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Acute changes in serum immune markers due to swimming in a chlorinated pool

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ABSTRACT

Background: Exposure to disinfectants and disinfection byproducts (DBPs) due to swimming in chlorinated water has been associated with allergic and respiratory health effects, including asthma.
Objectives: Biological mechanisms contributing to these associations are largely unknown. We hypothesized a potential pathway involving modulation of the immune system.
Methods: We assessed levels of immune markers (CCL11, CCL22, CXCL10, CRP, EGF, GCSF, IL-8, IL-17, IL-1RA, MPO, VEGF, Periostin) in serum collected from 30 women and 29 men before and after 40 min of swimming in a chlorinated pool. Exposure to DBPs was assessed by measuring bromodichloromethane, bromoform, chloroform, and dibromochloromethane in exhaled breath before and after swimming. Covariate data including information on physical activity was available through questionnaires and measurements. We assessed the association between indicators of swimming in a chlorinated pool and changes in serum immune marker concentrations using linear regression with bivariate normal distributions and adjusted for multiple comparisons by applying the Benjamini-Hochberg procedure.
Results: We observed a significant decrease in serum concentrations of IL-8 (−12.53%; q = 2.00e-03), CCL22 (−7.28%; q = 4.00e-04), CCL11 (−7.15%; q = 9.48e-02), CRP (−7.06%; q = 4.68e-05), and CXCL10 (−13.03%; q = 6.34e-14) and a significant increase in IL-1RA (20.16%; q = 4.18e-06) from before to after swimming. Associations with quantitative measurements of DBPs or physical activity were similar in direction and strength. Most of the observed associations became non-significant when we adjusted the effects of exposure to DBPs for physical activity or vice-versa.
Conclusions: Our study indicates that swimming in a chlorinated pool induces perturbations of the immune response through acute alterations of patterns of cytokine and chemokine secretion. The observed effects could not be uniquely attributed to either exposure to DBPs or physical activity. Evidence in the literature suggests that observed decreases in immune markers are possibly due to an immunosuppressive effect of DBPs, while the increase in IL-1RA might be due to physical activity.

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1. Introduction

Even though the beneficial effect of swimming as a form of physical activity on human health is undisputed, concerns have been raised with regards to potential negative effects on human health of swimming in pools in which water disinfectants are applied. Disinfectants such as chlorine react with organic matter in the water creating a range of disinfection by-products (DBPs), some of which (especially trichloramine) have been linked with chronic allergic and respiratory health effects, including asthma, in epidemiological studies (Villanueva et al., 2015; Villanueva and Font-Ribera, 2012). Biological mechanisms contributing to these observed associations are largely unknown though might involve modulation of the immune system.

Two studies previously assessed the effect of swimming in chlorinated pools on acute changes in immune marker concentrations. Font-Ribera et al. (2010) assessed a suite of markers (RANTES (regulated upon activation, normal T-cell expressed, and secreted), vascular endothelial growth factor (VEGF), tumor necrosis factor (TNF), interleukin (IL) 12p70, IL-4, IL-8, IL-10, interferon-gamma (IFN-γ), and IFN-γ–induced protein 10 (IP10) in exhaled breath condensate of nonsmoking adults, collected before and after for 40 min of swimming in a chlorinated pool. No significant change in any of the immune markers was observed. A significant change in lung damage marker club cell secretory protein 16 (CC16) levels in serum was observed. The authors mentioned that the concentrations of the immune markers in exhaled breath condensate was low and indicated that further validation of using these markers assessed in exhaled breath condensate as indicators of acute inflammation was needed (Font-Ribera et al., 2010). Pedersen et al. (2009) observed no significant changes in lung function, exhaled NO, pH of exhaled breath condensate, and cellular composition of sputum of 45 min of swimming in a chlorinated swimming pool. One study very similar in design to the study by Font-Ribera observed no significant associations between the effect of swimming in a chlorinated pool on oxidative stress and lung damage markers (serum surfactant proteins A and B) (Llana-Belloch et al., 2016).

Evidence for potential immunotoxic effects of DBPs is available from a handful of animal studies (Auttachoat et al., 2009; French et al., 1999; Munson et al., 1982), while studies among humans exposed to halocarbons that are structurally very similar to DBPs also provide evidence for immunotoxic effects (Bassig et al., 2013; Griffin et al., 2000; Iavicoli et al., 2005; Weber et al., 2003).

