TRENDS IN STREPTOCOCCUS PNEUMONIAE ANTIMICROBIAL RESISTANCE BEFORE AND AFTER THE IMPLEMENTATION OF THE 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV13), IN A GREEK TERTIARY CHILDREN'S HOSPITAL

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BACKGROUND

In Greece, PCV7 was introduced in the Greek National Immunization Schedule (GNIS) at 2006 and was replaced by PCV13 at 2010. PCV10 was introduced only for a short period of time before the implementation of PCV13, having therefore only a minimal effect on community serotype circulation

AIM

The goal of this study was to compare the antimicrobial susceptibility of pneumococcal strains colonizing the nasopharynx or causing pneumococcal disease in young children, between pre- and post- PCV13 eras

METHODS

An 11-year retrospective study (2007-2017) was carried out, recording antimicrobial susceptibility of pneumococcal clinical and non-clinical strains, from children (age range: 1 month-14 yrs) admitted or examined as outpatients at a busy Tertiary Children's Hospital in Athens, Greece, covering 4 years before and 7 years after PCV13 GNIS implementation. Oxacillin susceptibility of each isolate was determined using Sensi-Disc BD. Susceptibility to different antimicrobials was determined with VITEK 2 Card AST-GP68 (BioMerieux Inc.). Pneumococcal isolates were classified as susceptible, intermediate and resistant according to current CLSI breakpoints. GraphPad Prism version 6 and Fisher's exact test were used for statistical analysis (a $p < 0.05$ was considered significant)

RESULTS

A total of 434 pneumococci were isolated, 171 during the pre-PCV13 and 263 during the post-PCV13 era

➤ From pre- to post- PCV13 era, the prevalence of penicillin non-susceptible (intermediate/resistant) strains decreased (28.8% vs. 9.94%, $p < 0.05$) (Fig. 1)

➤ Resistance to erythromycin, tetracycline and cotrimoxazole decreased during the post-PCV13 era compared to the pre-PCV13 era, while resistance to clindamycin increased (Fig. 2)

➤ Pneumococcal isolates demonstrating multidrug (MDR) antimicrobial resistance (≥ 3 antimicrobial classes) also decreased in the post-PCV13 era compared to the pre-PCV13 era (Fig. 3)

Fig. 1. Percentage of Penicillin non-susceptible strains

Fig.3. Percentage of MDR pneumococcal strains

Fig. 2. Percentage of pneumococcal Resistance to other antimicrobials

DISCUSSION

❖ Our study suggests that, in accordance with findings from other research groups, **PCV13 introduction is associated with a significant reduction of pneumococcal nonsusceptibility to first-line antimicrobials**

❖ A possible explanation for this finding is that in the pre-PCV13 era, serotypes in PCV13 but not in PCV7, such as 19A, mainly associated with increased resistance to common antimicrobials, accounted for the vast majority of pneumococcal disease; therefore, **19A inclusion in PCV13 and the incorporation of the latter in GNIS, was the major contributor to the significant decrease in community circulation of nonsusceptible serotypes leading to substantial reduction of antimicrobial-nonsusceptible and multidrug-nonsusceptible pneumococcal disease**

❖ Current IDSA and ESPID guidelines regarding paediatric infectious diseases such as acute otitis media, bacterial rhinosinusitis and community acquired pneumonia, where *S. pneumoniae* is considered an important pathogen, in many clinical scenarios, recommend empiric treatment with high-dose amoxicillin. In agreement with these recommendations, **our findings support the use of high-dose amoxicillin as an effective empiric antimicrobial choice instead of broad-spectrum antimicrobials for non-meningitis pneumococcal infections, in the post-PCV13 era**

REFERENCES

- Angoulvant F, Cohen F, Doit C, et al. Trends in antibiotic resistance of Streptococcus pneumoniae and Haemophilus influenzae isolated from nasopharyngeal flora in children with acute otitis media in France before and after 13 valent pneumococcal conjugate vaccine introduction. BMC Infect Dis 2015;15:236.
- Kim L, McGee I, Tomczyk S, Beall B. Biological and Epidemiological Features of Antibiotic-Resistant Streptococcus pneumoniae in Pre- and Post-Conjugate Vaccine Eras: a United States Perspective. Clin Microbiol Rev 2016 ;29:525-52.
- Kaur R, Casey JR, Pichichero ME et al. Emerging Streptococcus pneumoniae Strains Colonizing the Nasopharynx in Children After 13-valent Pneumococcal Conjugate Vaccination in Comparison to the 7-valent Era, 2006-2015. Pediatr Infect Dis J 2016;35:901-6.
- Weinstein MP, Klugman KP, Jones RN et al. Rationale for revised penicillin susceptibility breakpoints versus Streptococcus pneumoniae: coping with antimicrobial susceptibility in an era of resistance. Clin Infect Dis 2009;48:1596-600.
- Grivea I, Sourla A, Ntokou E, et al. Macrolide resistance determinants among Streptococcus pneumoniae isolates from carriers in Central Greece. BMC Infectious Diseases 2012;12:255
- Syriopoulou V, Menegas D, Georgakopoulou T, et al. Pneumococcal disease in children: changing serotypes and antimicrobial resistance in a tertiary hospital in Greece (2002-2011). 8th International Symposium on Pneumococci and Pneumococcal Diseases (ISPPD), 2012. Poster number 195.
- Syriopoulou V, Syrogiannopoulos GA, Georgakopoulou T, et al. Serotype distribution and antimicrobial susceptibility of Streptococcus pneumoniae following introduction of 13-valent pneumococcal conjugate vaccine (PCV13) in Greece. 30th Annual meeting of the European Society for Pediatric Infectious Diseases (ESPID), 2012.
- Kaplan SL, Barson W, Lin P, et al. Early trends for invasive pneumococcal infections in children following the introduction of the 13-valent pneumococcal conjugate vaccine. IDSA 49th Annual Meeting, 2011, Boston. Presentation number LB-1.
- Andrews N, Kaye P, Slack M, et al. Effectiveness of the 13 valent pneumococcal conjugate vaccine against IPD in England and Wales. 8th International Symposium on Pneumococci and Pneumococcal Diseases (ISPPD), 2012. Poster number 148.
- Van der Linden M, von Kries R, Imöhl M. Effects of three years of immunization with higher valent pneumococcal conjugate vaccines on serotype distributions among reported IPD cases in German children and adults. 52nd Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), 2012 Poster number G-863.
- Georgakopoulou T, Menegas D, Tzanakaki G, et al. Epidemiology of bacterial meningitis in Greece, in the era of conjugate vaccines: a 7 year review 2005-2011. 52nd Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), 2012. Poster number G3-1543.

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