chloramphenicol's and trimethoprim-sulfamethoxazole's (TMP-SMX) have been subsequently reported [5]. The resistance against penicillins occurs as a result of genetic structural change in penicillin binding proteins reducing their affinity for the antibiotic molecules. Resistance in many clinical isolates of *S. pneumoniae* is due to changes in three main PBPs namely PBP2x, PBP2b and PBP1a [6,7]. Resistance to macrolides in pneumococcus arises due to the modification of target site in 23S rRNA encoded by gene erm(B), or efflux of antibiotic through an efflux pump encoded by mef(A) [8]. Around 20-40% of *S. pneumoniae* population is found resistant to macrolides [9]. The resistance against fluoroquinolones is low but steadily increasing accounting to acquisition of plasmid encoded genes, alterations in topoisomerases and efflux of antibiotic. As in fluoroquinolones, development of resistance in TMP-SMX is also attributed to mutations in bacterial genome. The prevalence of TMP-SMX resistance in *S. pneumoniae* is around 35% [9]. The rise of antimicrobial resistance in these pathogens is responsible for placing a substantial clinical and financial burden on the health care systems, patients, and their families.

To overcome the problem of antibiotic resistance, sensible use of present antibiotics and introduction of new antibiotics have become absolutely imperative. Many researches are being carried out around the world in search of novel ways to combat antimicrobial resistance in *S. pneumoniae*, some of which are mentioned here.

Solithromycin- A new fluoroketolide Solithromycin is a next generation macrolide showing potent *in vitro* activity against pneumococci including macrolide resistant strains. Like its predecessor telithromycin, solithromycin works by affecting 50S ribosomal subunit functioning but it has several structural modifications which helps it to escape macrolide resistance mechanism of bacteria [10]. Solithromycin has demonstrated strong *in vitro* activity against macrolide-, penicillin and fluoroquinolone-resistant isolates of *S. pneumoniae* [11]. It has proved effective and safe in phase II/III clinical trials in comparison

to fluoroquinolones and moxifloxacin for treatment of community acquired bacterial pneumonia. In addition to this it has shown low hepatotoxicity and lower affinity to nicotinic receptors unlike telithromycin. Current data presents solithromycin as a promising drug for treatment of CAP in adults nevertheless its safety has yet to be confirmed in larger populations [10,12].

Ceftaroline-ceftaroline is a newer generation cephalosporin recently approved by US Food and Drug Administration for treatment of CAP in children aged ≥ 2 months [13]. Like β-lactam antibiotics, ceftaroline interacts covalently with the PBPs to inhibit the bacterial cell wall synthesis. This binding in case of ceftaroline with PBP2b, PBP2x and PBP1a is found to be stronger than that of other cephalosporin group members [14]. Different independent clinical studies carried out in US to assess the efficacy of ceftaroline have found it to provide coverage against penicillin-resistant *S. pneumoniae*. Ceftaroline exhibited potent *in vitro* activity against ceftriaxone-non susceptible clinical isolates of *S. pneumoniae* causing CAP in children [15,16].

Zabofloxacin & Nemonofloxacin- Two novel members of class fluoroquinolone, zabofloxacin and nemonoxacin have been tested for their efficacy against clinically relevant gram-positive bacteria in the recent years. Results from the published data indicated potent *in vitro* and *in vivo* activity of zabofloxacin and nemonoxacin as compared to other quinolones against pathogens causing CAP [17,18]. Zabofloxacin showed better efficacy against strains resistant to levofloxacin but its activity was similar to that of gemifloxacin [17]. In clinical trials nemonoxacin was found to have similar efficacy as of levofloxacin for the treatment of CAP and good tolerance in patients [19]. The effect of these antibiotics however needs to be tested on larger populations for any adverse events nevertheless both zabofloxacin and nemonofloxacin appear promising new drug candidates.

Tigecycline- Tigecycline is the first glycylcycline of tetracycline antibiotic class. It has been used for treatment of complex skin, intraabdominal and soft tissue infections but its use can be extended to treat CAP. Studies have shown that efficacy of tigecycline was better than that of levofloxacin in treating CAP and that it was well tolerated in patients as well. Tigecycline can well provide an antibiotic option to treat mild to moderate CAP [20,21].

Development of resistance in *Streptococcus pneumoniae* is at a much greater pace than the development of new antibiotics. In addition to developing new antibacterial, coordinated efforts in minimizing the risk of spread of resistant pathogens and prevention from the disease through immunization are the pressing needs of the hour. It is important to raise awareness regarding pneumococcal vaccine which can prevent pneumococcal pneumonia and other pneumococcal infections especially in children and adults 65 years or older. Pneumonia is a global health issue and concerted efforts are required from government, health professionals and researchers so that no more lives are lost to it.

