Eradication of Methicillin-Resistant Staphylococcus Aureus-Forming Biofilm by Silver Sulfadiazine

Toyokazu TAJIRI [1)], Shiro JIMI [2)], Keika TANG [1)],
Ken SHIGEMORI [1)], Shuuji HARA [3)], Hiroyuki OHJIMI [1)]

[1)] *Department of Plastic Surgery, Faculty of Medicine, Fukuoka University*
[2)] *Central Lab for Morphology and Pathology, Faculty of Medicine, Fukuoka University*
[3)] *Department of Drug Informatics, Faculty of Pharmaceutical Science, Fukuoka University*

Abstract

Biofilm (BF) is a unique habitat for bacteria, and reveal a tolerance to many kinds of drugs. Staphylococcus aureus forms BF in necrotic tissue and/or on indwelling medical devices. Due to the difficulties in eradicating BF, more effective bactericidal drugs are necessary. In this study, we examined the effect of silver sulphadiazine on BF. A clinically isolated MRSA strain, great BF former, was used. BF on a plastic chip were prepared by incubation of bacteria at 37℃ for 18 and 36 hours, namely BF18H and BF36H, respectively. Bacteria in planktonic (PK) and BF were incubated in media containing serially diluted silver sulphadiazine (AgSD), $AgNO_3$ (Ag), or sulphadiazine (SD), and the minimum inhibitory concentration (MIC), minimum bactericidal concentration (MBC), and minimum biofilm eradicating concentration (MBEC) were analyzed. The AgSD-MIC against PK, BF18H, and BF36H were the same level (125 μg/mL), although MBC level increased in BFs compared to PK, and, in MBEC, a further increment was detected in BF36H. When comparing AgSD with Ag and SD, the same levels of MIC were found in AgSD and Ag, however SD did not induce growth inhibition in any concentrations. Whereas, Ag itself induced higher MBC and MBEC levels than AgSD. Microscopically, AgSD alone accumulated on the BF. In a wound infection mouse model, bacterial colonies formed on the wound surface were effectively eliminated by AgSD, but tissue damage was minimal. In conclusion, the present results show that in accordance with BF maturation, drug resistance property increases. AgSD, as a complex of Ag and SD, accumulates on BF formed by MRSA, and manifests eradicative property. AgSD may be thus a pharmacologically effective bactericidal drug for eradication of BF in wounds.

Key words: Biofilm, Silver sulfadiazine, MIC, MBC, MBEC, MRSA, Wound infection