Editorial

Potential application of electronic healthcare records to the effectiveness study of the treatment of emerging virus diseases

Zhongheng Zhang

Department of Emergency Medicine, Sir Run-Run Shaw Hospital, Zhejiang University School of Medicine, Hangzhou 310016, China
Correspondence to: Zhongheng Zhang. No. 3, East Qingchun Road, Hangzhou 310016, China. Email: zh_zhang1984@hotmail.com.
Comment on: Fedson DS. Treating the host response to emerging virus diseases: lessons learned from sepsis, pneumonia, influenza and Ebola. Ann Transl Med 2016;4:421.

Received: 17 April 2017; Accepted: 17 April 2017; Published: 26 May 2017.
doi: 10.21037/jeccm.2017.05.02
View this article at: http://dx.doi.org/10.21037/jeccm.2017.05.02

In a long review article entitled "Treating the host response to emerging virus diseases: lessons learned from sepsis, pneumonia, influenza and Ebola", Fedson provided insightful thoughts on the development of effective treatment drugs for emerging virus diseases (1). Since the development of novel drugs targeting each of the emerging viruses are costly, the target to the host response which is a common final pathway for the pathogenesis of virus diseases, would be a promising target. The author enumerated some successful drugs such as the statins and angiotensin receptor blockers. No matter what the upstream causes it is, the host responses to virus infection share the same mechanisms such as endothelial dysfunction, over-activation of the immune system. However, these potentially attractive drugs have not been proven to be effective in reducing mortality outcomes. In patients with acute respiratory distress (ARDS) and/or sepsis, none of the randomized controlled trials have reported the efficacy of statin in reducing mortality (2-4), though the statin was found to be safe in these patient populations. The futility of these trials may be attributable to the low dose and late initiation. In a study, the statin was initiated for a mean of eight days after mechanical ventilation (3). The host responses can be quite different at different stages of infection. Results from bench work have shown that the host experiences immunosuppression and immune hyperactivity phases. These phases can overlap with each other, and the potential targets of different phases can be different (5). Another example is the use of corticosteroids for the treatment of ARDS. In theory, corticosteroids are able to inhibit inflammatory response to exogeneous pathogens, and ARDS is associated with hyperactive response of the immune system. However, the biological efficacy has not been translated to clinical effectiveness and studies have failed to identify beneficial effects of corticosteroids in ARDS (6).

Due to the complexities of interactions between host response and drugs, it can be difficult to perform RCTs with sufficient power to detect difference between control and treatment arms. Also, there may be potential unknown interactions between anti-inflammatory drugs and other treatment strategies such as fluid resuscitation, vasopressors and mechanical ventilations. In other words, patients treated in the intensive care unit (ICU) typically require multi-disciplinary approaches. Given five interventions, there can be 2^5=32 combinations of two treatments. It is impossible to perform RCTs to investigate the effectiveness of combination therapies. In such a situation, the use of electronic healthcare records (EHR) big data can provide some useful insights into the potential interactions between treatments. If a certain combination of treatments is found to be effective in reducing mortality, further RCTs can be specifically designed for the combination. Since the use of existing EHR is resource-saving, with less ethical constraints than RCTs, the complex interactions between timing, dosing and type of drugs can be investigated. In an observational cohort study, Mansur A and colleagues found that statin was effective in severe sepsis-induced ARDS (7). Actually, the ARDS encompasses case mix with different causes and severities, and the effectiveness of statin can only be effective in a subgroup of the case mix. However, observational studies are subject to confounding and false positives. Thus, the results can only be served as hypothesis-

generating and subsequent RCTs are still mandatory for its validation.

Big-data study is a concept emerged with the development of information technology. The size of information that investigators can obtain in the era of big data is far bigger than the information collected and managed by hand. All conventional methodologies in epidemiology and statistics are applicable to big-data study. New analytics such as statistical learning and machine learning techniques are powerful when big-data is available. It has been proven that artificial intelligence surpassed human brain for medical diagnosis (8-11). Classification methods such as nearest neighbors, neural networks and decision tree are potentially useful for the determination of subgroup of sepsis/ARDS patients who will benefit the most from treatments with statin and/or angiotensin receptor blockers (12,13).

Acknowledgements

None.

Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

References

1. Fedson DS. Treating the host response to emerging virus diseases: lessons learned from sepsis, pneumonia, influenza and Ebola. Ann Transl Med 2016;4:421.
2. Novack V, Eisinger M, Frenkel A, et al. The effects of statin therapy on inflammatory cytokines in patients with bacterial infections: a randomized double-blind placebo controlled clinical trial. Intensive Care Med 2009;35:1255-60.
3. Papazian L, Roch A, Charles PE, et al. Effect of statin therapy on mortality in patients with ventilator-associated pneumonia: a randomized clinical trial. JAMA 2013;310:1692-700.
4. Tralhão AF, Cés de Souza-Dantas V, Salluh JI, et al. Impact of statins in outcomes of septic patients: a systematic review. Postgrad Med 2014;126:45-58.
5. Delano MJ, Ward PA. Sepsis-induced immune dysfunction: can immune therapies reduce mortality? J Clin Invest 2016;126:23-31.
6. Zhang Z, Chen L, Ni H. The effectiveness of Corticosteroids on mortality in patients with acute respiratory distress syndrome or acute lung injury: a secondary analysis. Sci Rep 2015;5:17654.
7. Mansur A, Steinau M, Popov AF, et al. Impact of statin therapy on mortality in patients with sepsis-associated acute respiratory distress syndrome (ARDS) depends on ARDS severity: a prospective observational cohort study. BMC Med 2015;13:128.
8. Zhang Z. Big data and clinical research: perspective from a clinician. J Thorac Dis 2014;6:1659-64.
9. Zhang Z. When doctors meet with AlphaGo: potential application of machine learning to clinical medicine. Ann Transl Med 2016;4:125.
10. Esteva A, Kuprel B, Novoa RA, et al. Dermatologist-level classification of skin cancer with deep neural networks. Nature 2017;542:115-8.
11. Gulshan V, Peng L, Coram M, et al. Development and Validation of a Deep Learning Algorithm for Detection of Diabetic Retinopathy in Retinal Fundus Photographs. JAMA 2016;316:2402-10.
12. Zhang Z. Decision tree modeling using R. Ann Transl Med 2016;4:275.
13. Zhang Z. A gentle introduction to artificial neural networks. Ann Transl Med 2016;4:370.

doi: 10.21037/jeccm.2017.05.02
Cite this article as: Zhang Z. Potential application of electronic healthcare records to the effectiveness study of the treatment of emerging virus diseases. J Emerg Crit Care Med 2017;1:8.

