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The influence of weather on the risk of pain exacerbation in patients with knee osteoarthritis – a case-crossover study

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SUMMARY

Objective: To quantify the risk of knee pain exacerbation associated with temperature, relative humidity, air pressure and precipitation in persons with knee osteoarthritis.
Method: A web-based case-crossover study was conducted. Participants with a diagnosis of symptomatic, radiographic knee osteoarthritis were measured at baseline and followed for 3 months. Participants were instructed to log on to the study website if they perceived experiencing knee pain exacerbation (hazard period). Pain exacerbation was defined as an increase of ≥2 on a 0–10 numeric rating scale (NRS) from the participant's mildest pain reported at baseline. A time-stratified case-crossover study was conducted to anchor the corresponding hazard date to four control periods within a particular 35-day interval. Data on maximum and minimum temperature (°C), relative humidity (%), barometric pressure (hPa) and precipitation (mm) were obtained for the hazard and control periods from the publicly available meteorological database of the Australian Bureau of Meteorology. The associations were assessed using conditional logistic regression.
Results: Of the 345 participants recruited, 171 participants (women: 64%, mean age: 62 years, mean BMI: 30.2 kg/m^2) experienced at least one episode of pain exacerbation, yielding 1,425 observations included in the analyses. There was no apparent association between temperature, relative humidity, air pressure or precipitation and risk of knee pain exacerbation.
Conclusion: Despite anecdotal reports from patients, change in weather factors does not appear to influence the risk of pain exacerbation in persons with knee osteoarthritis. Additional studies should quantify the association of weather and risk of pain exacerbation in regions with more extreme weather conditions.

Introduction

Osteoarthritic pain is typically episodic and often patients will report that weather conditions can trigger their symptom exacerbations[1]. Cold temperatures, air humidity and barometric pressure are among the top triggers for pain exacerbation, in the opinions of patients with osteoarthritis[1,2]. This phenomenon – common to a number of other chronic pain conditions (e.g., rheumatoid arthritis, gout, and fibromyalgia) has been reported by two in every three patients with knee, hip or hand osteoarthritis[3], and observed in regions of varying climate conditions[1,3].

However, despite the frequency with which this phenomenon is endorsed by patients, the scientific literature on the subject is vulnerable to bias and conflicting[4]. In fact, most evidence in the field derives from studies establishing the association between patients' self-perceived sensitivity to climate changes and self-reported pain intensity[1–3,5]. To date, only few studies have focussed on the association between osteoarthritic symptoms and observed climatic conditions. Again, these have important methodological limitations, including small and heterogeneous samples of clinical diagnoses[6–10]; and failure to blind participants regarding

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the research question (i.e., the influence of weather on self-reported symptom alteration)[8,9]. Guedj & Weinberg, for example, have assessed the association between weather and joint pain or swelling in a small ($n = 24$) sample of patients with multiple joint osteoarthritis (e.g., hip, knee and hand)[8]. Even though the authors concluded that 83% of the included participants presented symptom variations in response to weather changes, the magnitude of that association was not reported, and pain exacerbation was self-reported, although patients were not blinded to the research question. Past evidence is also conflicting. For instance, Timmermans *et al.* have recently shown a weak but significant association between humidity and joint pain, but no association between temperature or atmospheric pressure and joint pain in people with osteoarthritis of the knee, hand and/or hip[11], contradicting the findings of McAlindon *et al.*, who showed changes in temperature and atmospheric pressure were associated with increased knee pain in patients with knee osteoarthritis[12].

Therefore, past research has not yet provided undisputed evidence on the transient risk of experiencing an episode of pain exacerbation associated with changes in weather conditions, in persons with knee osteoarthritis. The case-crossover approach overcomes most of the limitations of previous studies as it is optimally designed to quantify the risk of an event associated with short duration and transient exposures[13–15], such as changes in climate conditions. This approach compares exposure to putative risk factors in periods of time preceding the event to those when no event is observed and has been previously used to identify the role of climate conditions in the increased risk of myocardial infarction[16], stroke[17], acute low back pain[18], and recurrent gout attacks[19].

