Original Article

Diurnal Temperature Range as a Novel Risk Factor for Sudden Infant Death*

CHU Chen[1], ZHOU WenHao[2], GUI YongHao[1,#], and KAN HaiDong[3,4,#]

1. Cardiovascular Center, Children's Hospital of Fudan University, Shanghai 201102, China; 2. Department of Neonatology, Children's Hospital of Fudan University, Shanghai 201102, China; 3. School of Public Health, Key Lab of Public Health Safety of the Ministry of Education, Fudan University, Shanghai 200032, China; 4. G_RI°CE (Research Institute for the Changing Global Environment) and Fudan Tyndall Centre, Fudan University, Shanghai 200433, China

Abstract

Objective To assess the relationship between diurnal temperature range (DTR) and sudden infant death (SID) between 2001 and 2004 in Shanghai, China.

Methods We conducted a time-stratified case-crossover analysis to estimate the percent increase of SID associated with changes in DTR after adjustment for daily weather conditions (temperature and relative humidity) and outdoor air pollution.

Results DTR was significantly associated with daily SID. An increase of 1 °C in the current-day (L0) and in the 2-day moving average (L01) DTR corresponds to a 1.56% (95% CI: 0.97%, 2.15%) and a 1.89% (95% CI: 1.17%, 2.60%) increase in SID, respectively.

Conclusion An increased DTR was associated with an increased risk of SID in Shanghai. More studies are needed to understand the effect of DTR on infant deaths.

Key words: Diurnal temperature range; Sudden infant death; Case-crossover

Biomed Environ Sci, 2011; 24(5):518-522 *doi:10.3967/0895-3988.2011.05.010* *ISSN:0895-3988*

www.besjournal.com(full text) *CN: 11-2816/Q*

INTRODUCTION

Sudden infant death (SID) is a leading cause of post-neonatal infant death. The rate of SID has decreased significantly since the launch of awareness campaigns that promote the supine sleeping position. However, the risk factors for SID have still not been fully elucidated[1]. Previously, maternal smoking[2], alcohol intake[3], and exposure to air pollution[4] have been associated with SID. Weather conditions were also associated with increased risk of SID[5].

It has been known for a long time that temperature can have an effect on human health. Global warming and other climate phenomena, such as El Nino, have sparked new interest in the weather–health relationship[6]. The relationship between temperature and adult mortality is well established[7]. Typically, a U-shaped relationship between temperature level and mortality risk is observed, with mortality risk decreasing from the lowest temperature to an inflection point and then increasing with higher temperatures. Of course, this relationship varies in areas that have different weather patterns, latitude, levels of air pollution and prevalence of air-conditioning systems[7].

Diurnal temperature range (DTR) is defined as

*This work was supported by the National Basic Research Program (973 program) of China (2011CB503802), the National Natural Science Foundation of China (81001228), the National High Technology Research and Development Program of China (863 Program) (2007AA02Z442), the Shanghai Pu Jiang Program (09PJ1401700), and the Program for New Century Excellent Talents in University (NCET-09-0314).

#Correspondence should be address to KAN HaiDong, E-mail: haidongkan@gmail.com; or GUI YongHao, E-mail: yhgui@shmu.edu.cn

Biographical note of the first author: CHU Chen, female, born in 1981, MD, majoring in pediatric cardiology.

Received: December 7, 2010; Accepted: May 3, 2011

the difference between maximal and minimal temperatures within one day. DTR is a weather parameter closely associated with urbanization and global climate change[8]. Previously, DTR was shown to be an independent risk factor for mortality from coronary heart disease[9], stroke[10], and chronic obstructive pulmonary disease (COPD)[11]. We hypothesized that large diurnal temperature changes might increase the environmental stress on infants, thereby representing a new risk factor for SID. We used daily DTR and SID data from Shanghai, China to test our hypothesis using a case-crossover analysis.

MATERIALS AND METHODS

Data

Our study area comprises the nine urban Districts of Shanghai (289 km^2). These urban Districts are Huangpu, Jin'an, Luwan, Xuhui, Yangpu, Changnin, Yangpu, Putuo, and Zhabei. Daily numbers of SID in the nine urban Districts of Shanghai from January 1, 2001 to December 31, 2004 were collected from the database of the Shanghai Municipal Center of Disease Control and Prevention (SMCDCP). In Shanghai, all deaths are required to be reported to appropriate authorities before cremation. The place of death for Shanghai residents can be considered as either hospital or home. In both cases, the hospital or community doctors fill in the Death Certificate Cards. The information on the Cards is sent to SMCDCP through their internal computer network. SID is defined as a sudden, unexplained death of a child<1 year of age for which a clinical investigation and autopsy fail to reveal a cause of death.

