Economic Evaluation of Immunoprophylaxis in Children with Recurrent Ear, Nose and Throat Infections

Kurt Banz,1 David Schwicker1 and Anne Marie Thomas2
1 HealthEcon, Health Care Consultants, Basle, Switzerland
2 Pierre Fabre Médicament, Castres, France

Summary

This study compares the costs of immunoprophylaxis versus no immunoprophylaxis in children with recurrent ear, nose and throat (ENT) infections (otitis media and rhinopharyngitis) using ribosomal immunotherapy ("RibomunyL"). The per-patient cost of ribosomal immunotherapy (FF297) is offset by direct savings garnered through the prevention of many acute infectious episodes. The net 6-month per-patient savings associated with immunoprophylaxis range from FF272 to FF1704, depending on the indication and the type of treatment-cost estimate. Saved healthcare resources include physician consultations and visits, laboratory tests, medicotechnical services (audiometric tests) and antibiotic therapy. Sensitivity analysis of efficacy and treatment-cost estimates enabled threshold ranges of incremental efficacy to be identified. Cost-equivalence between the 2 treatment options was found to exist when the incremental efficacy of immunoprophylaxis lay between 7.4 and 17.5% (recurrent otitis media), and between 8.9 and 26.1% (recurrent rhinopharyngitis). Thus, even when clearly lower incremental efficacy rates than those reported in controlled clinical trials (approximately 40 to 60%) are assumed, ribosomal immunotherapy can still be expected to be cost effective. An analysis of the perspectives of the various payers in the French healthcare system demonstrated that net savings occurred for all payers involved. However, social security insurance would gain most from an immunoprophylaxis programme. Based on the evidence presented here for France, physicians and payers should give increased attention to this treatment option.

Respiratory tract infections are among the most commonly reported diseases in children,[1-4] with most episodes occurring during the winter months. In childhood, recurrent ear, nose and throat (ENT) infections, particularly rhinopharyngitis and otitis, represent a major public health problem because of their prevalence and the risk of sequelae.[5,6] The frequency of these infections decreases as the immune system matures, peaking at age 2 years and falling rapidly after age 7 years.[7,8] As these diseases are associated with substantial utilisation of healthcare resources, and constitute an important cause of parental absenteeism from work, they can be expected to have a considerable economic impact.[9]

Generally, recurrent ENT infections are defined as 3 or more acute episodes occurring within a 6-month time period,[7,10] with up to 10 episodes during 1 season having been observed.[8] Most of these infections are caused by bacterial pathogens,[3] and are therefore often successfully treated.
with antibiotics. However, with a rising number of such acute episodes, there is an increasing risk of complications and major sequels. The long-term risks in children suffering from recurrent otitis media include structural middle ear damage, entailing partial or permanent hearing loss as well as impairment of speech and language, and cognitive or psychosocial disorders.111

An alternative to treating repeated attacks is to prevent them through immunostimulatory therapy. The primary clinical rationale for prevention is the avoidance of discomfort and, additionally, improvement of the long-term prognosis for children who experience recurrent ENT infections. Ribosomal immunotherapy (‘Ribomunyl’), which stimulates immunity against recurrent ENT infections, contains 2 biologically active fractions: ribosomes from 4 bacterial strains (Streptococcus pneumoniae, S. pyogenes, Klebsiella pneumoniae and Haemophilus influenzae), and proteoglycans extracted from K. pneumoniae. In in vitro and in vivo pharmacological studies, treatment with ribosomal immunotherapy appeared to stimulate both specific and nonspecific immune mechanisms.112-14

In children with recurrent otitis media and rhino-pharyngitis, clinical trials have demonstrated that ribosomal immunotherapy significantly reduces the number of episodes of acute respiratory infections.17,8,15-18

However, clinical practice shows that prophylaxis against recurrent ENT infections is not employed as frequently as might be expected,19 even though patient selection criteria, based on the number of infectious episodes,17,8,10 are relatively clear cut. Reasons for this include the fact that even after immunoprophylaxis, acute infectious episodes still occur, albeit with reduced frequency. Connected to this is the general problem of reproducing results from controlled clinical trials in routine practice, leading to some uncertainty concerning the achievable efficacy. Furthermore, physicians may feel that prophylaxis of these recurrent infections is not worthwhile, preferring instead to treat acute episodes when they occur. This stems from the view that acute episodes are readily managed, are not life-threatening, and decrease in frequency with advancing age.

Considering the epidemiology of recurrent ENT infections, the frequency of acute infectious episodes in children and the potential for long-term sequels, these arguments against prophylaxis would appear to be economically questionable. Overall, it seems that the economic importance of recurrent ENT infections and of the impact of immunoprophylaxis is under-recognised. To our knowledge, the economics of preventive therapy in this field have not been systematically investigated, in contrast to many other prominent interventions and immunisation programmes.20-23

Thus, this study was undertaken to compare the costs of 2 treatment options: immunoprophylaxis of recurrent ENT infections, using ‘Ribomunyl’, versus no immunoprophylaxis.

**Methods**

**Evaluation Framework**

Because children with recurrent ENT infections experience acute episodes mainly during the winter, a time horizon of 6 winter months was chosen. This was in keeping with the design of most of the clinical studies of ribosomal immunotherapy, and with the recommended treatment period. Each acute episode can lead to direct healthcare resource utilisation, as well as productivity losses (fig. 1). Thermal cures1 represent an exception, as they are not directly related to the occurrence of an acute episode but are prescribed to children with diagnosed recurrent ENT infections as a general treatment.

In this context, the objective of this economic analysis is to investigate whether prophylaxis with ribosomal immunotherapy is capable of offsetting its overall direct costs by creating savings in other

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1 A thermal cure is a course of treatment that takes advantage of the special properties of mineral waters administered in a spa. This specialised treatment is used for diseases such as ENT disorders, dermatoses and rheumatism. Because it is not usually available locally, patients are normally required to travel in order to receive it.