Corynebacterium diphtheriae is the main etiologic agent of diphtheria, an acute communicable infection of the upper respiratory tract, frequently fatal. As a result of increased vaccine coverage, the global incidence of diphtheria has reduced dramatically. Nevertheless, C. diphtheriae remains a concern worldwide due to its potential to cause endocarditis, osteomyelitis and catheter-related infections. C. diphtheriae abilities to adhere to and survive within diverse host cells, including macrophages and respiratory cells were previously described. C. diphtheriae is also capable of resist to high doses of tellurite (TeO$_3^-$), a general oxidant. These findings suggest that diphtheria bacilli tolerate high concentrations of reactive oxygen species (ROS). Nevertheless, C. diphtheriae oxidative stress response is poorly understood. In the present work, the resistance of ten C. diphtheriae strains to the oxidative agents, hydrogen peroxide (H$_2$O$_2$), paraquat and potassium tellurite (K$_2$TeO$_3$), was analyzed. Additionally, the ability of C. diphtheriae strains to adapt to ROS exposure through the induction of adaptive-response and/or cross-resistance and by modulation of biofilm formation was evaluated. C. diphtheriae strains exhibited different resistance levels to the oxidative agents tested. The two homologs strains ATCC 27010 and ATCC 27012, which differ in the presence of the corynephage β$^{tom}$, showed a major difference in H$_2$O$_2$ resistance: the toxigenic strain, ATCC 27012, presented a higher susceptibility. The H$_2$O$_2$ induced an adaptive-response in three diphtheria bacilli strains. Among the two homologs strains, ATCC 27010 was the only H$_2$O$_2$-adaptive-response positive. Bacterial cross-resistance was not induced by any oxidative agents. The presence of H$_2$O$_2$, paraquat and K$_2$TeO$_3$ led to a diverse modulation of biofilm formation. Paraquat and K$_2$TeO$_3$ influenced antagonistically the adherence of C. diphtheriae to the glass surface despite both agent present the ability to generate superoxide anion. The H$_2$O$_2$ was able to potentiate the biofilm formation on polystyrene surface of the ATCC 27012 strain. The heterogeneous oxidative stress responses indicated that C. diphtheriae might express varied strategies that establish differences in host-pathogen interactions and in adaptation under stressing environmental conditions.

Palavras-chaves: adaptive-response, biofilm, Corynebacterium diphtheriae, cross-resistance, oxidative agents.

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