

Review Article

Challenging Approaches in Combating *Streptococcus Pneumonia* Infection

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Abstract

Context: *Streptococcus pneumoniae* [pneumococcus] induces a large variety of the diseases burden such as bacteremia, meningitis, otitis media and pneumonia in human. Among these, the meningitis can be disclosed with long-lost diseases sequelae. Over the last decades, various recommendations and consensus were released to better manage this major respiratory disease.

Evidence Acquisition: However, there is a controversy among the clinicians about the best strategy in dealing with this chronic infection. In brief, using proper antibiotics or conjugate vaccine to battle this bacterium is a critical question for the clinical setting.

Results: Taken together, it seems that the best possible adopted strategy is to apply the pneumococcal conjugate vaccines in management due to the following two reasons: 1) reducing the bacterial antibiotic resistance rates and 2) decreasing the prevalence of pneumoniae mortality and morbidity at global scale

Conclusion: Conclusively, continuous surveillance surveys determining antibiotic resistance seem inevitable to track pneumococcal genetical variable populations for both successful antibiotic therapy and proper vaccination.

Keywords: *Streptococcus Pneumoniae*, Antibiotic Resistance, Vaccine, WHO, Serotype 19A

1. Context

Following the isolation of *Streptococcus pneumonia* [*S. pneumonia*] in 1881's by Louis Pasteur, it seems necessary to observe this bacterium as listed among the bacteria with yet hundreds of unanswered questions. This encapsulated gram-positive diplococci are genetically and phenotypically close to various species of streptococci habituated in the human oral cavity [1]. Notably, the colonization with this bacterium in the upper respiratory system stays asymptomatic in many of the colonized individuals [2]. Clinically, this facultative microbe is responsible for invasive and non-invasive diseases, ranging from mild ones

including simple sinusitis to more severe diseases including septicemia and meningitis [3, 4]. The *S. pneumonia* is a bacterium that basically remains commensal in the human nasopharynx; nonetheless, in a certain situations, it becomes pathogen and finally causes severe diseases such as meningitis and pneumonia with relatively higher mortality rates [5, 6]. *S. pneumonia* is estimated to be solely responsible for 35% of all kind of pneumonia [7]. Only in the developing countries, *S. pneumoniae* is a main causative agent of more than one million death after meningitis and sinusitis among children [8]. As already mentioned, there are still large amount of unknown

queries about this bacterium, listed as virulence factors and the pattern of antibiotic resistance. Nowadays, it is widely debated and some have agreed that strain-dependent capsule is an unforgettable virulence factor detected in this microbe [9, 10]. The capsule efficiently helps the pneumococcus to persist while facing active phagocytosis by immune cells, mainly alveolar macrophages [11]. *S. pneumonia* has been known as a dangerous infectious agent for children under 3 years old and also the most controllable bacteria by the vaccine for many years [12]. Morbidity and mortality reported by the colonization of *S. pneumonia* were sharply increased in recent years due to the i) emergence of antibiotic resistance, ii) lack of an ideal vaccine against all clinical strains, iii) increased aged patients with chronic illness and iv) hospitalization [13-15]. To now, there has been two main tools in battle with this persistent microorganism: antibiotic therapy and vaccination [16]. In brief, there is no clear determined strategy for how to deal with this infection in various patients. In this review, the main purpose was to address two items affecting the low success rate in the management of *S. pneumonia* infections. Moreover, likely prospective of this infection was concentrated on.

2. Evidence Acquisition

2.1 Antibiotics

As expected, antibiotics were applied to eradicate the *S. pneumonia* isolating from clinical samples while the emergence of resistance hampered successful treatment of this bacterium [17, 18]. Regarding bacterial populations, applying inappropriate antibiotics formula resulted in failed therapy and selection of resistant/persistent bacterial clones [antibiotic selection pressure]. Pneumococcal strains are usually exposed to the prescribed antibiotics available in the nasopharynx and mostly propagate in mucosal microniche [19-21]. Among the all gram positive and negative microorganisms, *pneumococcus* is highly potent to receive

