Early Treatment of Influenza by Combination Drug Therapy

E. Bart Tarbet*

In 2010, Ison and Lee described lessons learned from the 2009 pandemic [1]. It was noted that the clinical spectrum of influenza infection can overlap with other common respiratory infections making a clinical diagnosis of influenza difficult, especially in patients requiring hospitalization [2]. Ison and Lee suggested that influenza should be suspected as a cause of fever or respiratory symptoms in any hospitalized patient if influenza is circulating in the community [1]. In addition, they suggested that “antiviral therapy be started empirically and should not be delayed while awaiting test results” [1]. This is an idea that needs our support. However, fears of antiviral drug overuse leading to emergence of drug-resistant viruses prevent us from embracing the concept. Even though it has been shown that earlier treatment of high-risk individuals, and those requiring hospitalization, may result in improved clinical outcomes [3-5]. One early treatment option for influenza virus infections that could also reduce the threat of emerging drug-resistance is to use combination drug therapy [6].

During the 2009 influenza pandemic, the Institute for Antiviral Research at Utah State University held contracts from the National Institutes of Health to evaluate new antiviral drugs through the National Institute of Allergy and Infectious Diseases (NIAID) Collaborative Antiviral Testing Program. At that time we were asked to identify a treatment regimen for influenza using our animal models. Obviously, new antiviral drugs take years to develop, so our focus was on combinations of licensed drugs, or investigational drugs that were already in the process of licensure. We evaluated a number of therapeutic options and presented our results at the Influenza Combination Therapy Workshop, sponsored by the Division of Microbiology and Infectious Diseases (DMID/NIAID) in March of 2010. Those results, as well as the results from a number of other laboratories, suggests that combination antiviral therapy has the potential to improve the outcome following influenza virus infection, while also reducing the development of drug-resistance [7-13].

Concerns about emerging drug-resistance can lead to delays in effective therapy, and those delays are associated with higher rates of mortality, longer hospital stays, and increased medical costs [14-18]. In 1997, the Infectious Diseases Society of America (IDSA) and the Society for Healthcare Epidemiology of America (SHEA) jointly published recommendations for preventing and reducing antimicrobial resistance in U. S. hospitals [19]. In addition, it was recommended that each institution should have an effective antimicrobial stewardship program [20]. In 2007, the IDSA and SHEA released guidelines for the creation of antibiotic stewardship programs (ASPs) [21]. The major aim of these ASPs was to “optimize clinical outcomes while minimizing unintended consequences of antimicrobial use, including toxicity, and the emergence of resistance” [19]. Although mainly used to evaluate antibiotics, I suggest the use of the ASP model for evaluation of early antiviral treatment of high-risk patients and those requiring hospitalization for febrile respiratory illnesses. Ideally, an ASP will include an infectious disease-trained physician, a clinical pharmacist with infectious disease training, and a clinical microbiologist, who can provide surveillance data on drug-resistance patterns [22]. Use of the ASP model will provide a critical evaluation of early treatment on clinical outcome, and also ensure that early treatment regimens, including combination drug therapy, do not lead to emergence of new drug-resistant influenza viruses.

References


