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Climate and the eye: Case-crossover analysis of retinal detachment after exposure to ambient heat

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ABSTRACT

Background: Retinal detachment is an important cause of visual loss, but the association with outdoor heat exposure has not been studied. Our objective was to determine the relationship between acute exposure to high outdoor temperature and risk of retinal detachment.
Materials and methods: We analysed 14,302 individuals with inpatient procedures for retinal detachment from April through September between 2006 and 2013 in the province of Quebec, Canada. Using a time-stratified case-crossover study design, we examined the association of retinal detachment with outdoor summer temperature the preceding week. We estimated odds ratios (OR) and 95% confidence intervals (CI) for mean weekly temperature according to subtypes of retinal detachment (traction, serous, rhegmatogenous, breaks), and assessed associations by age and sex.
Results: Exposure to elevated temperature the preceding week was associated with a higher likelihood of traction detachment, but not other forms of retinal detachment. Associations were stronger at < 75 years of age in both men and women. Relative to 15 °C, a mean weekly temperature of 25 °C was associated with an OR for traction detachment of 2.71 (95% CI 1.56–4.71) before 55 years, 2.73 (95% CI 1.61–4.64) at 55–64 years, and 1.98 (95% CI 1.30–3.02) at 64–75 years.
Discussion: Elevated outdoor temperatures may be associated with an increased risk of traction retinal detachment. In light of climate change, a better understanding of the impact of heat waves on the eye and other sensory organs is needed.

1. Introduction

Few studies have addressed weather as a potential risk factor for ophthalmological disorders, including retinal detachment. Retinal detachment is a common ophthalmic emergency and a major cause of visual loss (Feltgen and Walter, 2014). The estimated annual incidence of retinal detachment is around 12.6 cases per 100,000 persons (D'Amico, 2008), with 90 eyes blinded by detachments every hour around the world (Shah, 2009). Prevention of retinal detachment is challenging because its causes are not fully understood, and known risk factors such as myopia, cataract surgery, and trauma explain only a fraction of cases (Feltgen and Walter, 2014). The role of environmental triggers is not well characterized, including the contribution of elevated outdoor temperature. Retinal detachment is an acute event, and sudden environmental stressors such as heat have the potential to contribute to their occurrence.

Ambient temperature may affect the risk of retinal detachment given an increased incidence in warm compared with cold seasons (Ghisolfi et al., 1986; Jensen, 1957; Laatikainen et al., 1985; Lin et al., 2011; Mansour et al., 2009; Paavola et al., 1983; Prabhu and Raju, 2016). The vitreous, a clear gel contained between the lens and back of the eye that holds the retina in place, is sensitive to variation in temperature (Deman and Bruyneel, 1977; Katsimpris et al., 2003). Animal studies have highlighted that cold temperatures increase adhesive forces in the eye which potentially prevent collapse of the vitreous gel, while hot temperature liquefies the vitreous, predisposing

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to detachment (Deman and Bruyneel, 1977; Katsimpris et al., 2003; Mansour et al., 2009). However, the few population studies relating average monthly or seasonal temperature to retinal detachment in humans produce conflicting results (Lin et al., 2011; Mansour et al., 2009; Prabhu and Raju, 2016). Furthermore, evidence that daily variation in temperature is associated with retinal detachment is sparse. As global warming is predicted to increase (Snyder, 2016), the potential for an increased risk of retinal detachment during high temperature has public health implications. We therefore studied the relationship of daily and weekly temperature during the warmest time of the year with risk of retinal detachment using medical records for the province of Quebec, Canada.

2. Materials and methods

We carried out a multicenter case-crossover study. We used data from the Maintenance and Use of Data for the Study of Hospital Clientele registry which contains all hospital discharge summaries in Quebec from 2006 to 2013. In Quebec, discharge summaries are coded by trained hospital personnel, and compiled by the Health Ministry which validates the data for all centers using rigorous algorithms (Ministère de la Santé et des Services sociaux, 2016). We selected individuals with retinal detachment between April and September, the hottest months of the year. Between October and March, temperatures are cold or below 0 °C in Quebec, making it difficult to assess effects of heat. The sample includes all patients who were treated for retinal detachment in hospitals, but not outpatient clinics (Auger et al., 2017).

