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Hypertension modifies the short-term effects of temperature on morbidity of hemorrhagic stroke

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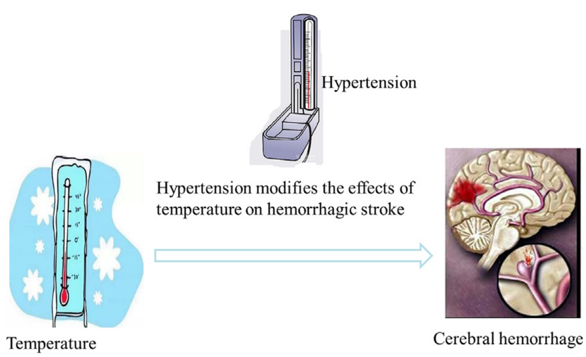
HIGHLIGHTS

- Low temperature might be one risk factor for hemorrhagic stroke.
- Decrease in the current day's temperature was associated with increase in daily hemorrhagic stroke.
- Hypertension may be one important effect modifier of this association mentioned above.

GRAPHICAL ABSTRACT



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ABSTRACT

Background: This study estimated the effects of ambient temperature on hospital admissions for hemorrhagic stroke during 2004–2009 in Jinan, China, and the effect modification of hypertension status.

Methods: The exposure–response relationship between temperature and hemorrhagic stroke was firstly examined, and then the association between daily mean temperature and hemorrhagic stroke was investigated using a generalized additive model. Stratified analyses were conducted to examine the potential effect modification of hypertension.

Results: A total of 1577 hemorrhagic stroke cases were observed between 2004 and 2009, among which, 1058 were hypertensive and 519 were non-hypertensive. We found an approximately linear relationship between ambient temperature and hemorrhagic stroke. Each 1 °C decrease in the current day's temperature was associated with 1.63% (95% CI: 0.33%, 2.95%) increase in daily hemorrhagic stroke. The stratified analyses observed that the association was significant among hypertensive hemorrhagic stroke, each 1 °C decrease in the current day's temperature was associated with 2.26% (95% CI: 0.57%, 3.98%) increase in daily hypertensive hemorrhagic stroke. While no significant effect was observed for non-hypertensive hemorrhagic stroke.

Conclusions: Low temperature might be one risk factor for hemorrhagic stroke and hypertension may be one effect modifier of this association in Jinan, China.

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1. Introduction

Being one leading cause of disability and mortality, stroke remains a major public health challenge in most parts of the world (Feigin et al., 2014). For example, stroke accounts for about one fifth of the overall mortality in China (Kim and Johnston, 2011). To reduce the disease burden of stroke, it is crucial to examine the risk factors in order to formulate corresponding prevention and control measures (Lin et al., 2017a; Poorthuis et al., 2017).

A number of studies have reported that some environmental factors were important determinants of the risk of stroke (Kyobutungi et al., 2005; Lin et al., 2016b). Among them, ambient temperature has attracted increasing attention in recent decades probably driven by the global climate change (Kan, 2011). Several epidemiological studies have examined the association between temperature and stroke with inconsistent findings; a few studies reported that both high and low temperatures were associated with increased risk of stroke (Chen et al., 2013; Hong et al., 2003), while some others did not find a significant association (Neidert et al., 2016).

As one important risk factor of stroke, blood pressure and hypertension were also closely related with temperature (Lewington et al., 2012). And some studies have suggested that hypertension or increased blood pressure may play an important role on the short-term association between ambient temperature exposure and risk of stroke (Wang et al., 2013). So it is reasonable to hypothesize that hypertension could modify the association between temperature and stroke, however, no such study has been conducted to examine this research question.

In one previous study, we have examined the effects of meteorological factors on morbidity of ischemic stroke (Wang et al., 2013). This study was conducted to examine two main research questions: 1) whether ambient temperature was associated with increased risk of hemorrhagic stroke; 2) whether hypertension could modify the association.

2. Materials and methods

2.1. Setting

Jinan is the capital city of Shandong Province. Its population in 2010 was about 6.95 million in Jinan City. Jinan has a temperate climate with dry winters and wet, hot summers. The annual mean temperature was about 15 °C during the study period. Two hospitals, namely Qilu Hospital and Jinan Fourth Hospital, were selected for this study.

