Vaccine 29S (2011) C35–C42

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

The pharmacoeconomics of pneumococcal conjugate vaccines in Latin America

Norberto Giglio[a,*], Paula Micone[b], Angela Gentile[a]

[a] Ricardo Gutierrez Children's Hospital, Buenos Aires, Argentina
[b] Hospital General de Agudos Carlos G Durand [General Hospital for Acute Illnesses], Argentina

ARTICLE INFO

Article history:
Received 17 June 2011
Accepted 24 June 2011

Keywords:
Pneumococcal conjugate vaccine
Latin America
Pharmacoeconomics
Cost-effectiveness

ABSTRACT

Streptococcus pneumoniae continues to be the most important causative agent of invasive bacterial infections in children and is the most common cause of vaccine-preventable deaths in children less than 5 years of age. Due to some conditions in the Latin America region, economic assessments of pneumococcal conjugate vaccines (PCVs) have unique characteristics. First, distribution of *S. pneumoniae* serotypes, and thus coverage by vaccines that incorporate certain serotypes, varies within the region and compared with other parts of the world. Second, the mortality rate of pneumococcal infections in developing countries is significantly higher than in the US and Europe. Third, the economies of the Latin American region are very different from those of developed countries. For these reasons, the Pan American Health Organization (PAHO) is promoting the need for economic valuation studies of the impact of pneumococcal vaccines Latin America. Given the importance of pneumonia in the burden of pneumococcal disease in Latin America, the number of pneumonia cases prevented by the vaccine has a large impact on the economic valuation of PCVs, due to a strong correlation with numbers of deaths averted, quality-adjusted life-years (QALYs) gained or disability-adjusted life-years (DALYs) avoided. In terms of cost, analysis of impact on acute otitis media (short-term) and sequelae (long-term) show a significant and important expenditure avoided by vaccination. Cost-effectiveness is significantly modified by vaccine cost, mortality due to pneumonia, vaccine efficacy/effectiveness and herd immunity. Finally the validity of certain assumptions based on the uncertainty of the data should be considered in economic assessments of new PCVs. These include assumptions related to the impact on otitis media, estimates of efficacy/effectiveness based on measured antibody levels and the extrapolation to PCV10 and PCV13 of previous experience with PCV7.

1. Introduction

Streptococcus pneumoniae continues to be the most significant causal agent of invasive bacterial infections in children under the age of 5 years, and is a relevant agent in common community infections. Since this is a frequent and in many cases severe infection, pneumococcal disease is a significant cause of morbidity and mortality, with a high economic impact on healthcare systems. Global figures from the World Health Organization (WHO) suggest that more than 700,000 children die each year from pneumococcal infections [1].

Since the highest morbidity and mortality rates from pneumococcal disease are seen in children under the age of 2, at the start of the 1990s, conjugate vaccines started to be developed with polysaccharides combined with a carrier protein in order to obtain an adequate immune response in this susceptible population. Three vaccines were developed, which contain 7, 10 and 13 (pneumococcal conjugate vaccine [PCV]7; PCV10 and PCV13, respectively) serotypes of *S. pneumoniae*.

From a pharmacoeconomic point of view, developing countries, such as those in Latin America have certain special conditions that set them apart from the United States and Europe. The mortality rate from pneumococcal infections is significantly higher than in developed countries; it is estimated that mortality in some of the poorest regions in the world it can be over 10 times higher than in developed countries [2,3].

The economies in the region are also very different from developed countries and variable across the Latin American region itself, which means that government investment in Healthcare Systems also varies significantly. Figures from the World Bank for Latin America and the Caribbean estimate that, in 2009, some countries in the region had a Gross Domestic Product (GDP) of between 8000 and 2000 US dollars (USD), while the average GDP in Europe and the United States is around 30,000 USD [4].

The distribution of *S. pneumoniae* serotypes shows regional variability. According to data from the SIREVA Network of the Pan

* Corresponding author at: Ricardo Gutierrez Children's Hospital, Epidemiology Department, Gallo 1330, Ciudad de Buenos Aires, ZC1426, Argentina.
Tel.: +54 1149649019; fax: +54 1149649019.
E-mail address: norbergiglio@gmail.com (N. Giglio).

0264-410X/$ – see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.vaccine.2011.06.095

American Health Organization (PAHO), it is estimated that PCV7, PCV10, and PCV13 would have an average coverage of 55%, 80%, and 87%, respectively, for invasive infections such as bacteremia, bacteremic pneumonia and meningitis in children aged under 5 [5]. This is why the PAHO has been using its ProVac Initiative to promote the need to carry out economic evaluation studies of the impact of pneumococcal vaccines in the different countries of Latin America and the Caribbean [6].

The economic impact that mortality from pneumococcal disease would have, the serotype distribution and potential coverage by available vaccines, and the costs associated with this disease are the points that will be discussed in this review, to assess the universal vaccination of children under the age of 5 years from the point of view of health economics.

