Arch Clin Infect Dis. 2016 January; 11(1): e36309. doi: 10.5812/archcid.36309

Published online 2016 January 23. **Editorial**

The Impact of Statin on Influenza Vaccine Efficacy in the Elderly and Patients With Acute Respiratory Illness

Masoud Mardani[1,*]

[1]Infectious Diseases and Tropical Medicine Research Center, Shahid Beheshti University of Medical Sciences, Tehran, IR Iran

*Corresponding author: Masoud Mardani, Infectious Diseases and Tropical Medicine Research Center, Shahid Beheshti University of Medical Sciences, Tehran, IR Iran. Tel: +98-2122439963-8, Fax: +98-2122439964, E-mail: drmasoudmardani@yahoo.com

Received 2016 January 13; **Accepted** 2016 January 13.

Keywords: Statin, Influenza Vaccine, Acute Respiratory Illness

Statins are a class of drugs used to lower cholesterol levels by inhibiting the enzyme HMG-CoA reeducates. Considering the association between elevated cholesterol levels and the risk of cardiovascular diseases and because of studies show that statins can lower this risk, it is given to a large number of adults (1). In fact, it is estimated that more than one billion people worldwide take statins (2). Although the primary goal of statin therapy was to lower cholesterol levels, it was recognized that this drug class had other effects, including suppression of T-cell activation and immunomodulatory and anti-inflammatory effects (3, 4). Many patients who routinely take statins are the elderly who are at higher risk for the complications of influenza (5).

Statins are beneficial for cardiovascular diseases due to their lipid-lowering effect (6). They also exhibit anti-inflammatory and immunomodulatory properties, which not only contribute to their impact on cardiovascular disease, but can also affect the clinical course of a variety of infectious processes, including sepsis, bacteremia, community-acquired pneumonia and laboratory-confirmed influenza. Furthermore, statins affect vaccine responsiveness in individuals, and their widespread use could influence overall vaccine effectiveness (VE) in a population (7-11).

Based on a study, the immunosuppressive effect of statins on the vaccine immune response was most dramatic in individuals receiving synthetic statins. These effects were observed in both the adjuvanted and non-adjuvanted vaccine groups in the clinical trial. These results, if confirmed, could have implications both for future clinical trial designs, as well as vaccine use recommendations for the elderly (12). Also in another study, statin therapy was associated with reduced influenza VE against medically attended acute respiratory illness (MAARI). Many cases of MAARI are not caused by influenza; studies on the impact of statins on influenza VE against laboratory-confirmed influenza are needed (13).

Researchers observed that statin users had a significantly reduced to immune response to vaccination compared to those not taking statins, as measured by the level of antibodies to the flu vaccine strains in the patients' blood three weeks after vaccination. The effect was most dramatic in patients on synthetic statins, rather than naturally derived statins (14).

Apparently, statins interfere with the response to influenza vaccine and lower the immune response, and it seems to also result in a lower effectiveness of influenza vaccines. If confirmed, the findings could support the preferential use of high-dose flu vaccine or vaccines containing adjuvants to boost immune response in the elderly, in an attempt to counteract the apparent effect (15, 16).

Researchers in a study observed that vaccine effectiveness, to prevent serious respiratory illness, was lower among the patients taking statins compared to the ones not on statins, particularly when flu was widespread in the region. The findings have potential implications for guidelines regarding statin use in older adults around the vaccination time, but additional studies, including researches examining laboratory-confirmed cases of flu, are needed to provide more guidance (12, 13).

In conclusion the results of these studies should be viewed as hypothesis-generating and should prompt further investigations on whether statins reduce inactivated influenza vaccine immunogenicity and, if so, the mechanisms by which immune responses and associated vaccine effectiveness are adversely affected.

Acknowledgments

The author of manuscript appreciates Bita Pourkaveh for her contribution in collecting data and manuscript editing.

