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Influenza vaccination and the endurance against air pollution among elderly with acute coronary syndrome

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A B S T R A C T

Objective: Air pollution, weather condition and influenza are known risk factors of acute coronary syndrome (ACS) among elderly people. The influenza vaccine (IV) has been shown to reduce major cardiovascular events. The purpose of this study was to compare resistance to air pollution and weather factors causing ACS between vaccinated and less-vaccinated elderly people.

Methods: A case–crossover design was applied to 1835 elderly ACS patients who were obtained from the 1-million sample of Taiwan National Health Insurance Research Data with inclusion criteria: (1) the first diagnosis of ACS was in cold season and at age 68 or more, (2) had received the free IV program at least once during the period 3 years before the ACS. They were stratified into two groups: 707 had received flu vaccinations for all the 3 years and the remaining 1128 had not. The measurements of air pollutants, temperature, and humidity corresponding to each of the 3 days prior to the ACS diagnosis date were retrieved from the data banks of the Taiwan Environmental Protection Administration and Central Weather Bureau.

Findings: Increases in air pollution concentrations of CO, NO_2, PM_{10} or $PM_{2.5}$ and decreases in temperature significantly influenced the risk of ACS for the non-continuously vaccinated elderly population; however, less significant effects were observed for the continuously vaccinated population.

Conclusion: Consecutive influenza vaccination may potentially offer resistance against the detrimental effects of air pollution and changes in temperature in frail elderly adults with ACS. Future studies are needed to directly assess the interaction effect between the vaccination and environmental factors on ACS.

1. Introduction

Air pollution is a major risk factor in public health [1]. Cardiovascular diseases caused by air pollution have emerged as a substantial threat to human health [2]. Elderly adults and people with existing diseases appear particularly susceptible to the deleterious effects of ambient air pollution [3]. There is increasing concern over air pollutant exposure and its association with infectious diseases. Of particular concern, influenza is a major global health problem [4] especially in elderly adults with comorbidities. Influenza is a dangerous infection for elderly people with chronic cardiovascular disease because it strongly correlates with mortality from coronary artery disease (CAD) and acute myocardial infarction [5]. Several case–control studies have also demonstrated the benefits of the influenza vaccine in CAD patients [6,7]. The influenza vaccine has reduced major cardiovascular events in patients with acute coronary syndrome (ACS), and studies have further

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implied that with higher patient risk, greater benefits of the influenza vaccine can be expected [8,9]. Influenza complications can lead to severe respiratory diseases; a health concern that has also been linked with $PM_{2.5}$ exposure [10]. Therefore, air pollution has been implicated in respiratory illness infections [11]. A recent study in Beijing suggested that human influenza occurrence was correlated with exposure to particulate matter measuring less than 2.5 μm ($PM_{2.5}$) [12]. The underlying possible mechanism is that air pollution exposure likely causes host defense disorders, leading to immune dysfunction against bacterial and viral infections [13,14]. $PM_{2.5}$ and PM_{10} are major components in ambient particulate matter air pollution; moreover, their nano-particle size is comparable to that of viruses [15]. Some nanoparticles such as $PM_{2.5}$ behave like viruses and can penetrate lung and dermal (skin) barriers, subsequently entering the circulatory and lymphatic systems in humans, reaching most tissues and organs, potentially disrupting cellular processes and causing disease [15]. We postulated that the human body defense mechanism may regard $PM_{2.5}$ as a virus, and virus vaccinations might produce beneficial effects against $PM_{2.5}$. However, no previous study has evaluated the association between influenza vaccination and air pollution or environmental temperature change.

Taiwan government implemented a vaccination program in 1996 and expanded it in 1998 to include all people aged 65 or older. Vaccines are delivered in health care settings by nurses or physicians, or in community settings through public health departments. The vaccination rate in Taiwan gradually increased from 9.9% in 1998 to 49.2% in 2007, reaching a peak of 70% in 2004, which approximated the national target level of 68% set by the Taiwan CDC for 2010. In this study, we hypothesized that elderly adults with ACS who receive an influenza vaccination could experience a tolerance increase against air pollution and temperature change. The relationship can be illustrated as Fig. 1. Since the purpose is to investigate the effect of continuous vaccination for 3 times versus the non-continuous, we considered only the elderly people aged 68 or older when ACS was diagnosed, and had received vaccination for at least once, to make sure that each ACS patients had been eligible and had the need or information for vaccination program for 3 years. The aim of the study was to test whether influenza vaccination could increase the endurance against the detrimental effects of air pollution and offer resistance to temperature change in frail elderly adults with ACS.

