HYPERIMMUNE INTRAVENOUS IMMUNOGLOBULIN TREATMENT: A MULTICENTRE DOUBLE-BLIND RANDOMISED CONTROLLED TRIAL FOR PATIENTS WITH SEVERE A(H1N1)PDM09 INFECTION

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BACKGROUND: Experience from influenza pandemics suggested that convalescent plasma treatment given within 4 to 5 days of symptom onset might be beneficial. However, robust treatment data are lacking.

METHODS: This was a multicentre prospective double-blind randomised controlled trial. Convalescent plasma from patients who recovered from the 2009 pandemic influenza [A(H1N1)pdm09] infection was fractionated to hyperimmune intravenous immunoglobulin (H-IVIG) by CSL Biotherapies, Australia. Patients with severe A(H1N1)pdm09 infection on standard antiviral treatment requiring intensive care and ventilatory support were randomised to receive H-IVIG or normal IVIG manufactured before 2009 as control. Clinical outcome and adverse effects were compared.

RESULTS: Between 2010 and 2011, 35 patients were randomised to receive H-IVIG (17 patients) or IVIG (18 patients). One defaulted patient was excluded from analysis. No adverse event related to treatment was reported. Baseline demographics and viral load before treatment were similar between the two groups. Serial respiratory viral load demonstrated that H-IVIG treatment was associated with significantly lower day 5 and 7 post-treatment viral load when compared to the control ($P = 0.04$ and $P = 0.02$, respectively). The initial serum cytokine level was significantly higher in the H-IVIG group but fell to similar level 3 days after treatment. Subgroup multivariate analysis of the 22 patients who received treatment within 5 days of symptom onset demonstrated that H-IVIG treatment was the only factor which independently reduced mortality (odds ratio = 0.14; 95% confidence interval, 0.02-0.92; $P = 0.04$).

CONCLUSIONS: Treatment of severe A(H1N1)pdm09 infection with H-IVIG within 5 days of symptom onset was associated with a lower viral load and reduced mortality.

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