Reply to Kadhiravan

TO THE EDITOR—We appreciate Dr Kadhiravan’s comments [1], which reflect the current debate on the efficacy of the neuraminidase inhibitor (NAI) antiviral drugs in the context of limited data from randomized controlled trials, including no trials conducted among hospitalized adults.

We reviewed records of adults requiring intensive care for influenza A(H1N1) pdm09 illness during a period when all such cases were required to be reported in California [2]. During the pandemic, patients’ hospital records were often incomplete. As an example, immunization status was documented in <5% of our cases. However, the proportions of survival in NAI-treated and untreated patients who became ill before 15 September 2009 (73% vs 55%; \( P = .0007 \)), prior to the largest wave of illness and to the availability of H1N1 pdm vaccine, were similar to the proportions during the entire pandemic (75% vs 58%; \( P < .0001 \)), suggesting that either strain-specific immunization or other differences between the early and later phases of the pandemic had limited effect on survival.

Dr Kadhiravan appropriately questions whether patients with influenza A (H1N1) pdm09 illness who were not treated had a lower rate of survival because they were sicker than those who received NAIs, irrespective of treatment. Although we cannot definitively resolve this concern, as reported in Table 1 of our article [2], we note that both groups were equally likely (62% vs 59%; \( P = .44 \)) to have received mechanical ventilation during their illness. Moreover, within the subset of intubated cases, patients treated with NAIs were more likely to survive than untreated patients (60% vs 34%; \( P < .0001 \)).

Dr Kadhiravan wonders whether the longer median length of hospital stay in NAI-treated versus untreated patients (10 days vs 6 days; \( P < .0001 \)) reflects more severe disease in untreated patients, as a higher mortality rate may have reduced average hospital stay. Further analysis of our data found that the median length of hospital stay was no shorter in treated than in untreated survivors, whether in all survivors (9 days vs 6 days; \( P = .0001 \)), or in the proportion of treated survivors with the briefest hospitalizations equal to the proportion of all untreated patients who survived (58% of each group, 7 days vs 6 days; \( P = .02 \)). This would be consistent with treated patients being at least as severely ill before therapy as untreated patients; clinicians’ decisions to initiate NAIs may have been based in part on their perception of severity of illness.

A recent systematic review of the evidence concluded that early initiation of NAI treatment reduced the likelihood of severe outcomes during the 2009–2010 influenza A (H1N1) pandemic, compared with late or no treatment [3]. We agree with Dr Kadhiravan that blinded-dose studies or placebo-controlled studies can help to resolve the uncertainty that we face with evidence from current observational studies.

Note

Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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References


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