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Association of elevated ambient temperature with death from cocaine overdose

Nathalie Auger[a,c,*], Marianne Bilodeau-Bertrand[a,b], Maud Emmanuelle Labesse[b], Tom Kosatsky[d]

[a] University of Montreal Hospital Research Centre, Montreal, Quebec, Canada
[b] Institut national de santé publique du Québec, Montreal, Quebec, Canada
[c] Department of Social and Preventive Medicine, School of Public Health, University of Montreal, Montreal, Quebec, Canada
[d] National Collaborating Centre for Environmental Health, British Columbia Centre for Disease Control, Vancouver, Canada

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ABSTRACT

Background: Ecologic data suggest that elevated outdoor temperature is correlated with mortality rates from cocaine overdose. Using non-aggregated death records, we studied the association of hot temperatures with risk of death from cocaine overdose.

Methods: We carried out a case-crossover study of all deaths from cocaine or other drug overdose between the months of May and September, from 2000 through 2013 in Quebec, Canada. We used conditional logistic regression to estimate odds ratios (OR) and 95% confidence intervals (CI) for the association between maximum outdoor temperature and death from cocaine or other drug overdose. The main outcome measure was death from cocaine overdose as a function of maximum temperature the day of death and the days immediately preceding death.

Results: There were 316 deaths from cocaine overdose and 446 from other drug overdoses during the study. Elevated temperature the preceding week was associated with the likelihood of death from cocaine but not other drug overdose. Compared with 20 °C, a maximum weekly temperature of 30 °C was associated with an OR of 2.07 for death from cocaine overdose (95% CI 1.15–3.73), but an OR of 1.03 for other drug overdoses (95% CI 0.60–1.75). Associations for cocaine overdose were present with maximum daily temperature the day of and each of the three days preceding death.

Conclusions: Elevated ambient temperature is associated with the risk of death from cocaine overdose. Public health practitioners and drug users should be aware of the added risk of mortality when cocaine is used during hot days.

1. Introduction

Case reports suggest that risk of death from cocaine overdose is heightened during warm weather (Menaker et al., 2011; Plush et al., 2015; Wetli et al., 1996). Cocaine is used by 0.4% of the world population (United Nations Office on Drugs and Crime, 2016), and is one of the main illicit substances causing death (International Narcotics Control Board, 2016; Martins et al., 2015). Recent evidence suggests that mortality from cocaine overdose is on the rise (International Narcotics Control Board, 2016; Martins et al., 2015), with a 12% increase in the United States between 2012 and 2013 alone (International Narcotics Control Board, 2016). Numerous studies have focused on understanding how route of administration and frequency of use affect risk of death (Degenhardt et al., 2011; de la Fuente et al., 2014; United Nations Office on Drugs and Crime, 2016), but external risk factors, such as temperature, have received less attention. Animal studies provide abundant support that cocaine induces hyperthermia during high ambient temperatures (Catravas and Waters, 1981; Gonzalez, 1993; Lomax and Daniel, 1993), but the impact of cocaine use during heat waves on humans is poorly understood.

Only two ecologic studies have evaluated the correlation of outdoor temperature with death from cocaine overdose, both in New York (Bohnert et al., 2010; Marzuk et al., 1998). Using aggregate data on unintentional cocaine overdoses, investigators found weak evidence of an increase of mean daily number of deaths due to cocaine when maximum outdoor temperatures were greater than 31.1 °C (Marzuk et al., 1998). The weekly number of fatal cocaine overdoses in New York also seemed to increase with average temperature (Bohnert et al., 2010). Both studies used aggregate or ecologic patient data, making it challenging to determine if the associations were biased by changes in

* Corresponding author at: 190 Cremazie Blvd E., Montreal, Quebec H2P 1E2, Canada.
E-mail address: nathalie.auger@inspq.qc.ca (N. Auger).

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climate, temperature, or cocaine use over time. In analyses of aggregate data, increasing temperatures may induce a spurious relationship with overdose mortality if cocaine use rises simultaneously, resulting in ecologic bias (Wakefield, 2008). Solid evidence of an association between elevated ambient temperature and death from cocaine overdose, therefore, has yet to be established. We studied the relationship of temperature during warm months with risk of mortality from cocaine overdose using individual death records for a large Canadian province.

2. Material and methods

We carried out a case-crossover analysis of all deaths from cocaine overdose between 2000 through 2013 in Quebec, Canada. We drew the data from death registration certificates that cover the entire population of Quebec. We used diagnostic codes of the 10th revision of the International Classification of Diseases to identify cases where cocaine (T40.5) was a principal or secondary cause of death. For deaths that did not involve cocaine, we used International Classification of Disease codes to capture cases where other narcotics or hallucinogens were primary or secondary causes (T40.0-T40.4, T40.6-T40.9, X42, Y12). We used other drugs as a comparison group to assess the plausibility of the hypothesis that temperature is associated with mortality from cocaine, but not other overdoses.

We focused on deaths between the months of May and September, the hottest period of the year in Quebec. In other months, temperatures are much colder and unlikely to reach 30 °C. As there are 18 health regions in Quebec and the residential region was available on death certificates, we obtained temperature data from Environment Canada for 18 meteorological stations representative of each health region. We paired the temperature data to individuals by region of residence at time of death.