Meteorological data (daily minimum, maximum and mean temperature, and relative humidity) were obtained from the Shanghai Meteorological Bureau. The weather data were measured at a fix-site station located in the Xuhui District of Shanghai.

As a possible confounding factor in studying the association between DTR and SID[12-14], daily air pollution data from 2001-2004, including levels of PM_{10}, SO_2, NO_2, and O_3, were collected from the Shanghai Environmental Monitoring Center.

Statistical Analysis

We analyzed the DTR and SID data with a time-stratified case-crossover design. The case-crossover design, which was first proposed by Maclure to study the transient effect of an intermittent exposure[15], has been used to study the health effects of acute environmental exposure[16]. The case-crossover approach is a design in which only cases are sampled, and their exposure at the time of their failure is compared with some estimate of their typical level of exposure. This approach only requires exposure data for cases and can be regarded as a special type of case-control study in which each case serves as his/her reference. Therefore, case-crossover design has the advantage of controlling for potential confounding factors caused by fixed individual characteristics, such as gender, race, diet, and age. Recently, time-stratified reference selection, (time is divided into fixed strata and the days in a stratum are used as references for a case that falls in that stratum) was shown to be able to avoid subtle selection bias issues and result in an unbiased estimate using conditional logistic regression models[17].

In our analysis, we selected control days matched to the same day of the week in the same month of the same year when a SID occurred (a case day). This control selection strategy was expected to adjust for the effects of long-term trends, seasonality, and the day of week[18]. The association between DTR and SID was measured by odds ratios (ORs) using conditional logistic regression. After control for current-day mean temperature, relative humidity and air pollutant concentrations, ORs were expressed for each 1 °C increment of DTR.

To present the lag pattern of the association between DTR and SID, we examined the effect of DTR with different lag (L) structures, including both single-day lag (from L0 to L6) and multi-day lag (L01 and L06)[19]. For example, in single-day lag models, a lag of 0 day (L0) corresponds to the current-day DTR, and a lag of 1 day (L1) refers to the previous-day DTR; in multi-day lag models, L01 corresponds to the 2-day moving average of DTR of the current and previous day, and L06 corresponds to 7-day moving average of DTR of the current and previous 6 days. Normally, there is a U-shaped relationship between mortality risk and temperature level[7]. Because the effect of DTR may vary between cold days (below the "inflection point") and warm days (above the "inflection point"), we conducted the analysis separately in these two periods.

We carried out time-stratified reference selection using the statistical software package SAS, version 9.1 (SAS Institute Inc, Cary, NC, USA), and conducted conditional logistic regression analysis using the *COXPH* procedure in R 2.11.0[20]. The results are presented as the percent change in SID per 1 °C increment of DTR.

RESULTS

From 2001 to 2004, a total of 1 728 SID cases were recorded in Shanghai. The mean temperature level ranged from -2.4 to 34.0 °C. The minimal, mean and maximal DTR were 1.0, 6.8, and 16.6 °C, respectively. The mean air pollution levels were 101.9 μg/m^3 for PM_{10}, 44.7 μg/m^3 for SO_2, 66.6 μg/m^3 for NO_2, and 63.5 μg/m^3 for O_3 (Table 1).

Table 1. Summary Statistics of Daily SID Number, Weather Conditions and Air Pollutant Concentrations in Shanghai in 2001-2004

		Mean	SD	Min	P(25)	Median	P(75)	Max
SID Counts		1.19	0.26	0	0	1	2	5
Meteorological Measures	DTR (°C)	6.8	2.7	1.0	4.8	6.8	8.7	16.6
	Mean Temperature (°C)	17.7	8.5	-2.4	10.3	18.3	24.7	34.0
	Relative Humility (%)	72.9	11.4	33.3	65.5	73.5	81.0	97.0
Air Pollutants Concentrations	PM_{10} (μg/m^3)	101.9	64.4	14.0	56.0	84.0	128.0	567.0
	SO_2 (μg/m^3)	44.7	24.2	8.0	27.0	40.0	56.0	183.0
	NO_2 (μg/m^3)	66.6	24.8	14.0	50.0	62.0	79.0	254.0
	O_3 (μg/m^3)	63.5	35.5	5.4	38.4	57.2	81.8	212.3

Table 2 shows results from the single-lag day (L0-L6) and the cumulative exposure models (L01 and L06) for the percent increase in SID per 1 °C increase in DTR. The effects of DTR on SID are statistically significant for most lagged days that we examined (Table 2). For example, an increase of 1 °C in the current-day (L0) and in the 2-day moving average (L01) DTR corresponds to a 1.56% (95% CI: 0.97%, 2.15%) and a 1.89% (95% CI: 1.17%, 2.60%) increase in SID, respectively. We did not find significant associations of air pollutants with SID (data not shown).