References

1. Lewington S, Whitlock G, Clarke R, Sherliker P, Emberson J, Halsey J, et al. Blood cholesterol and vascular mortality by age, sex, and blood pressure: a meta-analysis of individual data from 61 prospective studies with 55,000 vascular deaths. *Lancet.* 2007;**370**(9602):1829–39. doi: 10.1016/s0140-6736(07)61778-4. [PubMed: 18061058]
2. Ioannidis JP. More than a billion people taking statins?: Potential implications of the new cardiovascular guidelines. *JAMA.* 2014;**311**(5):463–4. doi: 10.1001/jama.2013.284657. [PubMed: 24296612]
3. Weitz-Schmidt G, Welzenbach K, Brinkmann V, Kamata T, Kallen J, Bruns C, et al. Statins selectively inhibit leukocyte function antigen-1 by binding to a novel regulatory integrin site. *Nat Med.* 2001;**7**(6):687–92. doi: 10.1038/89058. [PubMed: 11385505]
4. Jain MK, Ridker PM. Anti-inflammatory effects of statins: clinical evidence and basic mechanisms. *Nat Rev Drug Discov.* 2005;**4**(12):977–87. doi: 10.1038/nrd1901. [PubMed: 16341063]
5. Thompson WW, Shay DK, Weintraub E, Brammer L, Cox N, Anderson LJ, et al. Mortality associated with influenza and respiratory syncytial virus in the United States. *JAMA.* 2003;**289**(2):179–86. [PubMed: 12517228]
6. Taylor FC, Huffman M, Ebrahim S. Statin therapy for primary prevention of cardiovascular disease. *JAMA.* 2013;**310**(22):2451–2. doi: 10.1001/jama.2013.281348. [PubMed: 24276813]
7. Baigent C, Blackwell L, Emberson J, Holland LE, Reith C, Bhala N, et al. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170,000 participants in 26 randomised trials. *Lancet.* 2010;**376**(9753):1670–81. doi: 10.1016/s0140-6736(10)61350-5. [PubMed: 21067804]
8. Stroke Prevetion by Aggressive Reduction in Cholestrol Levels I, Karam JG, Loney-Hutchinson L, McFarlane SI. High-dose atorvastatin after stroke or transient ischemic attack: The Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Investigators. *J Cardiometab Syndr.* 2008;**3**(1):68–9. [PubMed: 18326981]
9. Bu DX, Griffin G, Lichtman AH. Mechanisms for the anti-inflammatory effects of statins. *Curr Opin Lipidol.* 2011;**22**(3):165–70. doi: 10.1097/MOL.0b013e3283453e41. [PubMed: 21412153]
10. Cannon CP, Braunwald E, McCabe CH, Rader DJ, Rouleau JL, Belder R, et al. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. *N Engl J Med.* 2004;**350**(15):1495–504. doi: 10.1056/NEJMoa040583. [PubMed: 15007110]
11. Ridker PM, Cannon CP, Morrow D, Rifai N, Rose LM, McCabe CH, et al. C-reactive protein levels and outcomes after statin therapy. *N Engl J Med.* 2005;**352**(1):20–8. doi: 10.1056/NEJMoa042378. [PubMed: 15635109]
12. Black S, Nicolay U, Del Giudice G, Rappuoli R. Influence of Statins on Influenza Vaccine Response in Elderly Individuals. *J Infect Dis.* 2015. doi: 10.1093/infdis/jiv456. [PubMed: 26516142]
13. Omer SB, Phadke VK, Bednarczyk RA, Chamberlain AT, Brosseau JL, Orenstein WA. Impact of Statins on Influenza Vaccine Effectiveness Against Medically Attended Acute Respiratory Illness. *J Infect Dis.* 2015. doi: 10.1093/infdis/jiv457. [PubMed: 26516141]
14. Hansson GK, Libby P. The immune response in atherosclerosis: a double-edged sword. *Nat Rev Immunol.* 2006;**6**(7):508–19. doi: 10.1038/nri1882. [PubMed: 16778830]
15. Nichol KL, Nordin JD, Nelson DB, Mullooly JP, Hak E. Effectiveness of influenza vaccine in the community-dwelling elderly. *N Engl J Med.* 2007;**357**(14):1373–81. doi: 10.1056/NEJMoa070844. [PubMed: 17914038]
16. Fedson DS. Pandemic influenza: a potential role for statins in treatment and prophylaxis. *Clin Infect Dis.* 2006;**43**(2):199–205. doi: 10.1086/505116. [PubMed: 16779747]