

PROJECT OVERVIEW

Project Name

Empirical therapy for respiratory tract infections in an era of increasing antimicrobial resistance: a decision and cost analysis.

Introduction

Community-acquired upper respiratory tract infections are one of the most frequent reasons to present to a practitioner's office. In the first decade of the 21st Century, major environmental changes have resulted into alterations in the bacterial pathogenic microflora, and this is likely to affect future treatment strategies.¹

The three key bacterial pathogens responsible for upper respiratory tract infections have been *Streptococcus pneumoniae*, *Haemophilus influenza* and *Moraxella catarrhalis*. In the 1990s, one of the most significant community-acquired upper respiratory pathogen was penicillin-resistant *S. pneumoniae*. For example, in the case of acute otitis media, common infection frequently caused by *S. pneumoniae*, recurrent episodes caused by resistant strains of this bacterium sometimes deteriorated to life/threatening invasive pneumococcal diseases, such as pneumonia, bacteremia and meningitis.²

Resistance increase is also current issue of Slovak community environment. Privately funded source MIKROMED is collecting community resistance data for a decade now and it is showing several disturbing patterns of increasing resistance for several pathogens and antibiotics. Most recent data show that we have declining susceptibility of macrolides toward most common respiratory pathogens e.g. *S. pneumoniae* but also to *Streptococcus pyogenes* and *Staphylococcus aureus*. Resistance levels are reaching 30% in community overall.³

¹ Hedrick JA. Community-acquired upper respiratory tract infections and the role of third-generation oral cephalosporins. *Expert Rev Anti Infect Ther.* 2010 Jan;8(1):15-21

² Cartwright K. Pneumococcal disease in western Europe: burden of disease, antibiotic resistance and management. *Eur J Pediatr.* 2002 Apr;161(4):188-95. Review. PubMed PMID: 12014384.

³ Babela R et al.: Infekcie horných dychacích ciest z pohľadu terapie cefalosporinom 3. Generacie - ceftibutenom. *Medical Practice* 2012 (5):20-23

Resistance of *Haemophilus influenzae* to ampicillin reached level of 12% and level of penicillin resistance *Streptococcus pneumoniae* is steady at level of 9%.³

Project goals and design

In Slovakia, there has not been published any study including cost analysis and decision pattern, where resistance in community was involved. Based on current practice in community, macrolides are overprescribed and it is showing negative effect within community resistance patterns. If there were cost-based models of respiratory tract infections (RTI) published, they did not address the issue of drug resistant respiratory pathogens. Understanding the impact of drug resistance is of critical importance, because the rates of antimicrobial resistance are continually changing and the prevalence of drug-resistant pathogens has a potentially large impact on the empirical antimicrobial regimen of choice.⁴

We would like to perform a cost-minimization analysis followed by sensitivity analysis to determine the precise level of macrolide resistance that should trigger a switch in empirical therapy for respiratory tract infections (uncomplicated) from macrolides to cephalosporins (3rd generation).

We would like to develop a decision tree model (using Tree Age Software). Model will be based on RTI (uncomplicated) caused by *Streptococcus pneumoniae* in adults >18 years of age. To obtain information on costs and clinical outcomes of RTIs, we will perform a systematic review of available literature by searching MEDLINE, PUBMED and local sources. We would also look for reliable data by insurance funds and by expert opinion in area of RTIs. Clinical response will be derived only from prospective clinical trials or investigations.

Model will most probably simulate 4 key scenarios (including 2 key sub-trees) – depending on the agent used and whether the organism will have in vitro

⁴ Gupta K, Scholes D, Stamm WE. Increasing prevalence of antimicrobial resistance among uropathogens causing acute uncomplicated cystitis in women. JAMA. 1999 Feb 24;281(8):736-8. PubMed PMID: 10052444.

susceptibility. First sub-tree will be dealing with macrolide treatment management and possible effects and second sub-tree will be dealing with cephalosporins treatment management and possible outcomes. Model will use susceptibility data of *Streptococcus pneumoniae*.

Probabilities and variables will be subject of further modeling using current published data or expert opinions if applicable.

Costs reviewed (can be subject of change):

- 1) Cost of antibiotics
- 2) Number of doctor's visit – initial and follow-up
- 3) Laboratory susceptibility tests
- 4) Hospitalization for complicated RTIs connected to resistant bacteria
- 5) Additional laboratory tests needed

Timeframe: Q1-Q2/2013 (3 – 4 months)

Data collection: MEDLINE, PUBMED, Expert opinion, insurance fund data, other local sources (e.g. HPL, MEDIREX)

Evaluation: Q2/2013, Dept. of Public Health and Healthcare Management, Bratislava

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Expected submission of results: ISPOR 2013 (Europe or USA, depends on
results availability), local presentations
where applicable

Project sponsorship: MSD Slovakia – research grant

Expected project budget: 9400 EUR