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Triggering of stroke by ambient temperature variation: A case-crossover study in Maputo, Mozambique

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ABSTRACT

Objectives: The effect of ambient temperature as a stroke trigger is likely to differ by type of stroke and to depend on non-transient exposures that influence the risk of this outcome. We aimed to quantify the association between ambient temperature variation and stroke, according to clinical characteristics of the events, and other risk factors for stroke.
Methods: We conducted a case-crossover study based on a 1-year registry of the hospital admissions due to newly occurring ischemic and hemorrhagic stroke events in Maputo, Mozambique's capital city ($N = 593$). The case-period was defined as the 7 days before the stroke event, which was compared to two control periods (14–21 days and 21–28 days before the event). We computed humidity- and precipitation-adjusted odds ratios (OR) and 95% confidence intervals (95%CI) using conditional logistic regression.
Results: An association between minimum temperature declines higher than 2.4 °C in any two consecutive days in the previous week and the occurrence of stroke was observed only for first events (OR = 1.43, 95%CI: 1.15–1.76). Stronger and statistically significant associations were observed for hemorrhagic stroke (OR = 1.50, 95%CI: 1.07–2.09) and among subjects not exposed to risk factors, including smoking, high serum cholesterol or atrial fibrillation. No differences in the effect of temperature were found according to the patients' vital status 28 days after the event.
Conclusions: First stroke events, especially of the hemorrhagic type, were triggered by declines in the minimum temperature between consecutive days of the preceding week.

1. Introduction

Most stroke events are attributable to a relatively small number of well identified risk factors, corresponding to exposures that are essentially stable throughout time, which contribute to a higher background risk of stroke and to its overall burden [1,2]; however, these do not explain why an event occurs to a certain individual at a specific time [3,4].

Transitory exposures, such as day-to-day variation in ambient temperature, have been shown to trigger the occurrence of stroke events [4–9], possibly by influencing, either directly or indirectly, biological factors that lead to an acute event (*e.g.*, blood pressure and heart rate; serum concentration of lipids and vasoactive peptides; platelet aggregation) [10,11]. Nevertheless, the mechanisms underlying this triggering effect remain poorly understood, namely regarding the potential interaction with conventional risk factors for stroke and differences according to stroke subtype.

In an earlier study we showed that sudden decreases in the minimum temperatures were associated with an increase in the incidence rates of stroke in Maputo within 5–10 days [12]. In the present study we further addressed this topic by quantifying the association between ambient temperature variation

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on stroke occurrence, according to clinical characteristics of the events and other risk factors for stroke, using a case-cross over methodology.

2. Patients and methods

We conducted a case-crossover study based on a 12-month registry of the hospital admissions due to newly occurring stroke events in Maputo, the capital city of Mozambique.

2.1. Identification of stroke events and data collection

Between August 1, 2005 and July 31, 2006, we prospectively evaluated all patients admitted to any governmental or private hospital in Maputo (the Maputo Central Hospital, three general public hospitals, the Military Hospital, and six private clinics), living in town for >12 months, and suspected of having an incident stroke. The investigation followed the STEPS Stroke protocol, Step 1 (registration of hospitalized patients) according to the STEPS Stroke Manual Version 2.0 [13] as previously described [14].

Stroke was defined according to the World Health Organization clinical definition: "a focal (or at times global) neurological impairment of sudden onset, and lasting more than 24 h (or leading to death), and of presumed vascular origin [15]". During the study period trained interviewers were permanently at the Maputo Central Hospital Emergency Department for data collection. At other medical facilities a trained nurse in each shift was in charge of gathering information regarding patients with suspected stroke.

During the study period 651 stroke events were registered; CT scan or autopsy were performed in 601 (92.3%), from which 351 (58.4%) were classified as ischemic, 242 (40.3%) as hemorrhagic and 8 (1.3%) as subarachnoid hemorrhages. For this investigation, subarachnoid hemorrhages ($n = 8$) and stroke events with no classification regarding subtype ($n = 50$) were excluded leaving a total of 593 ischemic or hemorrhagic stroke events for data analysis. The date of symptom onset, as reported by the patient or a next-of-kin, was recorded and considered the day of the event (index date), regardless of the admission date.

