Editorial

Pneumococcal vaccination in adults:
New perspectives for old problems

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It is widely accepted that infections of the lower respiratory tract represent a significant factor of morbidity and mortality. In particular, pneumococcal pneumonia bears a mortality rate of 15-20% which increases to nearly 60% in elderly[1]. In USA, the economic burden of the disease is estimated to be 1.3-2.2 billion dollars per year. The disease claims more than 1.6 million lives yearly, mainly among young children and elderly people. In Europe, the incidence of pneumococcal pneumonia appears to be higher than in other continents[2]. As it is projected that in 2050 the percentage of people aged above 65 years will reach 30.3% of the total European population (2000, 15.7%), it could be easily concluded that prevention of pneumococcal disease is by far more preferable than therapeutic intervention.

The cornerstone for prevention is the composition and wide uptake of a safe and effective vaccine. In adults, the current practice is based on the administration of the 23-valent polysaccharide vaccine, licensed in 1983. It contains purified pneumococcal capsular antigens from 23 types of pneumococcal bacteria that cause 88% of bacteremic pneumococcal disease. Immune response, including enhanced opsonization, phagocytosis and bacterial killing, is mediated through the activation of B-cells. Due to the T-cell independent immune response, polysaccharide vaccine does not induce neither immune memory nor mucosal immunity and devoid of booster effect. The safety of PPV23 is well documented and adverse events are usually mild and self-limited, including mainly local reactions. On the contrary, the vaccines' efficacy was always a controversial issue, as many studies report that antibodies production (or even their functional activity) in elder or immunocompromised patients' lies well beneath the desired level[3-5]. Certain (but not all) studies conclude that the gradual fall of antibody titers 5-10 years after initial vaccination is not restored by repeated administration of the vaccine[6]. In accordance to these discrepancies, clinical studies report conflicting results[7]. In a number of publications, PPV23 appears to offer significant protection against non-bacteremic pneumonia, while others (mainly metanalyses) conclude that protection is minimal, if any[8,9]. The effectiveness of PPV23 against bacteremic pneumonia is reported as considerable, being 63-83% for all adult population but only marginal (0-42%) for high-risk patients[10]. Notably, a recent 8-years long epidemiology study conducted at two counties in UK revealed an increase of invasive pneumococcal disease despite the improved uptake of PPV23 from 49%

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to 70%[11]. Nevertheless, a very recent interim report of an ongoing prospective study including more than 27,000 patients of >60 years of age, suggests that PPV23 appears to be somewhat protective against ischemic stroke and acute myocardial infarction[12]. The underlying mechanism of such protection is unknown, although several explanations are proposed.

Conjugated polysaccharide vaccine (PCV) on the other hand, initially licensed as 7-valent and currently as 13-valent, until recently was offered only for children use. PCV's clinical and laboratory evaluation is highly coherent and apparently positive. It is documented that conjugated vaccines are able to activate both B- and T-cells, eliciting strong immune stimulation and inducing immune memory. Although PCV was introduced in clinical use quite recently (2000), it has already proved its effectiveness in reducing both bacteremic pneumonia rates and nasal carriage in children, while being safe as much as PPV 23. The reduction in nasal pneumococcal carriage decreases the bacterial transmission and induces what is referred as "herd immunity" i.e. immunizing a proportion of the population in the community reduces the disease in unvaccinated individuals[13]. Equally impressive is the observed reduction in viral pneumonia rates, suggesting a strong interplay between pneumococcus and viral pathogens in the pathogenesis of the disease[14].

The remarkable success of PPV has raised the interest in the possible use in high-risk adults and elderly people. Indeed, initial studies in individuals above 70 years of age and COPD patients suggest that PPV elicits superior immune response to PPV23[15,16]. However, it was also revealed that prior vaccination with PPV23 attenuates the subsequent response to conjugated vaccine. There is no doubt that more and larger clinical studies such as CAPITA project in Holland are required before the extrapolation of safe conclusions about the actual efficacy of the PPV in adults. Nevertheless, the already existing evidence was considered by the FDA as adequate to justify its approval for prevention of pneumococcal disease in adults aged 50 years and older[17].

Of course there are concerns about some negative consequences that could rise from a potentially wide uptake of the conjugated vaccine in adults. First, a replacement of covered pneumococcal serotypes by others, not included in the vaccine is quite possible to occur. This is not only a theoretical speculation, since it is documented that actually happen (although at limited extent) after the wide spread of PPV vaccination in children. Another possible disadvantage is the relatively narrower serotype coverage provided by the currently available 13-valent PPV, due to manufacturing difficulties rising from its complex composition. Finally, conjugated vaccines are considerably more expensive, setting barriers to their availability in countries with limited resources. Nonetheless, there are indications that the expected greater effectiveness could designate PPV as a cost-effective choice[18].

It has to be underlined that beyond issues related to the right choice of pneumococcal vaccine, an improvement of vaccine's uptake is of great importance. According to the existing data, the percentage of vaccinated individuals in high-risk groups is still quite disappointing and, thus, there is still room for substantial improvement[19]. Possible solutions include the simultaneous administration of influenza and pneumococcal vaccine and the implementation of effective strategies to augment in-hospital vaccination[20,21].

Although the above mentioned concerns are of certain importance, yet they are not sufficient to blur the expectations raised by the recent approval of PPV for adult use. Moreover, there is accumulating evidence that reliable alternatives (such as protein-based vaccine) will be available in the near future, improving even further our ability to prevent pneumococcal disease.

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