We have conducted a web-based case-crossover study to quantify the transient increase in risk of knee pain exacerbation associated with a range of potential triggers[20]. This paper evaluates the association of selected weather conditions and the risk of knee pain exacerbation in people with knee osteoarthritis. Exposure to weather factors at the time of the pain exacerbation (defined as hazard periods) was compared with that in periods when no symptom exacerbations were reported (control periods)[14].

Methods

Participants

A web-based case-crossover study was conducted between June 2012 and July 2014 in Australia. A total of 345 participants with the diagnosis of symptomatic radiographic knee osteoarthritis were recruited through online advertisements posted on special interest group websites (e.g., Arthritis Australia, MyJointPain); and from existing databases of participants of previous studies on symptomatic knee osteoarthritis. Detailed information on patient recruitment can be found elsewhere[20]. To be included, participants needed to be aged 40 years or older; report having knee pain at least 5 days/week that fluctuates in intensity; meet at least one of the American College of Rheumatology criteria for knee osteoarthritis; have tibiofemoral (Kellgren and Lawrence Grade (KLG) $\geq$2) or patellofemoral osteoarthritis confirmed on a radiograph (confirmed by a study physician and based on the participant's most recent X-ray); and have access to the internet and an active email address. Participants on waiting lists for surgical knee replacement within 6 months or with a history of knee replacement on the most symptomatic knee; a history of secondary osteoarthritis (e.g., osteonecrosis) or those unable to communicate in English were excluded. Participants were advised the aim of the study was to assess the risk of knee pain flares associated with common triggers, but were not aware of which specific weather factors would be included or when and how these would be assessed. The study was approved by the Human Research Ethics Committees of the University of Sydney (protocol number: 14435) and the University of Melbourne (HREC number 1237429).

Knee pain exacerbation

All participants were asked to complete online questionnaires including demographic and clinical data at baseline and then every 10 days for 3 months. At baseline, participants were asked to indicate how severe their knee pain was at its mildest, usual and worst times of their current everyday life. Participants were also instructed to log on to the study website whenever they experienced a disabling increase in their knee symptoms that lasted for longer than 8 h without settling. Knee pain exacerbation was ascertained via the Pain Numeric Rating Scale (NRS 0–10) and defined as an increase of $\geq$2 on a 0–10 NRS compared with the mildest pain level reported at baseline. Those participants who experienced a disabling increase in symptoms and also reached the flare definition threshold of a 2-point increase in pain were automatically identified by our system – knee pain exacerbation (*hazard period*). Regular email reminders were sent to all participants prompting them to log in immediately after they experienced symptom exacerbation. The threshold for knee pain exacerbation was chosen based upon the OARSI Clinical Trials Response Criteria definition for a meaningful change in symptoms[21]. 'Pain at its mildest' was used as the comparator for our case definition (i.e., pain exacerbation) to enable the identification of the maximum number of meaningful events as possible. Participants were asked to provide zip codes for their location when they experienced knee pain exacerbation.

Climate data

Data on maximum and minimum temperature (°C), relative humidity (i.e., current amount of water vapour in the air relative to that if the air were completely saturated; %), barometric pressure (hPa), and precipitation (mm) for each specific zip code were obtained for each participant's hazard and control periods by querying from the publicly available meteorological database of the Australian Bureau of Meteorology (www.bom.gov.au/climate/data/index.shtml).

Our definition of hazard and control periods follows our previous work on the influence of weather on the risk of gout attacks[19]. Specifically, for the *hazard period*, the day of the reported pain exacerbation was used as the reference date to obtain climate data across 0–24 (index day), 25–48 (1 day before index), 49–72 (2 days before index) and 73–96 h (3 days before index) from the pain exacerbation date. For *control periods*, the calendar was divided into 35-day intervals, from twenty fourth of June 2012 (study inception) and within each 35-day interval, the day of the week knee pain exacerbation occurred, was used as the hazard period index date. The same day of the week was used as the index date for the control periods. For example, if knee pain exacerbation occurred on the second Monday of a 35-day time block, then the first, third, fourth, and fifth Mondays in that time block were used to define each of four control periods[19]. Although weather variations do not necessarily depend on the day of the week, other potential time-varying confounders (e.g., engagement in physical activity, shoewear) could potentially influence the risk of knee symptom exacerbation and vary according to the day of the week. Thus, the time-stratified case-crossover approach could appropriately account for cyclical variation of the underlying hazard of pain exacerbation according to day of the week. In addition,