2. Basic pharmacoeconomic concepts applied to vaccines

Currently, major concerns about the increased cost of healthcare have led to a range of possible solutions being put forward, which have the main aim of ensuring the rational use of healthcare funds. The fact that there are limited financial resources available means that we have to draw comparisons between the efficiency of different healthcare alternatives (for example, whether to vaccinate or not) in order to incorporate the idea that the money to be assigned to healthcare resources is ringfenced and that when money is spent on one type of technology, this sometimes means not spending money on another type of technology (opportunity cost principle) [7–11].

Vaccines represent an important group of healthcare interventions and a cost-effectiveness analysis is the most common way of assessing the efficiency of the incorporation of a vaccine into national immunization programs [12].

Cost-effectiveness studies use the results in terms of both health outcome (effectiveness) and the costs of different options in their assessments (as to whether to vaccinate or not in the majority of cases). Given that the most common unit of measurement of effectiveness refers to lives saved or deaths avoided, economic studies can be used to deduce the cost per life year gained, life saved or year, adjusted depending on quality of life or disability. This allows us to assess the investment involved in the incorporation of a vaccine into an immunization program [13].

Especially for the pediatric population, adjusting the number of years in terms of quality or disability of life is difficult and challenging for economic evaluation models. The different economic evaluations use the cost per disability-adjusted life year (DALY)[1] averted or quality-adjusted life year (QALY)[2] gained. This makes it possible to establish the differences between the subjective value of 1 year of life in perfect health (value = 1) and 1 year of life with a disability, chronic pain or a basic need which has not been met (value < 1) [14–17].

From the point of view of costs, economic evaluations focus on what is commonly known as perspective and may include the costs of the healthcare system only (from the perspective of the health sector) or may also include the loss caused by a disease in terms of the loss of working productivity, as, for example, in the case of pediatric illnesses, when the parents cannot go to work because they are taking their children to the doctor, or when they have to take time off to look after their children at home. In some cases, economic evaluations may even include the economic losses in labor terms of a death under the *concept of human capital* (perspective of society) [18].

Most economic evaluations of vaccines need to carry out a simplified analysis of the disease to deduce the impact of a vaccine and therefore use models which allow for a description of the incidence and the healthcare costs that this pathology causes when there is no sanitary intervention (base case).

The most frequently used instruments in the pharmacoeconomics literature are decision trees and Markov chains. The advantage of these types of instruments lies in their simplicity, but they have the drawback of assuming that the strength of the infection (rate of infection per susceptible individual) remains constant throughout the period studied [19,20]. In reality, the strength of the infection depends on the number of infected individuals at any time. Therefore, in order to carry out a more accurate estimation of the impact of an infectious disease, an alternative is to use dynamic models. These allow for the inclusion of both the direct effect derived from the reduction in the number of susceptible cases and the indirect effect (herd effect) associated with the decrease in the number of contacts between susceptible and infected people [21]. However, few economic evaluations have been carried out in Latin America based on dynamic models for vaccines.

The idea of investing in medical technology to improve the quality of life of the population (increase in QALYs or reduction in DALYs) is a relatively new concept in the field of immunization. For the first vaccines, such as the vaccines against diphtheria, tetanus and whopping cough, poliomyelitis and measles, the evaluations consisted of comparing the costs of the vaccine against the saving on the cost of treatment of the disease that they aimed to eradicate. For all of these vaccination strategies, monetary savings were achieved from avoiding cases of the disease. However, since the new vaccines require more complex technologies such as conjugation with polysaccharides, the cost of the manufacturing process is higher and, as a result, the prices paid for each dosage also increase [22]. Generally, it is more difficult to "save money" with the new vaccines, as more money is normally spent with the incorporation of a vaccine into an immunization calendar than is saved on the disease. In most countries in the Latin American region, the resources available to cover costs of the healthcare sector are becoming increasingly limited, which means they need to be applied efficiently and fairly (i.e., the investment to be made has to be justified by the health benefits that will be obtained). This is why the use of economic studies is promoted before the introduction of a vaccine into a given healthcare system.

The aim of the remainder of this work is to review the articles published on economic evaluations relating to pneumococcal conjugate vaccines in Latin America.

3. Methods

For this review, the PubMed database and the Lylacs Latin American database were searched from the dates they were created to 30 April 2011. The following keywords were used: *costs, economic, pneumococcal and vaccine*. This strategy was used to select the important articles for the review and information was gathered in terms of: type of economic evaluation; country or region where the economic evaluation was carried out; model used; details of the disease burden that are most relevant from a pharmacoeconomic point of view; type of vaccine; number of doses; duration of immunity; costs included; timeframe; coverage; cost per dose of the vaccine; and discount. Finally, following the guidelines of Drummond et al. [23], completed economic evaluations were also

[1] DALY: The unit of measurement of the impact of a disease in terms of time lost due to a premature death (mortality) and time spent with a disability (morbidity). The Global Burden of Diseases Study (GBD) sponsored by the World Bank and launched in 1992 aims to quantify the global burden of diseases. This quantification requires the standardization of the unit of measurement in terms of health, which is why the WHO uses the DALY concept for disease assessments.

[2] QALY is a universal validation form which is applicable to all diseases and which allows us to use a single measurement to assess the quantity and quality of life in years gained. Canada has been leading the way in developing this concept.