

EV1099

ePoster Viewing

Virology non-HIV/non-hepatitis

**Neutralizing antibody activity of human intravenous immunoglobulin (IVIG) against enteroviruses causing hand, foot and mouth disease**

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**Objective:** Microneutralization (microNT) and plaque reduction neutralization (PRNT) assays were conducted to determine the neutralizing antibody activity of intravenous immunoglobulin (IVIG) against various strains of enterovirus 71 (EV71) and Coxsackievirus A16 (CA16) isolated in Thailand.

**Methods:** Four lots of IVIG from manufacturers in 2 Asian countries were assayed against 4 strains of EV71 (B5/2011, B5/2013, C4a/2014 and C4b/2006); and 2 strains of CA16 (B2/2011 and B2/2012) for 50% inhibitory concentration (IC<sub>50</sub>) by cytopathic effect (CPE)-based microNT assay in Vero cell monolayers in duplicate. Moreover, PRNT assay for % inhibition was employed in triplicate as the supplementary test. IVIG at concentration of 10 mg/ml was cytotoxic; therefore, the initial concentration of 5 mg/ml was serially 2-fold diluted to the final concentration of 0.039 mg/ml and assayed against the test viruses at virus doses of 100, 25 and 10 TCID<sub>50</sub>. The last IVIG concentration that exhibited ≤50% CPE in the infected monolayers was defined as the IC<sub>50</sub> value. PRNT assay was performed using IVIG at concentrations of 2.5 and 5 mg/ml using the virus dose of 100 PFU/ml. % inhibitions were calculated based on % reduction in plaque numbers as compared to the virus control.

**Results:** This study showed that all 4 lots of IVIG yielded similar results as tested against all virus strains. At the virus concentration of 10 TCID<sub>50</sub>, 3 of 4 EV71 strains yielded the IC<sub>50</sub> values varying from 0.078 to 0.625 mg/ml and C4a/2014 was not inhibited at all; while both CA16 strains yielded the IC<sub>50</sub> values varying from 0.156 to 1.25 mg/ml. At the virus concentration of 25 TCID<sub>50</sub>, only EV71 B5/2011 and EV71 C4b/2006 were inhibited and yielded the IC<sub>50</sub> values varying from 0.078 to 0.625 mg/ml; and also, only one strain of CA16 isolated in 2012 was inhibited and yielded the IC<sub>50</sub> values varying from 0.625 to 1.25 mg/ml. At the virus concentration of 100 TCID<sub>50</sub>, EV71 B5/2011 was the only strain inhibited with IC<sub>50</sub> of 0.312 mg/ml; and none of CA16 was inhibited. EV71 C4a/2014, the only strain that was not inhibited by any IVIG concentrations was further investigated by PRNT, together with EV71 B5/2011 and CA16/2012 as the positive controls. The results showed that EV71 B5/2011 was inhibited and yielded % inhibition of 88 and 97% for IVIG concentration of 2.5 and 5 mg/ml, respectively; and CA16/2012 yielded 100% inhibition with both IVIG concentrations. Nevertheless, EV71 C4a/2014 was poorly inhibited with % inhibition of 31-32%.

**Conclusion:** In Thailand, IVIG is routinely prescribed as a therapeutic agent for HFMD patients who developed neurological and/or cardiopulmonary complications. Not only to modulate the immune response, we showed that IVIG prepared from blood of Asian people also contain neutralizing antibody activity against EV71 and CA16.