We identified individuals with retinal detachment using surgical codes from the Canadian Classification of Health Interventions (1.CN.59). In Quebec, hospital data include up to 20 surgical and 26 diagnostic codes documented during the admission. We searched primary and secondary diagnoses for codes of the International Classification of Diseases, 10th revision, to determine the subtype of retinal detachment, including traction (H33.4), serous (H33.2), rhegmatogenous (H33.0), breaks (H33.1, H33.3, H35.7), and unspecified. Traction retinal detachment occurs when the retina is pulled away by scar like bands due to disease processes such as diabetic or sickle cell retinopathy (Feltgen and Walter, 2014). Serous retinal detachment is due to fluid accumulation behind the retina from dysfunction in the blood-retina barrier (Feltgen and Walter, 2014). Rhegmatogenous retinal detachment, the most common form, occurs when liquefied vitreous humour passes through a retinal tear or break and accumulates under the retina (Feltgen and Walter, 2014). Reasons why breaks occur in the retina are varied and the exact pathogenesis is a subject of continuing research (D'Amico, 2008; Mitry et al., 2010). Commonly, liquefication of the vitreous with aging can separate and pull on the retina, causing breaks that allow fluid to seep under and produce rhegmatogenous detachment (Feltgen and Walter, 2014).

We obtained temperature data from Environment Canada for the 18 health regions of Quebec (Martel et al., 2010) (Table S1). Meteorologists of Environment Canada have identified 18 meteorological stations that provide temperature data representative of health regions in Quebec (Martel et al., 2010). We paired the region-specific temperature data directly to the patient's region of residence recorded on the hospital chart. We evaluated the temperature on the day of the retinal detachment procedure, and during each of the six preceding days. We expressed temperature as a continuous measure, using the mean temperature of the week as the primary exposure. We analysed the mean daily temperature of each day of the week as a secondary exposure. To assess the potential impact of cumulative heat or heat waves, we evaluated the total number of days in the week in which the maximum daily temperature reached at least 28 °C or 30 °C (e.g., 0, 1, 2, 3 or more days with ≥30 °C). We included percent relative humidity as a covariate in the analysis.

2.1. Study design

We used a time-stratified case-crossover study design to examine the association between elevated outdoor temperature and risk of retinal detachment. Case-crossover designs are ideal when the goal is to evaluate the association between an acute exposure and a disease that occurs shortly after (Levy et al., 2001). In our study, the exposure was outdoor temperature and the disease was retinal detachment. The case-crossover approach is similar to case-control analysis in which the exposure for cases is compared with exposure for controls. The difference, however, is that the case-crossover design assesses only cases of retinal detachment, with exposure before occurrence of the case contrasted with the case's exposure in comparable "control" periods (Maclure and Mittleman, 2000; Redelmeier and Tibshirani, 1997). Here, the case is defined as the day the patient was treated for retinal detachment, and the control as nearby days when the event did not occur. Case days are afterwards compared with control days for key differences in temperature exposure. Because patients with retinal detachment are their own controls, adjustment for unmeasured confounders such as age, socioeconomic status, myopia or history of intraocular interventions is automatic, as long as these do not vary between case and control days over time (Levy et al., 2001; Maclure and Mittleman, 2000; Redelmeier and Tibshirani, 1997).

In this study, we defined case days as the date of treatment for retinal detachment, and used a time-stratified approach to select control days. Thus, if the calendar date of the case was Monday July 18, 2006, the time-stratified approach defined controls as all other Mondays in the same month. Selecting controls in the same month as the case cancels out seasonal bias and minimizes the possibility of changes in unmeasured covariates (Janes et al., 2005). Selecting controls the same day of the week rules out the possibility of effects of the day of week (Janes et al., 2005; Levy et al., 2001). Finally, bidirectional sampling of controls both before and after the day of case prevents bias due to temporal trends in weather in any given month (Levy et al., 2001).

2.2. Data analysis

We examined the distribution of retinal detachment according to outdoor temperature, age, and sex. We used the X^2 test to examine differences between proportions. Using conditional logistic regression, we estimated odds ratios (OR) and 95% confidence intervals (CI) for the association between temperature and retinal detachment, adjusting for humidity. We carried out the analysis for all retinal detachments combined, and for each type of detachment separately, in addition to running models stratified by age and sex. We expressed temperature as a continuous variable using cubic splines with knots at the 5th, 50th, and 95th percentiles following thresholds recommended in literature (Durrleman and Simon, 1989).

In sensitivity analyses, we examined associations in the urban areas of Montreal and Laval, and trends for months restricted to June through August when heat is more prominent in Quebec. We further examined associations between temperature and retinal detachment for all twelve months of the year combined, including January through December. In addition, we tested models adjusted for the mean weekly hours of sunlight and mean weekly barometric pressure for the subset of retinal detachments which had data available (N = 7123). We did so because temperature may be correlated with sunlight and barometric pressure, which researchers have proposed may be additional triggers for retinal detachment (Al Samarrai, 1990; Lin et al., 2011; Prabhu and Raju, 2016). We carried out subgroup analyses for individuals with diabetes (ICD codes E10-E14) and pre-existing hypertension (ICD codes I10-I15). Finally, we examined apparent temperature, a measure that combines temperature with relative humidity (Anderson et al., 2013), in the event that perceived heat was more strongly related to risk of retinal detachment.