

## Protective effect of low-concentration chlorine dioxide gas against influenza A virus infection

Norio Ogata and Takashi Shibata

Research Institute, Taiko Pharmaceutical Co. Ltd, 3-34-14 Uchihonmachi, Suita, Osaka 564-0032, Japan

### ABSTRACT

Influenza virus infection is one of the major causes of human morbidity and mortality. Between humans, this virus spreads mostly via aerosols excreted from the respiratory system. Current means of prevention of influenza virus infection are not entirely satisfactory because of their limited efficacy. Safe and effective preventive measures against pandemic influenza are greatly needed. We demonstrate that infection of mice induced by aerosols of influenza A virus was prevented by chlorine dioxide (ClO<sub>2</sub>) gas at an extremely low concentration (below the longterm permissible exposure level to humans, namely 0.1 ppm). Mice in semi-closed cages were exposed to aerosols of influenza A virus (1 LD<sub>50</sub>) and ClO<sub>2</sub> gas (0.03 ppm) simultaneously for 15 min. Three days after exposure, pulmonary virus titre (TCID<sub>50</sub>) was 102.6±1.5 in five mice treated with ClO<sub>2</sub>, whilst it was 106.7±0.2 in five mice that had not been treated (*P*=0.003). Cumulative mortality after 16 days was 0/10 mice treated with ClO<sub>2</sub> and 7/10 mice that had not been treated (*P*=0.002). In *in vitro* experiments, ClO<sub>2</sub> denatured viral envelope proteins (haemagglutinin and neuraminidase) that are indispensable for infectivity of the virus, and abolished infectivity. Taken together, we conclude that ClO<sub>2</sub> gas is effective at preventing aerosol-induced influenza virus infection in mice by denaturing viral envelope proteins at a concentration well below the permissible exposure level to humans. ClO<sub>2</sub> gas could therefore be useful as a preventive means against influenza in places of human activity without necessitating evacuation.

### DISCUSSION

We have demonstrated that ClO<sub>2</sub> gas at an extremely low concentration can prevent influenza A virus infection of mice caused by aerosols. According to the US occupational Safety and Health Administration, the 8 h permissible exposure level of ClO<sub>2</sub> in human workplaces is 0.1 ppm. The level of ClO<sub>2</sub> gas (0.03 ppm) used in this study is well below this level, and our results indicate that ClO<sub>2</sub> at this level could be used in the presence of humans to prevent their infection by influenza A virus and possibly other related virus infections of the respiratory tract. Specifically, ClO<sub>2</sub> gas could be used in places such as offices, theatres, hotels, schools and airport buildings without evacuating people, thus not interrupting their normal activities.