Intensive Care Med (2011) 37:1563–1564
DOI 10.1007/s00134-011-2289-y

A. J. Petros
J. H. Rommes
L. Silvestri
N. Taylor
H. K. F. van Saene

Early steroid therapy for patients with H1N1 influenza A virus infection

Accepted: 3 April 2011
Published online: 21 June 2011

An author's reply to this comment is available at: doi:10.1007/s00134-011-2290-5.

Dear Editor,

We read with interest Martin-Loeches and colleagues' study on the use of early corticosteroid therapy in patients with H1N1 influenza A infection [1]. The authors retrospectively analysed data within the registry of the European Society of Intensive Care, and compared a mixture of patients with suspected, probable or confirmed H1N1 influenza A infection who received corticosteroids early, later or not at all. They conclude that the early use of steroids did not result in reduced morbidity or mortality and was associated with an increased risk of infection. We would like to comment on these conclusions.

With regard to morbidity, hospital-acquired pneumonia (HAP) was more frequent in patients receiving early steroids than those who did not (odds ratio [OR] 2.2, 95% confidence interval [CI] 1.1–4.5). However, patients included in the early corticosteroid group were significantly older; had received significantly more chronic steroid therapy; were significantly more affected by asthma and chronic obstructive pulmonary disease (COPD); and were significantly sicker than those in the control group.

After adjusting for severity of illness alone the OR was unchanged, but the CI widened and the lower confidence limit equalled unity (OR 2.2, 95% CI 1.0–4.8), less than unity would suggest non-significance. However, the authors did not describe any modelling for the other potential confounding variables of age, asthma, COPD and previous chronic use of steroids. These are all risk factors for carriage and overgrowth of abnormal flora, including *Pseudomonas aeruginosa* and *Acinetobacter baumannii*, and predispose to lower airway infection [2]. Had appropriate adjustment for these variables been made it is feasible that the results of the study might have not demonstrated a difference. In a recent French study on the same topic, patients with asthma, COPD and chronic use of steroids were correctly excluded [3].

The control group included a mixed population of patients, some who never received steroids but also some who received them subsequently. Data on this subgroup of patients who might have received later steroids were not available to the authors and therefore not taken into account while performing the multivariate analysis, both for HAP and mortality. The authors acknowledged this as an important limitation.

With regard to mortality, we are not surprised that this was not significantly reduced by early steroid therapy after adjusting for illness severity, age, COPD, asthma and chronic steroid use, including also the cohort of patients who presented with acute respiratory distress syndrome (ARDS). This may be due to a substantial number of patients receiving steroids in the control group, as there is evidence that low-to-moderate dose glucocorticoid therapy reduces mortality [4].

As the study was retrospective and observational, all imbalances both between and within the two groups should have been minimised. A proper statistical approach using a rigorous adjustment for the differences in baseline characteristics or a matched case–control analysis should be employed [3, 5]. We believe that as this study did neither, it is sadly flawed and hence no firm conclusions can be drawn about the use of early steroids in intensive care unit (ICU) patients.

References

1. Martin-Loeches I, Lisboa T, Rhodes A, Moreno RP, Silva E, Sprung C, Chiche JD, Barahona D, Villabon M, Balasini C, Pearse RM, Matos R, Rello J, CM ESI, H1N1 Registry Contributors (2011) Use of early corticosteroid therapy on ICU admission in patients affected by severe pandemic (H1N1)v influenza A infection. Intensive Care Med 37:272–283. doi: 10.1007/s00134-010-2078-z
2. Silvestri L, Mino G, van Saene HKF (2005) Colonisation and infection. In: van Saene HKF, Silvestri L, de la Cal MA (eds) Infection control in the intensive care unit, 2nd edn. Springer, Milan, pp 37–48
3. Brun-Buisson C, Richard JCM, Mercat A, Thiebaut ACM, Brochard L, for the 2009 REVA-SRLF A/H1N1v Registry Group (2011) Early corticosteroids in severe influenza A/H1N1 pneumonia and acute respiratory distress syndrome. Am J Respir Crit Care Med 4:2011. doi: 10.1164/rccm.201101-0135OC
4. Meduri GU, Annane D, Chrousos GP, Marik PE, Sinclair SE (2009) Activation and regulation of systemic inflammation in ARDS. Rationale for prolonged glucocorticoid therapy. Chest 136:1631–1643
5. Kim SH, Hong SB, Yun SC, Choi WI, Ahn JJ, Lee YJ, Lee HB, Lim CM, Koh Y, for the Korean Society of Critical Care Medicine H1N1 Collaborative (2011) Corticosteroid treatment in critically ill patients with pandemic influenza A/H1N1 2009 infection: analytic strategy using propensity scores. Am J Respir Crit Care Med 4:2011. doi: 10.1164/rccm.201101-0110OC

A. J. Petros
Paediatric and Neonatal Intensive Care Unit, Great Ormond Street Hospital for Children, London, UK
e-mail: petroa@cats.nhs.uk

J. H. Rommes
Department Intensive Care, Gelre Ziekenhuizen, Apeldoorn, The Netherlands
e-mail: h.rommes@gmail.com

L. Silvestri
Unit of Anesthesia and Intensive Care, Department of Emergency, Presidio Ospedaliero, Gorizia, Italy
e-mail: lucianosilvestri@yahoo.it

N. Taylor · H. K. F. van Saene (✉)
Institute for Ageing and Chronic Disease, University of Liverpool, Liverpool, UK
e-mail: nia.taylor@liv.ac.uk