The primary exposure was the maximum temperature the week preceding death. We calculated the maximum weekly temperature as the average of the day of death and the 6 preceding days. To further evaluate which days were more strongly associated with overdose mortality, we examined the maximum daily temperature for each day separately. As a secondary exposure, we included an indicator of heat waves, defined as the total number of days (0, 1, 2, 3 days or more) in which the maximum temperature reached at least 28 or 30 °C the week preceding death. We considered percent relative humidity a possible confounder, as well as public holidays because patterns of illicit drug use may change during such times.

We used a case-crossover study design, a method suitable for outcomes that are rare and acute, particularly when the outcome occurs shortly after a sudden exposure (Levy et al., 2001). This method is ideal to assess deaths from drug overdose following exposure to high temperatures. The case is defined as the day of death. Controls consist of nearby days when death did not occur. The temperature on case days is then compared with temperature on control days (Levy et al., 2001). This method resembles traditional case-control studies, but the difference is that cases are not matched to other individuals who serve as controls. Instead, in case-crossover studies individuals who experience the event are their own control. Ambient temperature and other factors that fluctuate in the short term are the main characteristics that differ between cases and controls. Because cases are self-matched, there is no need to adjust for measured or unmeasured confounders that do not change during the month (Levy et al., 2001; Maclure and Mittleman, 2000). Characteristics that are stable, such as age, sex, and socioeconomic status, cannot be confounders in a case-crossover study.

We used a time-stratified approach to select control days that were in the same calendar month and day of week as the case day. This approach prevents bias due to temporal changes in temperature, season, or the day of week (Janes et al., 2005; Levy et al., 2001). We used a bidirectional design to select control days that were both before and after the case day. For example, if the case day was Wednesday the 23rd of November, control days were every other Wednesday before and after the case day in the same month of the year. The bidirectional design prevents bias due to linear time trends in temperature (Levy et al., 2001).

We examined the distribution of overdose deaths from cocaine and other drugs according to temperature, age (< 35, 35–44, ≥45 years), and sex. We used conditional logistic regression to estimate odds ratios (OR) and 95% confidence intervals (CI) for the association between maximum weekly temperature and overdose mortality. To more accurately display the relationships, we expressed temperature as a continuous variable using cubic splines with knots at the 5th, 50th, and 95th percentiles (Durrleman and Simon, 1989). We selected 20 °C as the reference temperature in the spline models, following previous research (Bohnert et al., 2010; Gonzalez, 1993; Lomax and Daniel, 1993; Marzuk et al., 1998). Similarly, we evaluated the association of overdose mortality with maximum daily temperature the same day and the each of the six preceding days, as well as the association with heat waves. We adjusted all models for relative humidity and public holidays.

We performed several sensitivity analyses. We began by restricting the data to the urban regions of Montreal and Laval where temperatures are usually higher than the rest of the province, and where illicit drug use is concentrated. We repeated the analysis using mean rather than maximum temperature as the exposure. We examined associations with apparent temperature, a measure of perceived heat which combines both temperature and humidity (Anderson et al., 2013). We excluded 18 deaths which involved psychostimulants (ICD code T43.6) as some studies report that drugs such as ecstasy can affect heat regulation (Parrott, 2012). Finally, we assessed the consistency of the association between temperature and overdose mortality across age and sex groups.

We performed the analysis in SAS version 9.3 (SAS Institute Inc., Cary, NC) using the restricted cubic spline macro (Heinzl and Kaider, 1997). Patient data were de-identified and the institutional review board of the University of Montreal Hospital Centre waived ethics review. This study abided by Tri-Council Policy requirements for research on humans in Canada.

3. Results

There were 762 deaths during the period under study, including 41.5% involving cocaine and 58.5% involving other drugs (Table 1). Death from cocaine overdose was more common in men (77.5%) and before 45 years of age (62.0%). Among cases, 10.4% of cocaine deaths and 7.4% of other drug deaths occurred on days when temperature was 28 °C or greater. Similarly, 21.5% of deaths from cocaine overdose, but only 14.8% of deaths from other drugs, occurred during heat waves of 3 or more days of temperature ≥28 °C in the week.

Elevated maximum temperature during the preceding week was associated with a greater likelihood of death from cocaine overdose, but not other drugs (Fig. 1). Relative to 20 °C, a maximum weekly temperature of 28 °C was associated with an OR of 1.66 for death from cocaine overdose (95% CI 1.08–2.55) and 1.00 for other drugs (95% CI 0.68–1.46). A maximum weekly temperature of 30 °C was associated with an OR of 2.07 for death from cocaine overdose (95% CI 1.15–3.73) and 1.03 for other drugs (95% CI 0.60–1.75).

Maximum temperature the same day as well as each of the three preceding days was associated with risk of death from cocaine overdose (Fig. 2). Compared with 20 °C, a maximum daily temperature of 30 °C was associated with an OR of 1.53 the day of death from cocaine overdose (95% CI 1.03–2.27), 1.89 the day prior (95% CI 1.29–2.75), 1.76 two days prior (95% CI 1.24–2.49), and 1.51 three days prior (95% CI 1.03–2.19). Maximum temperature was not associated with mortality from other drugs any day of the week.

The likelihood of death from cocaine overdose was greater during heat waves with maximum temperature ≥30 °C (Table 2). Compared with 0 days, 3 days of maximum temperature ≥30 °C during the week was associated with an OR of 1.80 for death from cocaine overdose