Table 2. Percent Increase (Mean and 95% CI) of Daily SID Associated with a 1 °C Increase in the DTR

	Lag (L)	Mean (95% CI)	*P* value
Single-day Lag	L0	1.56 (0.97, 2.15)	<0.01
	L1	1.28 (0.68, 1.88)	<0.01
	L2	1.03 (0.45, 1.61)	<0.05
	L3	2.51 (1.95, 3.08)	<0.01
	L4	1.95 (1.39, 2.51)	<0.01
	L5	1.49 (0.93, 2.05)	<0.01
	L6	0.96 (-0.39, 2.31)	>0.05
Multi-day Lag	L01	1.89 (1.17, 2.60)	<0.01
	L06	3.44 (2.58, 4.31)	<0.01

Table 3 provides the regression results for DTR with respect to SID, stratified by the temperatures above ("warm days") or below ("cold days") the inflection point of 21 °C. For the cold days, a 1 °C increase of the 2-day moving average of DTR (L01) corresponded to a 2.15% (95% CI: 0.45%, 3.85%) increase in SID; for the warm days, an increase of 1 °C DTR corresponded to a 1.58% (CI: 0.68%, 2.48%) increase in SID.

Table 3. Percent Change in SID and 95% Confidence Intervals (CI) per 1 °C Increment in DTR at Different Temperature Levels

/	Mean (95% CI)	*P* value
All time	1.89 (1.17, 2.60)	<0.01
<21 °C	2.15 (0.45, 3.85)	<0.01
>21 °C	1.58 (0.68, 2.48)	<0.01

Figure 1 presents the exposure-response curve for the DTR-SID association. Generally, there was an almost linear relationship for most observed DTR levels (chi-square test for linearity, *P* value >0.05).

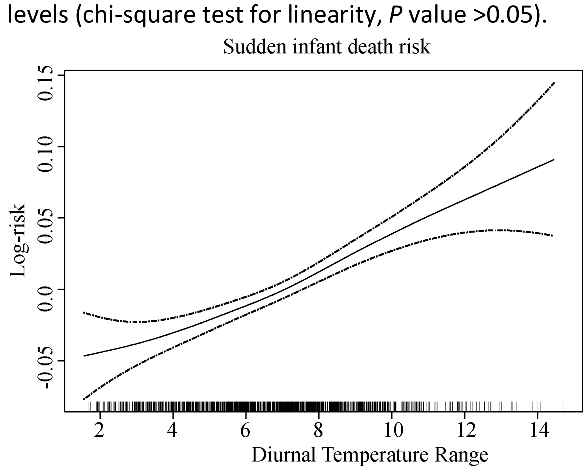

Figure 1. Smoothing plot of DTR against SID risk. X-axis is the DTR level (°C). The estimated mean percentage change in SID is shown by the solid line, and the dotted lines represent twice the point-wise standard error.

DISCUSSION

The acute effect on SID of environmental factors, such as ambient air pollutants (particles, SO_2, NO_2, O_3, and CO)[4] and weather conditions[5], have been previously reported. Evidence gained in this study shows that temperature variation within one day, the DTR, is also associated with increased risk of SID. Moreover, the association remained statistically significant after adjustment for temperature level and other covariates, suggesting that DTR is a new risk factor for SID, independent of the corresponding temperature level. To our knowledge, this is the first study to report the acute effect of DTR on SID.

Although the underlying mechanism is still unclear, previous studies have shown that sudden temperature change might increase cardiopulmonary workload and induce the onset of a cardiopulmonary event[21-22]. For SID, we hypothesized that a wide DTR might be a source of additional environmental stress, and stress on the cardiopulmonary system is increased during periods of high temperature change. For example, in a human study, a sudden temperature change of inhaled air has been associated with the release of inflammatory mediators associated with mast cells[23].

The limitations of our analyses should be noted, and substantial additional investigation of this association remains to be performed. As in other studies in this field, we used the available environmental monitoring data to represent the exposure of the population to DTR and other covariates. Numerous factors, such as air conditioning and ventilation rate between indoor and outdoor air, may affect the monitoring results from fixed stations, which are surrogates of personal exposure to DTR. The differences between these proxy values and the true exposures are an inherent and unavoidable type of measurement error. Also, it is uncertain whether air pollutants are confounders or effect modifiers (i.e., a synergistic effect) of the DTR-SID association. Future research should study an aggregate weather variable that incorporates temperature, temperature range (e.g. DTR), relatively humidity, dew point and wind speed. Investigation of the effects of air-conditioning and heating systems on the association between DTR and SID should be conducted given the wide use of these facilities in Shanghai.

