Environment International 78 (2015) 32–38

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Full length article

Association of Kawasaki disease with tropospheric winds in Central Chile: Is wind-borne desert dust a risk factor?

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ARTICLE INFO

Article history:
Received 18 March 2014
Received in revised form 17 January 2015
Accepted 4 February 2015
Available online 2 March 2015

Keywords:
Kawasaki disease
Tropospheric winds
El Niño Southern Oscillation
Chile

ABSTRACT

It has been found that Kawasaki disease (KD) cases diagnosed in Japan, Hawaii and San Diego, USA increase when tropospheric wind patterns arrive from central Asia, suggesting a common, wind-borne causal agent. We analyzed KD cases hospitalized in Santiago, Chile to look for associations with local, regional and large scale meteorological variables. We compiled monthly data of KD incidence rates, local meteorological variables, large scale wind patterns and several El Niño Southern Oscillation (ENSO) indices for 2001–2010; we considered standardized anomalies in all analyses and used linear time series models to account for data autocorrelation. We found that meteorological variables explain 38% of variance in KD rates. A unit increase in northerly wind at 3 lagged months, temperature at 1 and 3 lagged months and monthly change of ENSO 4 index are associated with changes in KD rates of 0.203 (95% CI 0.049–0.358), 0.181 (95% CI 0.014–0.347), 0.192 (95% CI 0.030–0.353) and −0.307 (95% CI −0.458–0.156), respectively. These results are robust when northerly wind level is changed or when a shorter period (2005–2010) is used to estimate model parameters. We found a statistical association of KD at Santiago, Chile with tropospheric, northerly wind patterns suggesting that dust transported from the Atacama Desert could include a causative agent. A novel result is that ENSO dynamics also explain part of KD variability with a decrease in KD when La Niña is dissipating or El Niño is on the rise; hence climate scale dynamics might be taken into account in future studies worldwide — at least as a potential explanatory variable that may confound KD seasonality on a global scale.

1. Introduction

Kawasaki disease (KD) is an acute, self-limited vasculitis that most commonly affects infants and young children. Its predilection to affect the coronary arteries has led KD to replace rheumatic fever as the most frequent cause of acquired heart disease in developed countries (Newburger et al., 2004). First reported in 1967 in Japanese children (Kawasaki, 1967), it is now known to occur worldwide with increasing incidence rates in many countries (Yanagawa and Nakamura, 2008), including Chile (Borzutzky et al., 2012); although it is unclear whether this is due to increased awareness or a true rise in incident cases. After more than 40 years of intensive research to find the cause of KD, its etiology remains elusive. The clinical characteristics of this mysterious disease share common patterns with several infectious diseases such as scarlet fever, measles, and adenovirus. Thus, it is thought that one or more infectious agents in individuals with genetic susceptibility may cause KD (Principi et al., 2013).

The incidence of KD appears to be affected by an interaction between host and environmental factors. Worldwide, over 75% of KD cases occur in children younger than 5 years of age and the disease is uniformly more frequent in boys than girls. Genetic factors definitely influence KD: incidence is at least 10-times higher in children of Asian ethnicity. Several genetic susceptibility loci and single nucleotide polymorphisms in genes related to immunity and inflammation have been associated with higher risk of KD (Rowley, 2011). However, genetic factors cannot completely explain seasonal and longitudinal variations in incidence or geographic clustering of KD cases. Epidemiological studies performed in multiple countries have supported the possibility of an elusive infectious etiological agent (Burgner and Harnden, 2005). KD has been reported to have seasonal variations in many different countries, as well as geographical and temporal clustering (Burns et al., 2005, 2013). In addition, epidemics of KD have occurred, most notably in Japan in 1982 and 1986 (Nakamura et al., 2012). Several reports have also documented an association with higher socioeconomic status, a characteristic that is also seen in several infectious diseases (Bell et al., 1981; Dean et al., 1982). Although associations of KD with several infectious agents

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http://dx.doi.org/10.1016/j.envint.2015.02.007

have been published (Principi et al., 2013), these reports have not been confirmed and so far no unique etiological agent has been identified.

Rodo et al. (2011) found an association of KD in Japan, Hawaii and San Diego, USA, with tropospheric wind patterns transporting air masses from central Asia's deserts and cities towards those locations. When air trajectories change – wind blowing to Japan from the southern ocean – KD incidence rates show a strong decrease there. Further research by this group has suggested that tropospheric winds from northeastern China carry a putative etiologic agent of KD to Japan (Rodo et al., 2014). These authors have postulated the hypothesis of a wind-borne aerosolized infectious agent, possibly a fungus of the *Candida* species, as a potential etiology of KD.

Why would desert dust pose a risk to human health? Griffin (2007) has summarized literature on the long-range transport of bacteria, fungi and viruses in desert dust in the Northern hemisphere; he states that "…the risk from other pathogenic microorganisms is unknown, due to the limited number of studies and study design – all to date have been culture based, and none have been risk oriented – (page 472)". Goudie (2014) has summarized the scientific evidence of dust storms on respiratory and cardiovascular disorders (KD is not cited), along with other diseases, reported in the literature; he concurs with Griffin's opinion that dust-borne pathogen risks are still largely unknown.