the new DNA using the transformation approach [22]. This DNA update helped the *pneumococcus* to survive regardless of the environmental antibiotics existence; thus, new offsprings emerged rapidly causing the epidemic pneumoniae among both adults and infants [23, 24]. The problem with streptococci is that human nasopharynx can be an immense territory for commensal bacteria carrying the resistant elements with potency of transforming to the *pneumococcus*. In 1912, Optochin resistance was reported from experimental assays, being an alarming sound for clinical practice concerning difficulty in treating this bacterium in close future [25]. During the 1935s and 1940s, patients with meningitis caused by *S. pneumonia* showed high resistance rate into the sulfonamide [26]. Interestingly, occurrence of resistance to the penicillins lasted until 1968s as reported [27]. Later, resistance to the chloramphenicol was found among the clinical isolates while tetracycline susceptibility rates were also reduced in many of geographical regions [28, 29]. Broadly defined, multidrug-resistant [MDR] pneumococci are characterized by resistance to 3 or more antibiotics at the same time. Although MDR isolates were firstly defined among the pediatric cases, later other research groups were able to identify these classes of antibiotic-resistant strains from the adult groups [30-33]. Reports on antibiotic resistance of *S. pneumonia* to the macrolides have increasingly come into the media and scientific communities. Since *S. pneumoniae* is the first ranked bacterium among causative agents of community-acquired pneumonia, an efficient antibiotic therapy would be preferable by clinicians. To date, the macrolides are the first and most effective choice in elimination of this bacterium in colonized hosts. On the other side, current evidence manifesting the rate of macrolides resistance is getting close to alarming levels in global scale. Previous inappropriate usages of macrolide is the

main risk factor escalating the trend of failed therapy using this antibiotics against *S. pneumoniae*. As such, better prescription policies in clinics and increased awareness of patients about the threats of the uncontrolled drug consumptions will be the main solution in this unfair war! Relatively high rate of resistance among the clinical strains of *S. pneumoniae* to the cephalosporins and macrolides is a critical concern which needs intensive attention to have better insight into diseases-associated statics about this respiratory system bacterium [19, 20, 34-38].

3. Results

The important rationale for using the vaccine against *S. pneumoniae* infection are as follows: i) large burden of aged population in the world, ii) increased health status after proper vaccinations, and iii) lack of proper antibiotic therapy in clinical practice. Having capsular based design is a pitfall for general dissemination of this application among the candidates. From the beginning, pneumococcal conjugated vaccines [PCV] were designed to reduce the prevalence of this persistent bacterium, but rapid emergence of different circulating serotypes led to the defeated vaccines projects worldwide [39-42]. Another basic problem was the decreased immunogenic response to the polysaccharides composition of PCV among the young individuals and also infants. Since twenty years ago, certain proteins were conjugated into the available vaccine, thus T-cell mediated immunity was initiated subsequently [43-45]. The main concern is that despite wide spread usage of PCV, pneumococcal-associated death rate is still increasing, according to the recent WHO released news [46]. In 2014, Tabatabaei *et al* reported that limited success rate of PCV 13, mainly among the young population, is a major threat for public health in Iran. However this finding is contradictory and confirmatory in comparison with different groups [47-50]. Although the status for Iran

is quite different, in Japan, the [PCV-7] they announced recommendations for volunteers in order to increase the hygiene situation. In total, introducing the seven-valents PCV [14, 18C, 23F, 19F, 6B, 4 and 9V] conjugate vaccines, which was a main cause of reduced incidence of pneumococcal associated diseases worldwide, was the main cause of the emergence of non-vaccine serotypes of *S. pneumoniae*. For example, 19A was a dominant non-vaccine strain which caused pneumonia with high rate of antibiotic resistance [mostly MDR-strains] at national and international levels [51-54]. Moreover, 19A was recently emerged as a dominant serotype with antibiotic resistance among the patients with invasive diseases [55, 56]. A large body of evidence indicate that the universal spread of 19A is a major clinical issue and it needs further attentions, especially in developing and low income countries. Pneumococcus is considered to be the first rank agent in pneumonia acquired from the community in comparison with other human respiratory pathogens. Not only because of failures in establishment of routine antibiotics susceptibility tests in clinical settings, but also for inconsistent national programs, there is no clear guideline to address this problematic and killing diseases, especially for children under 2-4 years old, mainly in developing countries. Although it is more than a century that the scientists have knowledge about the *S. pneumoniae*, still the questions exist about how to manage this infection among the patients especially high risk individuals. It is frequently stated that nasopharyngeal carriage of pneumococcal isolates is the main route of transmission into new hosts [57-59]. Therefore, determining the circulating serotypes among the vaccine-target persons would be a novel strategy before starting the vaccination projects, particularly in developing and low-income countries. Presently, most of attempts to produce a preventive vaccine were devoted to suggest a conjugate vaccine; and yet in reality,

pneumococcal diseases, mainly with invasive prognosis, pose huge death rates worldwide. The first available idea is to shift in strategy to produce a vaccine from conjugate to the novel alternative ones. Using the proteins in combination with selective bacterial antigen is a new era which may answer today's frequent queries in the management of pneumococcal-associated diseases. Last but not least, continuous follow-up programs about antibiotic resistance are necessary to track pneumococcal genetical variable populations for both a successful antibiotic therapy and proper vaccination.

4. Conclusion

The antibiotic resistance of *S. pneumoniae* has become a major public health dilemma, even for developed countries. In this line, countries such as the United States reported that the prevalence of drug-resistant strains has increased and in response with this problem, different strategies to compensate are required.

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Conflict of Interest

The authors declare no conflict of interest.

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