In summary, although the relationship between climate change and DTR varies across the globe and our findings about DTR and SID might not necessarily apply to other areas of world, our data suggest that even a slight increase in DTR is associated with an increased risk of SID. By focusing on the preventative aspects of SID, e.g. DTR, we can reduce SID more significantly. Public health programs should be implemented to prevent heat and cold-related health problems, including the effects of the DTR. Of course, our findings require replication, especially in areas with different weather patterns and in areas where air conditioning systems are prevalent.

REFERENCES

1. Sahni R, Fifer WP, Myers MM. Identifying infants at risk for sudden infant death syndrome. Curr Opin Pediatr, 2007; 19, 145-9.
2. Dietz PM, England LJ, Shapiro-Mendoza CK, et al. Infant morbidity and mortality attributable to prenatal smoking in the U.S. Am J Prev Med, 2010; 39, 45-52.
3. Phillips DP, Brewer KM, Wadensweiler P. Alcohol as a risk factor for sudden infant death syndrome (SIDS). Addiction, 2010; 106, 516-25.
4. Tong S, Colditz P. Air pollution and sudden infant death syndrome: a literature review. Paediatr Perinat Epidemiol, 2004; 18, 327-35.
5. Auliciems A, Barnes A. Sudden infant deaths and clear weather in a subtropical environment. Soc Sci Med, 1987; 24, 51-6.
6. Haines A, Kovats RS, Campbell-Lendrum D, et al. Harben Lecture - Climate change and human health: impacts, vulnerability, and mitigation. Lancet, 2006; 367, 2101-9.
7. Basu R, Samet JM. Relation between elevated ambient temperature and mortality: a review of the epidemiologic evidence. Epidemiol Rev, 2002; 24, 190-202.
8. Easterling DR, Horton B, Jones PD, et al. Maximum and minimum temperature trends for the globe. Science, 1997; 277, 364-7.
9. Cao J, Cheng Y, Zhao N, et al. Diurnal temperature range is a risk factor for coronary heart disease death. J Epidemiol, 2009; 19, 328-32.
10. Chen G, Zhang Y, Song G, et al. Is diurnal temperature range a risk factor for acute stroke death? Int J Cardiol, 2007; 116, 408-9.
11. Song G, Chen G, Jiang L, et al. Diurnal temperature range as a novel risk factor for COPD death. Respirology, 2008; 13, 1066-9.
12. Dales R, Burnett RT, Smith-Doiron M et al. Air pollution and sudden infant death syndrome. Pediatrics, 2004; 113, e628-31.
13. Koehler SA. Air pollution and sudden infant death syndrome. Pediatrics, 1996; 98, 796-8.
14. Wang L, Pinkerton KE. Air pollutant effects on fetal and early postnatal development. Birth Defects Res C Embryo Today, 2007; 81, 144-54.
15. Maclure M. The case-crossover design: a method for studying transient effects on the risk of acute events. Am J Epidemiol, 1991; 133, 144-53.
16. Carracedo-Martinez E, Taracido M, Tobias A, et al. Case-Crossover Analysis of Air Pollution Health Effects: a Systematic Review of Methodology and Application. Environ Health Perspect, 2010; 118, 1173-82.
17. Levy D, Lumley T, Sheppard L, et al. Referent selection in case-crossover analyses of acute health effects of air pollution. Epidemiology, 2001; 12, 186-92.
18. Zanobetti A, Schwartz J. The effect of particulate air pollution on emergency admissions for myocardial infarction: a multicity case-crossover analysis. Environ Health Perspect, 2005; 113, 978-82.
19. Wong CM, Vichit-Vadakan N, Kan H, et al. Public Health and Air Pollution in Asia (PAPA): a multicity study of short-term effects of air pollution on mortality. Environ Health Perspect, 2008; 116, 1195-202.

20. R Development Core Team. R: A Language and Environment for Statistical Computing, version 2.11.0. Vienna: R Foundation for Statistical Computing. 2010.
21. Luurila OJ. Arrhythmias and other cardiovascular responses during Finnish sauna and exercise testing in healthy men and post myocardial infarction patients. Acta Med Scand, 1980; S641, 1-60.
22. Imai Y, Nobuoka S, Nagashima J, et al. Acute myocardial infarction induced by alternating exposure to heat in a sauna and rapid cooling in cold water. Cardiology, 1998; 90, 299-301.
23. Togias AG, Naclerio RM, Proud D, et al. Nasal Challenge with Cold, Dry Air Results in Release of Inflammatory Mediators - Possible Mast-Cell Involvement. J Clinical Investigation, 1985; 76, 1375-81.