A key issue in connecting Asian dust emissions with downwind population exposure is to show that they would reach ground levels at a receptor site while other Asian emissions would not. Dust emissions are generated by synoptic-, meso- and small-scale motions (Schepanski et al., 2009); then turbulence injects dust into the free troposphere; in the Northern hemisphere westerly winds transport dust across the Pacific Ocean above the marine boundary layer (MBL) so dust is subject to lower wet scavenging than urban pollution plumes — which are transported within the MBL. Hence, pollution levels on the coast of China decrease by 50–100 times when arriving to North America as compared with only a 20 times reduction for Asian dust (Chin et al., 2007). Whenever air masses reach the North American west coast, subsidence motion and mountain waves bring dust down to the ground (McKendry et al., 2008). This framework has been supported by dispersion modeling of trans-Pacific dust transport (Uno et al., 2011) and by observations: VanCuren and Cahill (2002) have found a distinctive spring peak of crustal aerosol reaching remote sites in western North America; Zhao et al. (2008) found a correlation of 0.83 between ground level PM_{10} at US sites and frequency of Asian desert storms in 2000–2006; and Cottle et al. (2013) have used lidar and sunphotometer network data to backtrack Asian dust plumes reaching Canada and northern USA in spring 2010.

The above evidence suggests that desert dust may be an environmental trigger for KD increases in the Northern hemisphere and that other pollution sources – Asian cities – would not contribute to that onset. In this study we evaluated possible associations of KD in central Chile with tropospheric wind patterns to test the hypothesis that desert dust exposure may contribute to increase KD cases; we also consider local and large-scale meteorological variables that may also explain part of KD variability, including its seasonality.

2. Materials and methods

2.1. Study population

We conducted a retrospective review of national hospital discharge databases from the Department of Health Statistics and Information of the Chilean Ministry of Health (2013). We examined hospital discharges for KD (ICD-10 code M30.3) between January 2001 and December 2010 for patients younger than 18 years of age. A total of 1274 cases of KD occurred in Chile during this 10-year period. Fifty percent of the national KD caseload (641 cases) occurred in the population living in the Metropolitan Region that includes the capital city of Santiago (33.5°S, 70.6°W) with a regional rate of 3.34 per 100,000 children younger than 18 years for the period. Nineteen cases were excluded because of missing data and thus 622 cases were finally included in the study. Cases were then grouped by month of discharge and monthly KD incidence rates were calculated in children (i.e. population younger than 18 years) for the entire study period. Raw and standardized anomalies of KD incidence rates were calculated for quantitative analyses.

2.2. Tropospheric wind data

We downloaded wind data from the USA's National Oceanic and Atmospheric Agency (NOAA) NCAR/NCEP reanalysis data at a 0.5° resolution – http://rda.ucar.edu/datasets/ds093.0/#!description – these are generated by data assimilation of all available meteorological observations using a global circulation model so they represent an optimal estimate of the actual state of the atmosphere. We selected the values at 33.5°S and 71°W that are close to Santiago's metropolitan area and representative of air masses en route to the city. We chose the following height levels: 1000, 925 and 850 millibars (mb) and 2743 and 3658 m above sea level (masl). Winds on the lowest two levels (1000 and 925 mb) are usually within the planetary boundary layer (PBL) and those on the two highest levels (2743 and 3658 masl) are above the PBL, within the free troposphere. Therefore lower level winds stand for local wind circulations such as the valley-mountain breeze whereas free troposphere winds stand for long-range transport of air masses to Santiago. In this way we include the dominant large scale wind patterns arriving at Santiago.

2.3. Local weather data

We compiled SYNOP reports at Santiago's international airport (WMO station 85574, 33°23′S, 70°47′W) that contain meteorological records for the period 2001–2010. These data are subject to QA/QC protocols by local meteorological officers and were downloaded from a specialized website (www.ogimet.com).

2.4. El Niño indices

El Niño Southern Oscillation (ENSO) is a feature of the ocean–atmosphere system in the tropical Pacific causing climate variability on seasonal to inter-annual time scales (NOAA, 2014). To include the ENSO climate effect we have chosen the Multivariate ENSO Index (MEI) that is based upon six meteorological variables (Wolter and Timlin, 2011). We have also chosen the Southern Oscillation Index (SOI), which is a standardized sea level pressure difference between Tahiti and Darwin, Australia. Finally, sea surface temperature (SST) anomalies in four tropical Pacific Regions (1 + 2, 3, 4 and 3.4) were also included in the analysis. Data were downloaded from NOAA's Climate Prediction Center – http://www.esrl.noaa.gov/psd/enso/enso.current.html#indices – where further details about those indices are provided.

3. Results

3.1. Seasonal variation of actual KD and meteorological variables

Fig. 1 shows the monthly averages of KD incidence rates at Santiago, Chile and zonal and meridional wind components, respectively. Fig. 2 (top panel) shows temperature, relative humidity and total rainfall; these data are distinctive of a temperate climate with rainy winters and dry summers. Fig. 2 (bottom panel) shows the ENSO indices considered here – SOI was reversed in sign for consistency – all of them indicate El Niño/La Niña events – warmer/cooler ocean temperatures in Equatorial Pacific – when the index is positive/negative — see Wolter and Timlin (2011) for further details. Meridional winds above the PBL show a distinct northerly jet (~2000–5000 masl) that results from the