ASSOCIATION BETWEEN PFAS CONCENTRATIONS AND LIVER FUNCTION BIOMARKERS IN THE HYPER-EXPOSED POPULATION OF THE VENETO REGION

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Background:

Per- and polyfluoroalkyl substances (PFAS) are a ubiquitous group of chemical substances that have proven to be associated with several adverse health effects, depending on the characteristics of exposure and on individual factors. PFAS can dysregulate immune, endocrine, cardiometabolic and reproductive systems and pose increased risk for cancer and developmental effects [1,2]. Epidemiological and animal studies highlight the presence of consistent associations between PFAS exposure and markers of liver damage, suggesting that the liver is one of the main target organs for PFAS [3,4]. Additional studies are required to further explore PFAS possible hepatotoxic effect. In 2013, in a large area of Veneto Region (Italy), public water works and private wells were found to be contaminated by PFAS, due to the presence of a fluorochemical manufacturing plant operating in the area since the 1960s. A biomonitoring programme (the Health Surveillance Programme) was implemented in 2017 to investigate the associations between PFAS exposure and several health outcomes in the hyper-exposed population [5]. Participants completed a questionnaire regarding their socio-demographic characteristics and provided serum and urine samples for PFAS quantification and biomarkers evaluation.

Aim:

The primary objective is to investigate the association between exposure to PFAS, namely PFOA, PFOS, PFHxS and PFNAe and alanine aminotransferase (ALT) and aspartate aminotransferase (AST), with ALT being considered as a specific biomarker of liver injury, using both single-pollutant and mixture approaches. The secondary objective is to investigate the role of body mass index (BMI) as a possible mediator of PFAS exposure effect on liver function.

Methods:

The study population is composed by 42,094 subjects aged ≥20 years participating to the Surveillance Program and residing in the contaminated area, after exclusion of pregnant women and subjects with reported liver diseases. To investigate the association between PFAS and ALT aspartate AST, we used generalized additive models, with thin plate splines for continuous variables. Models were adjusted for a set of possible covariates, including age, education level, smoking habit, alcohol consumption, laboratory of analysis and distance between PFAS measurement and the end of exposure. The joint effect of PFAS exposure was investigated using Quantile G-computation. PFAS concentrations and biomarkers levels were natural log-transformed and results were back-transformed to predicted percentage changes in the outcome for a 1% increase in PFAS concentration [3,6,7]. Furthermore, a mediation analysis was conducted to investigate the role of BMI in the abovementioned associations, decomposing the total effect in direct and indirect effect. All analyses were stratified according to sex after testing for interactions.

Results:

A 1% increase in PFOA concentration was associated with a 0.59% (95%CI: 0.04, 1.15) and a 0.41% (95% CI: 0.05, 0.77) increase in ALT and AST levels in males; a 1% increase in PFHxS concentrations was associated with a 0.84% (95% CI: 0.26, 1.43) and a 0.55% (95% CI: 0.17, 0.93) increase in ALT and AST levels in females. A negative association between PFOS and ALT and AST levels was found in males. Similarly, a 1% increase in PFNA concentrations was associated with a 1.02% decrease in AST levels in males. Results were confirmed when PFAS were considered as categorical variables, according to their quartiles of distribution. In Quantile G-computation, an interquartile increase in the PFAS mixture exposure was associated with a 2.82% increase (95% CI: 1.52, 4.14) in ALT and a 1.70% (95% CI: 0.78, 2.63) increase in AST levels, in females. Mediation analysis showed that BMI mediates 36.8% of the association between PFOA and ALT in males and 15.2% of the association between PFHXS and ALT in females, showing a positive direct effect which was higher than the total effect.

Conclusions:

Our findings suggest the presence of sex-specific associations between PFAS exposure and liver function biomarkers in the Italian cohort and highlight the necessity for additional studies investigating the role of possible mediators.

References:

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