2. Material and methods

2.1. Data sources

Two data banks were linked in this study: the National Health Insurance Research Database (NHIRD) in Taiwan for the period 2000–2013, and the Air Quality Monitoring Network (AQMN) established by the Taiwan Environmental Protection Administration (EPA). The NHI program was implemented in Taiwan in 1995, and the coverage rate among the whole population was 96% in 2000, and over 97% at the end of 2003, at which time more than 21.9 million residents were enrolled. For research purposes, precisely 1 million residents of Taiwan enrolled in NHI in 2005 were randomly selected by the National Health Research Institutes of Taiwan by using a stratified sampling scheme to ensure that the data were representative of the national population. The individual healthcare records for clinical and hospital visits are fully digitalized. The rationale for employing post-2000 NHIRD data is that as of January 1, 2000, in accordance with the rules of the Bureau of NHI, the NHI data have been encoded using the standardized International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM) or A-code.

Longitudinal medical records of patients who had received an ACS diagnosis during 2000–2013 were acquired from the NHIRD with inclusion criteria: (1) the first diagnosis of ACS was in cold season and at age 68 or more, (2) had received the free IV program at least once during the period 3 years before the ACS. In results 1835 ACS patients were included into the study and they were stratified into two groups: 707 had received flu vaccinations for all the 3 years and the remaining 1128 had not.

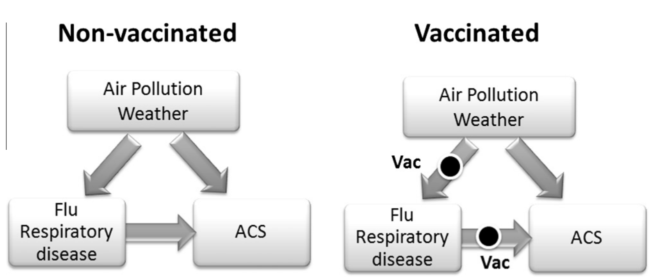

Fig. 1. Hypothetical relationship among influenza, vaccination, air pollution/weather and ACS.

2.2. Determination of ACS and flu vaccination

All ACS patients were ascertained through either treatment by an emergency unit (CU) or hospitalized with a diagnosis of coronary artery disease (ICD-9 code 410 or A-code A270), and CU treatment was identified by NHI codes (in Appendix A). Flu vaccination was verified by ICD-9 code V048, or NHI card sequence number (CARD SEQ NO) code:01 or case typecode:92. Comorbidities included diabetes, hypertension, chronic obstructive pulmonary disease, arrhythmia, heart failure, and cardiac disease; each was ascertained through at least five diagnoses from clinical visits that took place prior to the first ACS diagnosis, and the patient records were traced back to 1996.

2.3. Exposure assessment

The AQMN was launched by the EPA in September 1993. To date, a total of 77 monitoring stations have been placed throughout 75 townships and precincts in Taiwan. We archived the complete monitoring data for air pollutants, including SO_2, NO_2, O_3, CO, and $PM_{2.5}$, as well as daily temperature and relative humidity (RH) from the AQMN database. Concentrations of each pollutant were measured continuously and reported hourly by using the following methods: non-dispersive infrared absorption for CO, chemiluminescence for NO_2, ultraviolet absorption for O_3, ultraviolet fluorescence for SO_2, and β-gauge for $PM_{2.5}$. A daily (24-h) average concentration was calculated when at least 13 valid hourly values were available with no more than six successive hourly values missing, and an 8-haverage concentration was calculated when at least six valid hourly values were available. The measurement of exposure was calculated on the basis of the average of 24-h daily records of NO_2, CO, SO_2, $PM_{2.5}$ concentrations, and the 8-h daily records of O_3 concentrations (10:00 AM to 6:00 PM). The hourly weather records, including temperature and RH, were also obtained through the network.

2.4. Methods

We applied a case-crossover design to the ACS patients; each patient served as both an individual case and a control. This design facilitated assessing the effects of short-term factors such as ambient air quality, temperature, and humidity. The advantage of this design was that all long-term confounders, including comorbidities, body-mass index, habits (e.g., smoking), and demographical