

Authors: E. AGABITI-ROSEI - G. AMBROSIO - L. BADIMON - JP. BASSAND - A. BAYÉS DE LUNA - M.E. BERTRAND - E. CHAZOV - S. CHIERCHIA - J. CLELAND - D. CLEMENT - D. COKKINOS - N. DANCHIN - R. DIETZ - P. DOMINIAC - I. EDES - E. ERDMANN - R. FERREIRA - H.R.FIGULLA - W. FLAMENG - I. GRAHAM - G. JACKSON - W. JANUSZEWICZ - J.C. KASKI - P. KEARNEY - W. KLEIN - F. KOLBEL - M. KOMAJDA - W. KÜBLER - J.L.LOPEZ-SENDON HENTSCHEL - G. MANCIA - W.J. MCKENNA - T. MEINERTZ - J.MLCZUCH - D. MULCAHY - E. O'BRIEN - A. OTO - J. PAPP - W.J. PAULUS - J. POLONIA - I. PRÉDA - L.A. PROVIDENCIA - J. REID - W.J. REMME - W. RUZYLO - Z. SADOWSKI - P. SERRUYS - P. SLEIGHT - J. SOLER-SOLER - J. SOMERVILLE - P.G. STEG - H.A.J. STRUIJKER BOUDIER - B. SWYNGHEDAUW - L. TAVAZZI - M. TENDERA - P. TOUTOUZAS - A. VAHANIAN - J.L. VANOVERSCHELDE - J. WIDIMSKY - M. YACIOUB

Influenza vaccination and cardiovascular disease

Inflammation has been identified as a major atherogenic mechanism, and infectious agents have been postulated as potential triggers of the inflammatory process that can lead to acute cardiovascular events.¹

The “infectious” hypothesis for atherogenesis, however, appears now to have been abandoned by the research community after the negative results of antibiotic trials that have shifted the attention of researchers towards other pathogenic mechanisms. However, a link between infection—not necessarily related to bacterial agents—and cardiovascular disease is likely to exist, as elevated cardiovascular death rates are observed during influenza epidemics.² A recent article by de Diego et al³ has addressed this important issue, looking in particular at the effects of annual influenza vaccination on winter mortality in elderly subjects with chronic heart disease. The present article summarizes their findings.

Influenza and cardiac events

The influenza infection has been suggested to trigger autoimmune (both humoral and cellular) responses leading to accelerated atherosclerosis⁴ and contributing to higher mortality rates.⁵ Influenza affects both the younger and the elderly, but its debilitating effects are more apparent in the elderly, particularly in those individuals with comorbidities.⁵ Interestingly, despite the association described between influenza and heart disease and current recommendations regarding influenza vaccination in the elderly, there is a lack of large, definitive, trials on the effect of influenza vaccination on chronic heart disease and its complications.³ There have been a few small-sized trials, but these have produced controversial results and were therefore unable to provide a categorical answer to the question of whether the influenza vaccine reduces cardiovascular mortality in the elderly, particularly in subjects with heart disease.

Findings in a recent large trial

Very recently, de Diego et al³ evaluated the effects of annual influenza vaccination on all-cause mortality in 1340 individuals over 65 years of age, 47% men, all of whom suffered from chronic heart disease. A variety of comorbidities were present in 82% of the subjects. Patients in the study were followed up from Jan 2002 to April 2005. The incidence of all-cause death throughout the study period was 68.8 deaths per 1000 person-years. The attributable risk of all-cause death in nonvaccinated

individuals was 47.7 deaths per 100 000 person-weeks. Multivariable Cox proportional-hazard models adjusted by sex, age, and comorbidity showed that influenza vaccination was associated with a reduction of 37% in the adjusted risk of winter death. The attributable mortality risk reduction in vaccinated individuals was 8.2 deaths per 1000 person-winters. The authors estimated that 122 annual vaccinations were needed to prevent one death during one influenza period. The present study found a reduction of 25% in the unadjusted rate of all-cause winter mortality in vaccinated subjects compared to nonvaccinated individuals. These results are concordant with findings in other studies conducted in the Netherlands (24% reduction in risk for all-cause death)⁶ but disagree with studies carried out by Simonsen et al in the United States.⁷

Interpretation of the findings

Unfortunately, de Diego et al³ could not establish the cause-specific mortality risk associated with vaccination, and therefore only all-cause mortality has been reported in their paper. The study has other limitations that reduce the applicability of the findings to real-life patient groups: for example, its nonrandomized nature and the fact that patients were subdivided broadly into two groups: ie, “vaccinated” or “nonvaccinated,” but without attempting to further classify the subjects as to whether vaccination was first-time or revaccination, for example.

Conclusion

Thus, this study has demonstrated a reduced risk of all-cause winter mortality among vaccinated individuals with chronic heart disease compared with subjects who did not receive the influenza jab. Unfortunately, however, the study did not provide a definitive answer regarding cause-specific mortality, and thus the question as to whether influenza vaccination leads to a decrease in cardiovascular mortality remains to be answered.

**N. ABDULKAREEM and J.C. KASKI -
London, UK**

References: 1. Ross R. *N Engl J Med.* 1999;340:115-126. 2. Madjid M et al. *Eur Heart J.* 2007;28:1205-1210. 3. De Diego C et al. *Eur Heart J.* 2009;30:209-216. 4. Gurevich VS. *Autoimmun Rev.* 2005;4:101-105. 5. Sprenger MJ et al. *Int J Epidemiol.* 1993;22:334-340. 6. Voordouw AC et al. *JAMA.* 2004;292: 2089-2095. 7. Simonsen L et al. *Arch Int Med.* 2005;165:265-272.

All texts for *The European Cardiologist - Journal by Fax* are available on our website: www.servier.com

In the event of any questions, or if you wish to receive the referenced publications, please contact fax n° 01 55 72 56 84

Medical service from Serdia Pharmaceuticals
Makers of

COVERSYL[®]
PERINDOPRIL *Once daily*

NATRILIX *SR*
1 TABLET DAILY

FLAVEDON *MR*
2 tablets daily

SERDIA PHARMACEUTICALS (INDIA) PVT. LTD.
Serdia House, Off Dr. S.S. Rao Road, Parel, Mumbai 400 012.
Under Licence from: Les Laboratoires Servier, France. Visit us at: www.serdiapharma.com

