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## Corticosteroids do not cause harmful increase of viral load in severe H1N1 virus infection

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Dear Editor,  
Detractors of corticosteroids use in patients affected by severe H1N1 virus infections advocate the World Health Organization (WHO) statements to support their argumentations [1]. However, it should be noted that some of WHO's recommendations are not evidence-based. WHO recommendations that "corticosteroids should be avoided" in severely ill H1N1-infected patients seem to be based on the possibility of viral

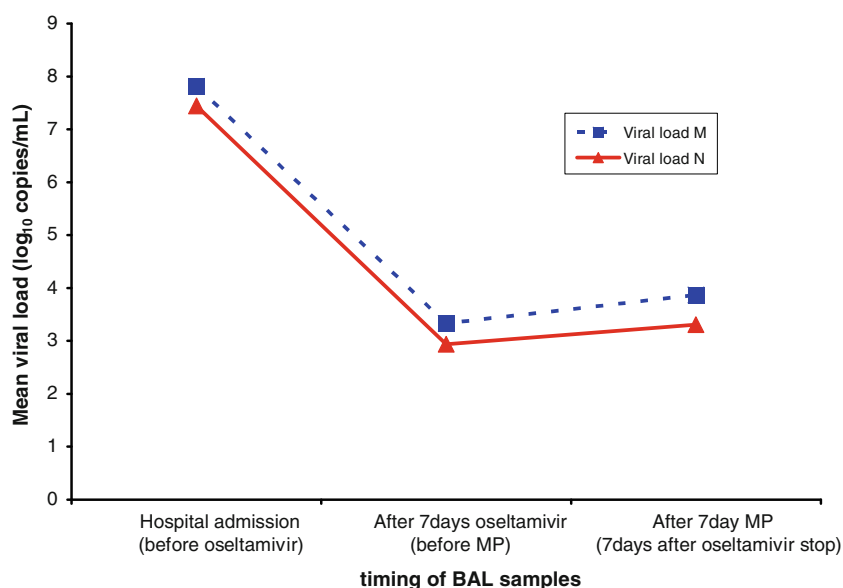
shedding by using corticosteroids during severe H1N1 infection [2]. Really, there is not any evidence in the literature that the viral load could return to peak levels for the administration of corticosteroids, whilst only the detection of some viral RNA in body samples during convalescence may have no clinical significance [3]. Moreover, data from quantitative analysis of viral shedding may have more important implications for formulating clinical prognosis and risks.

We had the opportunity to treat with methylprednisolone (MP) infusion (1 mg/kg/24 h) a previously healthy 30-year-old man with H1N1-related acute respiratory distress syndrome (ARDS) and severe sepsis who did not respond to oseltamivir (150 mg bid for 7 days) started 4 days after the onset of symptoms.

Molecular diagnosis of pandemic influenza H1N1 virus infection was performed on bronchoalveolar lavage (BAL) with the CDC Realtime RTPCR (rtPCR) on hospital admission and a viral load profile was assessed on weekly repeated BAL samples. The quality of RNA purified from the samples was assessed by an rRTPCR

primers/probe panel directed to the human RNase P gene (Invitrogen SuperScript™ III Platinum® One-Step Quantitative Kit). At ICU admission, the physician in charge avoided treating the patient with corticosteroids in accordance with the recommendations of WHO, but after a week of oseltamivir, protective mechanical ventilation (MV), pronation, and extracorporeal membrane oxygenation (ECMO), the patient was still in a life-threatening condition, so MP infusion was initiated. Within a few days, the patient significantly improved and, after 6 and 10 days, respectively, he was weaned from ECMO and MV without any major adverse effect. The initial viral load in BAL before oseltamivir was  $6.54 \times 10^8$  copies/ml, then reduced to  $2.14 \times 10^3$  copies/ml when oseltamivir stopped and MP started, and mildly increased to a maximum of  $7.40 \times 10^3$  copies/ml after 7 days of MP infusion (Fig. 1). The magnitude of virus copies amount was consistent with a clear reduction in comparison to the initial viral load in spite of adjunct corticosteroids. The viral load was determined by using the Quantification of Swine H1N1 Influenza Human

**Fig. 1** Treatment time course and viral load profile on BAL samples. Quantification of viral load was performed by using M1 (viral load M) and N1 (viral load N) primers/probes directed to regions of matrix and neuraminidase genes, respectively. MP methylprednisolone, BAL bronchoalveolar lavage, M matrix gene, N neuraminidase gene



Pandemic Strain-Advanced Kit (PrimerDesign, Southampton, UK). No viral mutations associated with virulence (D222G) and resistance to oseltamivir (H274Y) were detected by sequencing Ha and NA genes.

The efficacy of corticosteroids needs to be adequately demonstrated in patients with severe influenza. Nevertheless, at least a third of H1N1 cases in the literature were treated with corticosteroids [4] with some indication of a favourable outcome [5] and no report of harmful consequences [4]. The supposed viral shedding by corticosteroids use should not be advocated to avoid corticosteroid therapy in H1N1 severe infections, but it should be determined with quantitative viral load profile.

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