In addition to DPBs, physical activity might also have an effect on the immune system. A bout of physical activity has been reported to induce an anti-inflammatory environment including acute elevations in production of interleukin 6 (IL-6) from muscle tissue, stimulating the production of anti-inflammatory cytokines such as IL-1 receptor antagonist (IL-1RA), and downregulation of the number of monocytes in blood reducing the production of pro-inflammatory cytokines (Gleeson et al., 2011). Long-term exposure to regular bouts of physical activity has been linked to immunosuppression thought to be induced by the anti-inflammatory effects of exercise (Gleeson et al., 2011).

In this study we assessed the impact of 40 min swimming in a chlorinated pool on changes in a set of 13 serum immune markers. We attempted to disentangle the effects of physical activity and exposure to DBPs on the immune markers by quantitative assessment of both markers of exposure to DBPs and physical activity and by controlling potential confounding factors such as age, sex, and Body Mass Index (BMI).

2. Methods

2.1. Design

We recruited 59 nonsmoking adults through open advertisements at local universities. A screening questionnaire was used to verify eligibility among subjects (nonsmoking, non-professional swimmers, 18–40 years of age). Participants were asked to swim for 40 min at a calm pace in an indoor 25 m long chlorinated swimming pool in Barcelona, Spain. Participants did not swim during the week before the swimming session and did not shower or conduct intense physical activity on the day of the study. Up to four participants were evaluated between 09:00 and 14:00 each day (before lunch) in June, September–December 2013. Exhaled breath and blood were collected before and after the subjects swam in the chlorinated pool in a room inside the sports center. The study was approved by the ethics committee of the research center following the international regulations, and all volunteers signed an informed consent before participation.

2.2. Assessment of physical activity

Physical activity was estimated by measuring the distance swum by each participant, calculating energy expenditure (in kilocalories) using the swimming speed and the weight of the participant, assuming that swimming at 46 m/min equals 8.3 metabolic equivalent tasks (METs; kilocalories per kilogram per hour) (Ainsworth et al., 2000):

$$Kcal = weight\ (kg) \times \frac{distance\ swam\ (m)}{minute} \times swimming\ duration\ (hr) \times 8.3 \left(\frac{^{kcal}/_{kg}}{hr} \right) \Big/ 46\ (^{m}/_{min})$$

Study participants also wore a RCX5 heart rate (HR) monitor while swimming (Polar, Kempele, Finland). We calculated the percentage of monitored heart rate values during swimming that was higher than 69% of the individual theoretical maximum heart rate according to sex and age, indicating high intensity physical activity (%HR; 220-age for males, 206–0.88*age for females) (Gulati et al., 2010). Two participants did not register HR data. We imputed the missing values with the median value of the %HR calculated for the remaining study participants.

2.3. Markers of exposure to DBPs

We measured concentrations of four trihalomethanes (THMs)–chloroform ($CHCl_3$), bromodichloromethane (BDCM), dibromochloromethane (DBCM), bromoform ($CHBr_3$)–in exhaled breath before swimmers entered the swimming pool and right after (median 4 min) they left the pool (median 4 min). We used the THMs as surrogate for DBP exposure because they are easily measured in exhaled breath. Measurement of THMs in exhaled breath for this study has been described before (Font-Ribera et al., 2016). Briefly, exhaled breath samples were collected using a portable system for exhaled breath sampling (Bio-VOC™ Sampler, Markes International Ltd., UK). A total of 600 mL exhaled breath volume was collected. THM concentration were detected using a Gas Chromatograph 7890 (Agilent Technologies) coupled to Mass Spectrometer 5975C Inert XL MSD with a source in Electron Impact Mode (Agilent Technologies). Concentrations were expressed as micrograms per cubic meter.

In addition swimming water concentrations of a range of DBPs, including the THMs measured in exhaled breath, were measured on the days the study was conducted. A detailed description of sampling and analytical methods for DBPs in the poolwater in this study was provided in Font-Ribera et al. (2016).

To measure trichloramine, air samples were collected every day with a sampling pump at a constant flow rate of 1.2 L/min for 115 min within 1 m of the pool at a height of 60 cm above the water level. Trichloramine was collected on a quartz fibre filter, reduced to chloride ions and subsequently analyzed by ion chromatography. Further details on the applied methods are provided in Jacobs et al. (2007).