Do We Really Understand the Pathophysiology and Clinical Impact of Poststroke Infection?

To the Editor:

We read with interest the article by Vargas et al,1 which reported the results of a prospective study of poststroke infection. Poststroke infection was found to correlate with stroke severity but not short-term outcome. There are several points about this study that require further discussion.

The authors need to clarify whether the clinical outcome was measured at hospital discharge (as mentioned in the Abstract and Table 3) or on day 7 (as mentioned in the Methods and Results sections). Clinical outcomes assessed at these 2 time-points could potentially be significantly different, especially because the median time to discharge was 9 days, and one-quarter of patients stayed for over 13 days. If outcome was indeed assessed on day 7, the authors should also explain how they handled the data for those patients who were discharged before day 7.

According to Table 1, acute bronchitis accounted for 38 of 90 (42%) poststroke infections. In contrast, pneumonia only accounted for 37% and urinary tract infections for 14%. Inclusion of acute bronchitis could potentially be problematic because of its nonspecific definition (ie, fever + bronchial secretions + leucocytosis + normal chest x-ray). Because fever, bronchial secretions and leucocytosis are all common findings after stroke, even without systemic infection, it is potentially difficult to clearly differentiate between infectious and noninfectious cases. Moreover, the systemic impact of acute bronchitis is unlikely to be as great as bacterial pneumonia.2 Therefore, inclusion of acute bronchitis might have contributed to the study’s failure to find a correlation between poststroke infection and outcome. Future studies should also explore other important aspects of poststroke infection, such as the impact of multiple infections, infection of different organs, noninfectious pyrexia, and the relationship with coagulation, inflammation and neurodegeneration.

There is another possible explanation for an apparent lack of correlation between poststroke infection and outcome. The authors used an outcome measure that might not be sensitive enough to detect a relatively small effect size (which is probably the case for poststroke infection). The modified Rankin Scale score (mRS) was dichotomized to ≥ or ≤2 to define poor or good outcome, respectively. Such dichotomization could reduce the statistical power and introduce bias, because the final mRS for each patient depends heavily on the baseline mRS on admission. Consequently, some experts have advised against the use of dichotomized outcomes in clinical trials.3 Future studies could also consider assessing other outcomes such as change in National Institutes of Health Stroke Scale (NIHSS; eg, between baseline and 1 week), and other surrogate markers of neuronal damage such as infarct volume. Moreover, it is important to assess longer term outcomes, recruit a larger number of patients, and include a wider range of stroke severity.

There is currently a deficiency in the basic understanding of the pathophysiology and clinical impact of poststroke infection. The authors have suggested several possible mechanisms that poststroke infection could cause further neuronal damage, such as electrolyte imbalance, fever and hypoxia, but these hypotheses are largely unproven. Poststroke infection is an important clinical problem because it is both common (occurring in up to 65% of stroke patients) and can impact on rehabilitation and outcome.4 However, whether, how and why poststroke infections can affect neurological and functional recovery remains unclear; for example, why do some patients experience severe neurological deterioration after an infection, whereas others are totally unaffected? Moreover, what is the therapeutic value of minocycline, which has been shown in animal experiments to have beneficial effects on inflammation, microglial activation, matrix metalloproteinases, nitric oxide production, and apoptotic cell death?5 More basic neuroscience and clinical research is needed in these important areas.

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