Macrolide Resistance in Pharyngeal Isolates of Group A Streptococcus (GAS) from Nova Scotia, Canada

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ABSTRACT

Objectives: Penicillin is considered first line management for treating S. pyogenes (GAS) bacterial pharyngitis. For penicillin-allergic patients, macrolides are frequently used as an alternative for the treatment of non-invasive (pharyngeal) GAS. However, unlike penicillin, macrolide and clindamycin resistance are frequently reported. This study was performed to determine the prevalence of erythromycin and clindamycin in pharyngeal isolates of GAS in Nova Scotia.

Methods: GAS were prospectively collected in Nova Scotia between April 2019 and August 2019. Susceptibilities to erythromycin and clindamycin were performed using Kirby Bauer disk diffusion. Phenotypes were determined using a double disk diffusion method. Resistant isolates were genotyped by PCR (mefA, erm A/B/C/TR).

Results: Six-hundred-seventy-eight (678) GAS were collected in 2019. Nineteen-point-four percent (19.4%) of isolates were resistant to erythromycin, 18.1% were resistant to clindamycin. Among clindamycin resistant isolates, the majority (69.5%) exhibited a constitutive (cMLS\textsubscript{B}) phenotype whereas the remaining 30.5% displayed an inducible (iMLS\textsubscript{B}) phenotype. The M phenotype only accounted for 1.3% of macrolide resistant isolates. All isolates with an iMLS\textsubscript{B} phenotype were positive for ermTR; all cMLS\textsubscript{B} strains were positive for ermB. All isolates with the M phenotype were positive for mefA. In 2005, our last formal surveillance, macrolide resistance was 22.2%. Interestingly, the majority (95%) of clindamycin resistant isolates in 2005 were inducible, whereas now most are constitutive.

Conclusions: No significant differences were observed in overall macrolide resistance in 2019 compared to our historic data. However, a change in the predominant mechanism of resistance was observed. Resistant isolates are more likely to be resistant via a constitutive mechanism (cMLS\textsubscript{B}) compared to an inducible mechanism (iMLS\textsubscript{B}) seen previously. Although this study examined pharyngeal isolates of GAS, it underscores the importance of susceptibility testing, particularly in invasive GAS.

INTRODUCTION

Penicillin is the drug of choice for treating Streptococcal (GAS) pharyngitis. Penicillin resistance in GAS has not been described. Alternatively, for penicillin-allergic patients, the macrolides are frequently prescribed. Macrolides and lincosamides exert their antibacterial effects by binding to the 50S ribosomal subunit and inhibiting protein synthesis. They block the growth of nascent peptide chains by stimulating dissociation of the peptidyl- tRNA from the ribosome. Macrolide resistance in GAS primarily occurs via one of two mechanisms: by target site modification through acquisition of an erm-encoded methytransferase, or via a mefA-encoded energy dependent efflux pump. Efflux results in resistance to 14- and 15-membered macrolides only and is characterized by the M phenotype, while ribosomal modification results in resistance to macrolides, lincosamides and streptogramin B antibiotics and is characterized by the MLS\textsubscript{B} phenotype. Erm-mediated resistance can be inducible (iMLS\textsubscript{B} phenotype) or constitutive (cMLS\textsubscript{B} phenotype). We last performed an extensive survey in the Halifax area in 2005. This study was undertaken to determine if macrolide resistance in GAS had significantly changes during the intervening years.

RESULTS

Between April and August 2019, 678 unique isolates were collected. Nineteen-point-four percent of isolates were resistant to erythromycin and 18.1% were resistant to clindamycin. Ninety-three percent of the macrolide resistant isolates displayed the MLS\textsubscript{B} phenotype. Approximately 50% of the isolates were from the pediatric population (<16 years). No significant difference was observed in macrolide resistance between adult and pediatric populations.

The overall rate of macrolide resistance has not significantly changed in Nova Scotia since 2005.

The majority of resistant isolates had an inducible MLS\textsubscript{B} phenotype. In 2019, the constitutive MLS\textsubscript{B} phenotype accounted for only 28.4% of resistant isolates.

CONCLUSIONS

- The overall rate of macrolide resistance has not significantly changed in Nova Scotia since 2005.
- Target site modification accounts for 93% of all macrolide resistance among GAS in Nova Scotia.
- No significant differences were observed between the adult and pediatric populations.
- There was a major shift in the ratio between inducible and constitutive resistance between 2005 and 2019.