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Effectiveness of clindamycin and epidemiology of invasive beta-haemolytic streptococcal infections in a region of eastern Canada, 1996-2016

Antoine Couture-Cossette*[1], Jacques Pépin[2], Claudine Desruisseaux[2], Adam Mercier[2], Alex Carignan[2], Louis Valiquette[2]

[1]*Université de Sherbrooke; Chus; Infectious Diseases and Medical Microbiology*

[2]*Université de Sherbrooke*

Background: Shifting trends in the epidemiology of β-hemolytic streptococcal infections have been described in various countries since the turn of the century, notably with an increase in the incidence of infections caused by Lancefield group C and G organisms (*Streptococcus dysgalactiae* ssp. e*quisimilis*). There remains a paucity of data in the literature pertaining to treatment of these life-threatening illnesses. The objectives of this study were to characterize the epidemiology of invasive β-hemolytic streptococcal infections over the last 20 years in a region of Eastern Canada (population: 322,099) as well as to evaluate risk factors for mortality and estimate various treatment effects, notably for adjunctive treatment with clindamycin and intravenous immunoglobulin (IVIg).

Material/methods: A retrospective observational study of invasive β-hemolytic streptococcal infections from 1996 to 2016 was performed in the two hospitals of a tertiary care, 683-bed academic center with a near-complete catchment rate for severe illness in its geographic area. Age-adjusted incidence rates by Lancefield group were calculated for each 2-year interval from 2002 to 2015. Multivariate analysis was performed to identify significant risk factors for mortality and to evaluate treatment effects.

Results: The 20-year study period yielded 741 cases, corresponding to 249 episodes due to Lancefield group A streptococci (GAS) as well as 304, 48 and 140 episodes respectively due to group B, C and G organisms. Summary demographic and clinical characteristics are presented in Table 1. After adjusting for age, few significant baseline differences were seen between cases due to different groups of streptococci, apart from the prevalence of diabetes. The incidence of invasive GAS

infections was stable during the study, with a decrease in associated mortality over time. Age-standardized incidence rates significantly increased for infections due to non-GAS β-hemolytic streptococci. In multivariate analysis of GAS cases, mortality was significantly associated with increasing age (p≤0.001), high-risk clinical entities as defined by presence of any of fasciitis, myositis, endometritis, pneumonia, empyema, endovascular infection or toxic shock (AOR 5.4, p=0.04) and need for ICU admission (AOR 18, p=0.002). Adjunctive treatment with clindamycin was associated with a marked reduction in mortality (AOR 0.09, p=0.01), whereas IVIg had no significant effect.

Table 1. Characteristics of invasive β-hemolytic streptococcal infections

Characteristics	GAS (n=249)	GBS (n=304)	GCS (n=48)	GGS (n=140)	p-value[1]
Age	43 (24-65)	60 (38-75)	69 (60-80)	71 (62-83)	<0.001
Comorbidity (CCI[2])	0 (0-2)	2 (0-5)	3 (1-6)	3 (1-5)	<0.001
ICU[3] admission	123 (49%)	100 (33%)	12 (25%)	32 (23%)	<0.001
Infection-related mortality	20 (8%)	24 (8%)	3 (6%)	14 (10%)	NS[4]

Data presented as number of cases (%), with ages and comorbidity as median (interquartile range).
[1]Two-tailed Fischer's test; [2]Charlson comorbidity index; [3]Intensive care unit; [4]Not significant

Conclusions: This study supports adjunctive treatment with clindamycin in severe streptococcal disease due to GAS, but similarly to other studies failed to show an effect of IVIg on mortality. Invasive β-hemolytic streptococcal infections due to non-A groups are more frequent in older patients with comorbid conditions and their age-standardized incidence significantly increased in the study region. Their mortality rate similar to GAS potentially reflects incidence in a population with a limited physiological reserve.