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Harvesting Convalescent Plasma for Hyperimmune Intravenous Globulin Production: A Multicentre, Randomised Double-Blind Controlled Trial for Treatment of Patients with Serious S-OIV H1N1 Infection

Ivan Fan-Ngai Hung[1,2], Kelvin Kai-Wang To[1], Cheuk-Kwong Lee[3], Kar-Lung Lee[4], Wing-Wa Yan[5], Kenny Chan[5], Wai-Ming Chan[6], Chun-Wai Ngai[6], Kin-Ip Law[4], Fu-Loi Chow[7], Raymond Liu[8], Kang-Yiu Lai[9], Candy CY Lau[1], Shao-Haei Liu[10], Kwok-Hung Chan[1], Che-Kit Lin[2], Kwok-Yung Yuen[1]
[1]Carol Yu Centre for Infection and Division of Infectious Diseases, Queen Mary Hospital, State Key Laboratory of Emerging Infectious Diseases, The University of Hong Kong, Hong Kong, [2]Department of Medicine, Queen Mary Hospital, The University of Hong Kong, Hong Kong, [3]Hong Kong Red Cross Blood Transfusion Service, Hong Kong, [4]Department of Intensive Care Unit, United Christian Hospital, Hong Kong, [5]Department of Intensive Care Unit, Pamela Youde Nethersole Eastern Hospital, Hong Kong, [6]Department of Anaesthesia and Intensive Care Unit, Queen Mary Hospital, Hong Kong, [7]Department of Medicine and Geriatrics, Intensive Care Unit, Caritas Medical Centre, Hong Kong, [8]Department of Medicine, Ruttonjee Hospital and Tang Shiu Kin Hospitals, Hong Kong, [9]Department of Intensive Care Medicine, Queen Elizabeth Hospital, Hong Kong, [10]Department of Infection, Emergency & Contingency, Hospital Authority, Hong Kong

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 is lacking.

Methods: This is a multicentre prospective double-blind randomized 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 randomized to receive H-IVIG or normal IVIG manufactured before 2009 as control. Clinical outcome and adverse effects were compared.

Results: Between 2010 and 2011, thirty-five patients were randomized 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 [OR:0.14, 95% CI, 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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In Silico Structure-based Screening and Characterization of Inhibitors for Influenza A Virus Nucleoprotein

Chun-Yeung Lo[1], Ming Liu[1], Lit-Man Poon[2], Pang-Chui Shaw[1]
[1]Centre for Protein Science and Crystallography, School of Life Sciences, The Chinese University of Hong Kong, Hong Kong, [2]Centre of Influenza Research and School of Public Health, The University of Hong Kong, Hong Kong

The trend of drug resistance developed in different strains of influenza viruses is worrying, and it is of utmost importance and urgency to develop new drugs against this virus. The viral nucleoprotein (NP) is a major component of the ribonucleoprotein (RNP) complex for the transcription and replication of the virus. In order to maintain a stable RNP structure, NP forms homo-oligomers by inserting its tail-loop to the tail-loop insertion site of another NP. In this study, we have employed structure-based virtual screening on the influenza A NP tail loop insertion site and found two hit compounds number 7 and 16 that can subdue influenza RNP activities. Subsequently, two analogs from compound 16 were identified which inhibit RNP activities of various influenza A subtypes and viral growth at micromolar levels. These analogs were also shown to directly interact with NP at 12.0 ± 1.25 and 41.6 ± 1.93 μM respectively by surface plasmon resonance assay. These novel anti-influenza compounds would provide a template for designing drug candidates with higher potency.

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A Detailed Longitudinal Study of Infection Attack Rates among Healthy Adults in Hong Kong during the Epidemic of the Human Swine Influenza A/H1N1 Virus in 2009

Joseph Wu[1], Andrew Ho[1], Edward Ma[1], Cheuk Kwong Lee[2], Daniel Chu[1], Po Lai Ho[1], Ivan Hung[1], Lai Ming Ho[1], Che Kit Lin[2], Thomas Tsang[3], Su Vui Lo[4], Yu Lung Lau[1], Gabriel Leung[1], Benjamin Cowling[1], Malik Peiris[1]
[1]The University of Hong Kong, Hong Kong, [2]Red Cross Blood Transfusion Services, Hong Kong, [3]Centre for Health Protection, Hong Kong, Hong Kong, [4]Hospital Authority, Hong Kong

Background: In an emerging influenza pandemic, estimating severity (the probability of a severe outcome, such as hospitalization, if infected) is a public health priority. As many influenza infections are subclinical, sero-surveillance is needed to allow reliable real-time estimates of infection attack rate (IAR) and severity.

Methods and Results: We tested 14,766 sera collected during the first wave of the 2009 pandemic in Hong Kong using viral microneutralization. We estimated IAR and infection-hospitalization probability (IHP) from the serial cross-sectional serologic data and hospitalization data. Had our serologic data been available weekly in real time, we would have obtained reliable IHP estimates 1 wk after, 1-2 wk before, and 3 wk after epidemic peak for individuals aged 5-14 y, 15-29 y, and 30-59 y. The ratio of IAR to pre-existing seroprevalence, which decreased with age, was a major determinant for the timeliness of reliable estimates. If we began sero-surveillance 3 wk after community transmission was confirmed, with 150, 350, and 500 specimens per week for individuals aged 5-14 y, 15-19 y, and 20-29 y, respectively, we would have obtained reliable IHP estimates for these age groups 4 wk before the peak. For 30-59 y olds, even 800 specimens per week would not have generated reliable estimates until the peak because the ratio of IAR to pre-existing