Environmental Research 148 (2016) 7–14

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

The influence of pre-existing health conditions on short-term mortality risks of temperature: Evidence from a prospective Chinese elderly cohort in Hong Kong

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ARTICLE INFO

Article history:
Received 9 September 2015
Received in revised form
22 January 2016
Accepted 8 March 2016

Keywords:
Distributed lag nonlinear model
Elders
Medical condition
Mortality
Temperature
Nested case-control study

ABSTRACT

Background: Both cold and hot temperatures are associated with adverse health outcomes. Less is known about the role of pre-existing medical conditions to confer individual's susceptibility to temperature extremes.

Methods: We studied 66,820 subjects aged ≥ 65 who were enrolled and interviewed in all the 18 Elderly Health Centers of Department of Health, Hong Kong from 1998 to 2001, and followed up for 10–13 years. The distributed lag nonlinear model (DLNM) combined with a nested case-control study design was applied to estimate the nonlinear and delayed effects of cold or hot temperature on all natural mortality among subjects with different pre-existing diseases.

Results: The relative risk of all natural mortality associated with a decrease of temperature from 25th percentile (19.5 °C) to 1st percentile (11.3 °C) over 0–21 lag days for participants who reported to have an active disease at the baseline was 2.21 (95% confidence interval (CI): 1.19, 4.10) for diabetes mellitus (DM), 1.59 (1.12, 2.26) for circulatory system diseases (CSD), and 1.23 (0.53, 2.84) for chronic obstructive pulmonary disease (COPD), whereas 1.04 (0.59, 1.85) for non-disease group (NDG). Compared with NDG, elders with COPD had excess risk of mortality associated with thermal stress attributable to hot temperature, while elders with DM and CSD were vulnerable to both hot and cold temperatures.

Conclusions: Elders with pre-existing health conditions were more vulnerable to excess mortality risk to hot and/or cold temperature. Preventative measures should target on elders with chronic health problems.

1. Introduction

Climate change is likely to bring extreme temperature events more frequently with increased intensity and widespread distribution. It was observed that global warming not only increased the frequency of heat waves, but also led to increase in cold spells with a steeper rate than in hot spells from 1981 to 2010 worldwide (Song et al., 2013). Temperature extremes had short-term adverse impacts on health in that heat waves were associated with increased mortality, hospital admissions, and emergency room visits (Astrom et al., 2011; Khalaj et al., 2010; Knowlton et al., 2009; Williams et al., 2012). However, only a few studies have assessed the effects of cold temperature (Medina-Ramon and Schwartz, 2007; Medina-Ramon et al., 2006; Ou et al., 2013; Rocklov et al., 2014).

Extreme temperature events affect vulnerable populations most, amplifying social disparities in health, both within and between countries (Meehl and Tebaldi, 2004). Understanding susceptibility to extreme temperature is of importance in environmental public health researches (Anderson and Bell, 2009; Gasparrini, 2014). However, there were few studies for effects of thermal stress on susceptible subgroups (Astrom et al., 2015; Bateson and Schwartz, 2004; Ma et al., 2015), fewer were studies for effects of cold temperature and in persons with medical conditions. This may be due to: a lack of personal information to define susceptible groups in conventional studies with ecological designs

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Abbreviations: DLNM, the distributed lag nonlinear model; CI, confidence interval; COPD, chronic obstructive pulmonary disease; BMI, body mass index; ICD-9, Ninth Revision of the International Classification of Diseases; $PM_{2.5}$, particulate matter with aerodynamic diameter less than or equal to 2.5 μm; TPU, tertiary planning unit; AIC, Akaike Information Criterion; DM, diabetes mellitus; CSD, circulatory system diseases; NDG, non-disease group; SD, standard deviation; RR, relative risk

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http://dx.doi.org/10.1016/j.envres.2016.03.012
0013-9351/

(e.g. time-series, case-crossover, or case-only approaches); a lack of suitable statistical methods to assess effect modifiers of time-varying exposure in studies with cohort design; also the difficulties encountered in analyzing nonlinear and delayed effects for the relationship between temperature and mortality.

Among studies to explore whether medical conditions may confer susceptibility to temperature, most of them did not directly assess effects in persons with pre-existing health problems but instead indirectly through assessing mortality outcomes for specific causes (Atsumi et al., 2013). This approach is not appropriate, since the underlying cause of death may not necessarily provide the information of existing medical conditions before death. For example, people died from cardiovascular diseases may have diabetes mellitus and persons with diabetes mellitus not be reflected in the underlying cause. Thus vulnerability of persons with specific health problems cannot be assessed.

In the study, we aimed to assess the nonlinear and delayed mortality effects of cold or hot temperature among elders in a prospective Chinese elderly cohort in Hong Kong, and to comparatively assess effect modification of pre-existing diseases.