References

1 Weinberger DM, Harboe ZB, Sanders EAM, Ndiritu M, Klugman KP, et al. (2010) Association of serotype with risk of death due to pneumococcal pneumonia: a meta-analysis. Clin Infect Dis 51: 692-699.

2 Hamborsky J, Kroger A, Wolfe S (2015) Centers for Disease Control and Prevention. Epidemiology and prevention of vaccine-preventable diseases, 13th Edn, Washington DC: Public Health Foundation.

3 Lynch JP, Zhanel GG (2010) Streptococcus pneumoniae: epidemiology and risk factors, evolution of antimicrobial resistance, and impact of vaccines. Curr Opin in Pulm Med 16: 217-225.

4 Hansman D, Glasgow H, Sturt J, Devitt L, Douglas R (1971) Increased resistance to penicillin of pneumococci isolated from man. N Engl J Med 284: 175-177.

5 Charpentier E, Tuomanen E (2000) Mechanisms of antibiotic resistance and tolerance in streptococcus pneumonia. Microbes Infect 2: 1855-1864.

6 Hakenbeck R (1998) Mosaic genes and their role in penicillin resistant streptococcus pneumonia. Electrophoresis 19: 597-601.

7 Grebe T, Hakenbeck Rb (1996) Penicillin-binding proteins 2b and 2x of streptococcus pneumoniae are primary resistance determinants for different classes of beta-lactam antibiotics. Antimicrob Agents Chemother 40: 829-834.

8 Canu A, Malbruny B, Coquemont M, Davies TA, Applebaum PC, et al. (2002) Diversity of ribosomal mutations conferring resistance to macrolides, clindamycin, streptogramin and telithromycin in streptococcus pneumoniae. Antimicrob Agents Chemother 46: 125-131.

9 Cherazard R, Epstein M, Doan TL, Salim T, Bharti S, et al. (2017) Antimicrobial resistant streptococcus pneumoniae: prevalence, mechanisms, and clinical Implications. Am J Ther 24: e361-e369.

10 Van Bambeke F, Tulkens PM (2016) The role of solithromycin in the management of bacterial community-acquired pneumonia. Expert Rev Anti Infect Ther 14: 311-324.

11 Zhanel GG, Hartel E, Adam H, Zelenitsky S, Zhanel MA, et al. (2016) Solithromycin: a novel fluoroketolide for the treatment of community-acquired bacterial pneumonia. Drugs 76: 1737-1757.

12 Viasus D, Ramos O, Ramos L, Simonetti AF, Carratalà J (2017) Solithromycin for the treatment of community-acquired bacterial pneumonia. Expert Rev Respir Med 11: 5-12.

13 Pfaller MA, Mendes RE, Castanheira M, Flamm RK, Jones RN, et al. (2017) Ceftaroline activity tested against bacterial isolates causing community-acquired respiratory tract infections and skin and skin structure infections in pediatric patients from united states hospitals: 2012-2014. Pediatr Infect J Dis 36: 486-491.

14 Kosowska-Shick K, McGhee PL, Appelbaum PC (2010) Affinity of ceftaroline and other β-lactams for penicillin-binding proteins from staphylococcus aureus and streptococcus pneumoniae. Antimicrob Agents Chemother 54: 1670-1677.

15 Corey A, So TY (2017) Current clinical trials on the use of ceftaroline in the pediatric population. Clin Drug Investig 37: 625-634.

16 Farrell DJ, Castanheira M, Mendes RE, Sader HS, Jones RN (2012) In vitro activity of ceftaroline against multidrug-resistant staphylococcus aureus and streptococcus pneumoniae: a review of published studies and the aware surveillance program (2008-2010). Clin Infect Dis 55: S206-S214.

17 Park HS, Oh SH, Kim HS, Choi DR, Kwak JH (2016) Antimicrobial activity of zabofloxacin against clinically isolated streptococcus pneumoniae. Molecules 21: e1652.

18 Quin X, Huang H (2014) Review of nemonoxacin with special focus on clinical development. Drug Des Devel Ther 8: 765-774.

19 Van Rensburg DJ, Perng RP, Mitha IH, Bester AJ, Kasumba AJ, et al. (2010) Efficacy and safety of nemonoxocin versus levofloxacin for community acquired pneumonia. Antimicrob Agents Chemother 54: 4098-4106.

20 Cilli A (2013) The yield of tigecycline in the treatment of community-acquired pneumonia. Tuberk Toraks 61: 155-161.

21 Moya Cordero P, Ruiz-Aragón J, Molina Linde JM, Márquez-Peláez S, Motiva Sánchez V (2013) Evaluation of the efficacy and safety of tigecycline for treatment of respiratory tract infections: systematic review of literature. Rev Chilena Infectol 30: 591-597.