O064
Oral Session
Basic science: pathogenesis and epidemiology of Gram-positive bacteria

CLINDAMYCIN AND INTRAVENOUS IMMUNOGLOBULIN INFLUENCE GROUP A STREPTOCOCCUS VIRULENCE FACTOR ACTIVITY

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Objectives

Through the production of a vast array of virulence factors (VFs), Group A *Streptococcus* (GAS) can cause life-threatening invasive infections such as necrotizing fasciitis. In addition to surgical debridement, the current treatment envisages a combination of the antibiotics penicillin and clindamycin, acting on the inhibition of bacterial cell wall formation and protein synthesis respectively. However, lethality remains high and alternative or complementary treatment strategies are therefore required. Addition of intravenous immunoglobulin (IVIG) is one option although its efficiency has not yet been fully established. This work aimed to investigate the effect of IVIG and sub-inhibitory concentrations of clindamycin, as found in necrotic tissues, on the activity and expression of key GAS VFs such as SLO, Sda1, SpyCEP and SpeB.

Methods

The GAS strain M1T1 5448 was used. SLO activity was measured by assessing red blood cells hemolysis. Sda1 activity was estimated using a DNA degradation assay. IL-8 degradation was quantified by ELISA as a measure of SpyCEP activity and a colorimetric reaction involving the protease substrate BZ-Pro was employed to assess SpeB activity. Expression of virulence factors was assessed by real-time PCR and/or Western blot.

Results

Exposure of GAS M1T1 5448 to sub-inhibitory concentrations of clindamycin led to increased activity of the VFs SLO, Sda1 and SpyCEP but to decreased SpeB expression and activity. Sub-inhibitory concentrations of linezolid, tetracyclin and chloramphenicol had the same effect as clindamycin on VFs activity while no increase in activity was observed for gentamycin and tigecyclin. Physiological concentrations of IVIG blunted SLO, Sda1 and SpyCEP activities. The effect of sub-inhibitory clindamycin concentrations on the enhancement of VFs activity was confirmed in two GAS M1 clinical isolate strains resistant to clindamycin. Here, higher clindamycin concentrations were used and a concentration-dependent activity increase of all VFs tested was observed.

Conclusions

We demonstrate *in vitro* that bacteria exposed to sub-inhibitory concentrations of clindamycin, as found in poorly perfused necrotic tissues, display increased VFs activity and expression. On the other hand we demonstrate *in vitro* that IVIG is efficient in inhibiting GAS VFs involved in the progression and aggravation of invasive infections. Further work including the use of murine *in vivo* models is necessary to assess the role of VFs activity modulation by IVIG and clindamycin in real-time infections.