2. Methods

2.1. Study subjects

We included a total of 66,820 adults aged 65 years or older (≥ 65 years), about 9% of people aged ≥ 65 years in Hong Kong, who enrolled at one of the eighteen Elderly Health Centers of the Department of Health from 1998 to 2001 and followed up until 31st of December 2011. Body mass index (BMI) was collected by physical examinations, and socio-economic conditions, lifestyle characteristics (smoking, physical activity, education), and morbidity status were collected by face-to-face interview during enrollment and follow-up visits by registered nurses (Schooling et al., 2014; Wong et al., 2015). Ethics approval was obtained from the Ethics Committee of the Faculty of Medicine, The University of Hong Kong and of the Department of Health of Hong Kong.

Self-reported active chronic disease was collected through face-to face interview, which included hypertension, heart diseases, stroke, diabetes mellitus, and COPD and/or asthma. Self-reports of chronic diseases were confirmed and supplemented by clinical diagnoses based on history (Schooling et al., 2006). All natural mortality was coded as 1-799 according to the International Classification of Diseases, Ninth revision (ICD-9) before 2001 or A00-R99 based on ICD-10 from 2001 by the Department of Health. Subjects who died within the first year after recruitment were excluded from our analysis.

2.2. Air pollutants and meteorological data

We obtained air pollutants data of ten general monitoring stations from Environmental Protection Department of Hong Kong from 1999 to 2011. We took daily 24-h average concentration of particulate matter with aerodynamic diameter less than or equal to 2.5 μm ($PM_{2.5}$) and nitrogen dioxide (NO_2), and daily 8-h (10:00–18:00 h) average concentration of ozone (O_3). Data were regarded as missing if numbers of hourly concentration for one particular day were less than 75% (18 h for $PM_{2.5}$ and NO_2, and 6 h for O_3). Daily concentrations of air pollutants were evaluated by averaging the daily concentrations across all valid monitoring stations.

Daily mean air temperature and relative humidity in percent were measured by digital thermometers with platinum resistance sensors at the Hong Kong Observatory. The historical temperature data have been used in the previous population studies of temperature effects in Hong Kong (Goggins et al., 2015; Yi and Chan, 2014).

2.3. Statistical analysis

The nested case-control design employs a case-control approach within an established cohort to obtain estimates from a sample of the cohort that are similar to estimates obtained from analysis of the entire cohort (Goldstein and Langholz, 1992). This design has become popular because it allows for computationally efficient analysis of data from a cohort with substantial savings in cost and time; it is a useful alternative for cohort analysis with studying time-varying exposures (Essebag et al., 2005). The nested case-control design has already been used to studying time-varying exposure, such as $PM_{2.5}$ (Beverland et al., 2012).

In this study, we used nested case-control design to assess short-term effects of temperature. We constructed nested case-control data sets as follows: (1) controls selected randomly from among the cohort subjects whose follow-up time at least as long as the case for each death in the cohort; (2) the associated date of controls (the date when the control reached the exact follow-up time as the case) was in the same calendar year and month as the death date of case to control long-term trend and seasonality; (3) the date of birth of controls was within 1 calendar year of the date of birth of the case. We excluded controls when associated date was outside the follow-up period of the cohort. We randomly selected 9 controls to each case from all eligible subjects in the cohort (Beverland et al., 2012). For all participants (including persons with and without morbidity status), about 98% of cases had the full complement of 9 controls, and for diabetes mellitus (DM), circulatory system diseases (CSD), chronic obstructive pulmonary disease (COPD), and non-disease group (NDG), about 92%, 97%, 80%, and 93.4%, respectively.

Temperature appears a nonlinear and delayed relationship with mortality (Guo et al., 2011). A distributed lag nonlinear model (DLNM) has been developed based on a “cross-basis” function, which allows simultaneously estimate the nonlinear and delayed effects of temperature on mortality or morbidity in time-series data, and this approach was expanded to apply to cohort study recently (Gasparrini, 2014).

We used conditional logistic regression to incorporate a DLNM in a nested case-control study design to assess the nonlinear and delayed mortality effects of temperature among subjects in a prospective Chinese elderly cohort, and to comparatively examine the effect modification of morbidity status and the extent of mortality displacement related to high temperature.

$$\log itp = T_{t,l} + \beta_1 X_i + \beta_2 X_i(t) + Strata(Strata) \tag{1}$$

where t is the day of death for case or an associated day of each control; $T_{t,l}$ is a matrix obtained by applying the DLNM to temperature, and l is the number of lag days; X_i is the vector of time-independent variables, including individual-level factors: gender, BMI (three levels), smoking (three levels), physical exercise (four levels), education (three levels), tertiary planning unit (TPU)-level factors: proportion of the population ≥ 65 years of age, proportion with tertiary education, and the average monthly income in each TPU, and district level factor: proportion of smokers in each district; X_i *(t)* is the vector of time-dependent variables, including dummy variable of day of the week on day t, and natural cubic B-splines with 3 d.f. for relative humidity (Guo et al., 2011; Stafoggia et al., 2008). β_1 and β_2 are vectors of coefficients for time-independent and time-dependent variables; *Strata (strata)* is a categorical variable of each risk set.

$T_{t,l}$ in model (1) was the term to estimate both the nonlinear and delayed effects of temperature. In order to completely capture