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## Corticosteroids for H1N1 associated acute lung injury: is it just wishful thinking?

Accepted: 3 December 2009  
Published online: 30 March 2010  
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The author's reply to this comment is available at:  
doi:10.1007/s00134-010-1816-6.

Dear editor: When challenged by a potentially life-threatening infection, intensivists are frequently inclined to prescribe adjunctive therapies with so called immunomodulating effects. However, the story of anti-inflammatory therapies in severe infections has been so far a story of disenchantment. Most of it may be ascribed to an incomplete knowledge of immune and acute phase responses. Corticosteroids have recently been caught in the midst of a huge controversy regarding their indication for severe sepsis. Despite clear evidence of anti-inflammatory effects and of clinical benefit in small single center trials, the alleged survival benefits were not subsequently confirmed by the CORTICUS study. In a paper published in *Intensive Care Medicine*, Dr Quispe-Laime et al. [1] report their findings regarding the use of corticosteroids in patients with H1N1 influenza A virus-associated acute lung injury. The authors found significant improvement in oxygenation and a relatively low mortality rate. However, we have several concerns regarding the study's rationale, methodology, results and conclusions.

Recent systematic reviews do not support the use of corticosteroids for severe community-acquired pneumonia. Recent experimental data showed no beneficial effect on acute respiratory distress syndrome caused by the H5N1 infection [2]. A review evaluating the effects of adjunctive therapies in SARS patients concluded that among 29 trials of systemic corticosteroids, 25 were inconclusive and four were associated with harm [3]. Also, the recent WHO guidelines disapprove the use of corticosteroids as they are “of unproven benefit and potentially harmful” for patients with H1N1 infection. Therefore, the use of corticosteroid as adjunctive therapy for patients with severe H1N1 infection should be viewed as experimental and with extreme caution.

Therefore, we believe that according to the current rules from the International Committee of Medical Journal Editors, patients included in an evaluation of the potential benefits of corticosteroids as adjunctive therapy in H1N1 influenza A virus-associated acute lung injury should have been asked to give written informed-consent [1]. Even in the event of the use of corticosteroids as a rescue therapy for refractory or persistent ARDS, close supervision to identify potential harms frequently associated with corticosteroids should have been implemented.

The present study has additional methodological shortcomings, namely a very small sample size of proven H1N1 infection; only eight patients! The small sample size and the lack of a control group (not treated with corticosteroids) preclude any sound conclusion on the hypothetical benefits of this therapy in H1N1 infection. Moreover, although the authors state that their mortality rate was low (15%), it is actually similar to the rates reported by the Canadian [4] and ANZICS [5] cohorts, where

barely half of the patients received corticosteroids.

In conclusion, we believe that data from this small case series from Quispe-Laime et al. [1] is, at best, a hypothesis-generating one and should not be translated into clinical practice. The assessment of the hypothetical beneficial role of corticosteroids in H1N1 infection should be done with a more careful methodology. This will avoid unnecessary risk and harm to highly susceptible patients.

## References

1. Quispe-Laime AM, Bracco JD, Barberio PA, Campagne CG, Rolfo VE, Umberger R, Meduri GU (2009) H1N1 influenza A virus-associated acute lung injury: response to combination oseltamivir and prolonged corticosteroid treatment. *Intensive Care Med* 36:33–41
2. Xu T, Qiao J, Zhao L, He G, Li K, Wang J, Tian Y, Wang H (2009) Effect of dexamethasone on acute respiratory distress syndrome induced by the H5N1 virus in mice. *Eur Respir J* 33:852–860
3. Stockman LJ, Bellamy R, Garner P (2006) SARS: systematic review of treatment effects. *PLoS Med* 3:e343
4. Kumar A, Zarychanski R, Pinto R, Cook DJ, Marshall J, Lacroix J, Stelfox T, Bagshaw S, Choong K, Lamontagne F, Turgeon AF, Lapinsky S, Ahern SP, Smith O, Siddiqui F, Jovet P, Khwaja K, McIntyre L, Menon K, Hutchison J, Hornstein D, Joffe A, Lauzier F, Singh J, Karachi T, Wiebe K, Olafson K, Ramsey C, Sharma S, Dodek P, Meade M, Hall R, Fowler RA (2009) Critically ill patients with 2009 influenza A(H1N1) infection in Canada. *Jama* 302:1872–1879
5. Webb SA, Pettila V, Seppelt I, Bellomo R, Bailey M, Cooper DJ, Cretikos M, Davies AR, Finfer S, Harrigan PW, Hart GK, Howe B, Iredell JR, McArthur C, Mitchell I, Morrison S, Nichol AD, Paterson DL, Peake S, Richards B, Stephens D, Turner A, Yung M (2009) Critical care services and 2009 H1N1 influenza in Australia and New Zealand. *N Engl J Med* 361:1925–1934

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