ANTIBIOTIC EXPOSURE AND RISK OF MULTIPLE SCLEROSIS: A POPULATION-BASED CASE-CONTROL STUDY IN THE EMILIA ROMAGNA REGION

Ippazio Cosimo Antonazzo[1], Elisa Baldin[2], Corrado Zenesini[2], Luca Vignatelli[2], Emanuel Raschi[1], Roberto D'Alessandro[2], Elisabetta Poluzzi[1]

[1]Pharmacology Unit, Department of Medical and Surgical Sciences, University of Bologna, Bologna - Italy, [2]Epidemiologia e BioStatistica, IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna - Italy

Background and aim: Multiple sclerosis (MS) is a multifactorial inflammatory and neurodegenerative disease. Several environmental risk factors have been already associated with MS onset: low blood vitamin D concentration, smoking and Epstein-Barr virus. In this intricate scenario, the role of other external risk factors should be further assessed; for instance, others infections could trigger MS onset or drugs used to treat infections may have a role in MS disease by altering the immune system or the intestinal microbiota functions. The aim of this study was to investigate the possible association between antibiotic exposure and MS onset in Emilia Romagna, a large Italian region.

Methods: We conducted a population-based case-control study by including all residents in Emilia Romagna between 2002and 2017. Cases were represented by patients aged ≥ 18years with MS diagnosis since 2005. The MS diagnosis was done by neurologists who also provided demographic and clinical data: patient code, age, sex, date of onset (index date) and type of disease (relapses-remitting (RR-MS) or primary progressive (PP_MS)). For each patient, 5controls were matched by age, sex, place of residence, and time in the cohort before the index date. Antibiotic exposure was assessed by analysing the prescription reimbursement database from 2002to 2016. The exposure was defined as sum of days covered in the 3and 8years before the index date. Conditional logistic regression model was undertaken to estimate the odds ratio (OR) with relevant 95% confidence intervals (95%CI). Analyses were adjusted for the matching variables among cases and controls. Possible influence of deprivation index and chronic disease score were also evaluated, by including these covariates in the model.

Results: In the observed period, we selected 877cases and 4,205controls. Cases were mainly females (66%, in line with epidemiological features of the disease), with a mean age of 36years, and many of them lived in Bologna (24%). Thirty-three percent of cases were diagnosed in the 2014-2017and the RR-MS was the most frequent type of MS (817; 93%). Among the cases, 403(46%) were smokers. In the 8years before the index date, 468out of 529cases used at least 1antibiotic, showing an OR of 1.95(95%CI: 1.44-2.63). When the exposure to antibiotics was assessed in the 3years before OR was 1.52(1.29-1.79). As regards deprivation index, inverse association with MS was found for the 5th quintile (more deprived; 0.63; 0.49-0.82). The restricted analysis preformed only for Bologna residents showed a positive association between penicillin exposure and MS onset (1.59; 1.09-2.33). An association was also found for chronic disease score and MS, in particular for heart disease (1.65; 1.03-2.65) and peptic ulcers (1.83; 1.13-2.97).

Discussions and conclusions: This study showed a positive association between antibiotic exposure and MS onset. Our results are in contrast with a previous study performed in United Kingdom that included fewer cases of MS. On the other hand, our findings confirm a previous study performed in a Danish cohort. Future basic researches can investigate the role of antibiotics in MS pathology, contributing to understand if these drugs are cause per se of disease or represent a proxy of concomitant or previous diseases that trigger MS development.