2.2. Materials

Daily data on hospital admissions for hemorrhagic stroke were obtained from two referral hospitals in Jinan City, Qilu Hospital and Jinan Fourth Hospital. The data covered the period between 1 January 2004 and 31 December 2009. Patient data captured from the medical record system included age, sex, date of admission, hypertension status, and principal diagnosis on discharge. The data recording system in the study area has been proved to be of high validity (Geng, 2012). Only hemorrhagic stroke hospital admissions among residents living in Jinan City were included in this analysis. Data were collected as part of government mandated health surveillance and we only got the daily number of the hospitalization, no individual information was available, so ethical approval was not required.

The hemorrhagic stroke cases were grouped into hypertensive or non-hypertensive in this study. Hypertension was defined as systolic blood pressure ≥ 140 mm Hg, or diastolic blood pressure ≥ 90 mm Hg, and/or current treatment of hypertension with antihypertensive medication before the hospital admission (Lin et al., 2017b).

Daily meteorological data for Jinan for the same period were extracted from China Meteorological Administration Climatic Dataset Centre. The variables included daily mean temperature (°C), absolute humidity (g/m^3), rainfall (mm), wind speed (m/s) and duration of sunshine (h). The absolute humidity was defined as the amount of water vapor included in a unit volume of air (Davis et al., 2016).

2.3. Statistical analysis

As the daily number of hospital admissions usually followed a Poisson distribution, we applied generalized additive models (GAM) to examine the short-term association between daily mean temperature and bacillary stroke morbidity; a quasi-Poisson link was used to account for the over-dispersion in daily stroke count (Dominici et al., 2002).

Univariate model was firstly conducted, and then multivariate models were used to control for potential confounding factors. In accordance with previous time-series studies, we controlled for day of the week (DOW) and public holidays using categorical indicator variables (Lin et al., 2013). In addition, we used penalized smoothing splines to adjust for seasonal pattern and long-term trend in daily stroke morbidity with degree of freedom (df) selected a priori based on previous studies (Wang et al., 2013). Specifically, we used 6 df per year for time trend. For the smooth function of calendar time, 6 df per year was chosen so that we filtered out the information at time scales of two months (Curriero et al., 2002). We also controlled for absolute humidity (df = 3), wind speed (df = 3), rainfall (df = 3) and sunshine (df = 3). If there was high correlation (correlation coefficient larger than 0.8) between two meteorological factors, they would not be included in the same model to avoid the concerns of collinearity (Li et al., 2015). The risk estimates were presented as excess risk (ER) with 95% confidence interval (95% CI). The model can be specified as follows:

$$\begin{aligned}\log[E(Yt)] = {} & \alpha + s(t, df = 6/\text{year}) + \beta_1 * DOW + \beta_2 * PH \\ & + s(\text{humidity}, df = 3) + s(\text{wind}, df = 3) \\ & + s(\text{rainfall}, df = 3) + s(\text{sunshine}, df = 3)\end{aligned}$$

where $E(Y_t)$ is the expected daily hemorrhagic stroke morbidity count on day t, α is the model intercept, s() indicates a smoother based on penalized splines, and β is the regression coefficient.

We examined the shape of the association between the logarithm of daily stroke morbidity and daily mean temperature, based on which, we quantified the relationship across different lag days. We graphically examined exposure–response relationships which were derived using a smoothing function of daily mean temperature (Tian et al., 2016). To account for possible delayed effects, we examined the impact of up to 21 days.

To examine the effect modification of hypertension, stratified analyses were performed by hypertension status (yes or no). The statistical difference of the associations between the subgroups was examined by calculating the 95% confidence interval as:

$$(b_1 - b_2) \pm 1.96\sqrt{(se_1)^2 + (se_2)^2}$$

where b_1 and b_2 were the effect estimates for each stratum, and se_1 and se_2 were their corresponding standard errors (Lin et al., 2016a).

A series of sensitivity analyses was performed by changing degrees of freedom (5, 7 and 8 df/year) for temporal adjustment, and meteorological factors (4 and 5) to examine the robustness of the effect estimates. We also applied a distributed lag non-linear model (dlnm) to further examine the robustness of the results.

All statistical tests were two-sided and values of $P < 0.05$ were considered statistically significant. The "mgcv" and "dlnm" packages in R software Version 3.2.2 was used to fit all models and estimate the exact standard errors of regression coefficients.