Hypertension and diabetes were considered present when reported by the patients or their next of kin or when pharmacological treatment was prescribed on an inpatient or post-discharge basis. Information on socio-demographic characteristics, high serum cholesterol and current smoking was gathered using a standardized questionnaire, based on self-report. Atrial fibrillation was assessed through an electrocardiogram (EKG) performed to 416 patients at baseline or during the in-hospital stay. Glasgow score at admission was recorded and patients were followed up until the 28th day post-event (either through a pre-scheduled medical appointment or by telephone) to assess their vital status.

Data on the temperature in Maputo (maximum, minimum and mean temperatures for each day) were obtained from the Meteorological Institute of Mozambique, for the period between July 1, 2005 and July 31, 2006, along with mean relative daily humidity (%) and total daily precipitation (mm^3) data.

2.2. Case-crossover study design

For each stroke event, a period of 7 days before the index date was defined as the case period, which was compared with two distinct event free periods, namely between day 14 and day 21 before the event (D14–D21) and between day 21 and day 28 before the event (D21–D28) (Fig. 1). To define the maximum daily variation in the minimum temperature in each 7-day case or control periods, we computed the difference between the minimum temperature in each day and the day before, and selected the figure corresponding to the highest decrease in any consecutive days. A 7-day case-period was selected because it corresponds to the midpoint of the 5–10-day period within which we previously observed a higher incidence of stroke after sudden temperature declines [12], and to facilitate the matching by day of the week, since it may also be associated with transitory exposures. Two control periods were selected to improve the statistical power of the study.

We computed the decrease in the minimum temperature between every two consecutive days, in the case period (D0–D7) and in each of the control periods (D14–D21 and D21–D28) [12], and the highest decrease in minimum temperature in each period was selected to define the exposure to temperature variation in case and control periods. In the present report we considered only the minimum temperature decreases as our previous analysis of incidence of stroke according to temperature in this setting identified the decline in minimum temperature as the most important trigger [12].

2.3. Statistical analyses

We computed odds ratios (OR) and 95% confidence intervals (95%CI), crude and adjusted for mean relative daily humidity (%) and total daily precipitation (mm^3) in the case and control periods, as applicable, for the association between the decline in minimum temperature and stroke occurrence, using conditional logistic regression; the median of the distribution of the maximum day-to-day decrease in the minimum temperature in the case period was used as the cutoff to define the exposure to higher declines. Analyses were stratified by stroke subtype (first or recurrent and ischemic, hemorrhagic) age ($\leq$44; 45–64 or $\geq$65 years), sex, and the presence of several stroke risk factors (hypertension, current smoking, high serum cholesterol, diabetes and atrial fibrillation), stroke severity (based on patients' Glasgow score at admission) and vital status assessed at the 28-day post-event (alive or dead). For stratified analyses the OR estimates were computed using all participants with available information for each variable.

All analyses were conducted using STATA, Version 11.0 (Stata Corporation, College Station, TX, USA).

2.4. Ethics

The study protocol was approved by the National Mozambican Ethics Committee and written informed consent was obtained for all participants.

3. Results

Nearly half the patients were women and aged between 45 and 64 years. A total of 86.2% of the patients had hypertension, 9.5% were current smokers, 12.6% had high serum cholesterol and 13.4% had diabetes. Atrial fibrillation was present in just over 5% of the patients, mostly among those with ischemic stroke (Table 1).

During the 12-month study period, the median minimum temperatures were highest in February (22.8 °C) and lowest in June (14.2 °C). The monthly median of the highest decrease in minimum temperature between every 2 consecutive days in each 7-day period ranged from 1.3 °C in July to 4.2 °C in December (Fig. 2). When considering the cases among whom the highest decline in minimum temperature was higher for the case than for the control periods, the mean of the differences between each case period and the corresponding control periods D14–D21 and D21–D28 were 1.53 °C and 1.42 °C, respectively.

Minimum temperature declines higher than 2.4 °C in any consecutive days in the previous week were associated with the occurrence of stroke (crude OR = 1.23, 95%CI: 1.02–1.49; adjusted OR = 1.28, 95%CI: 1.05–1.56). However, no significant