The Institute of Environmental Medicine, Unit of Cardiovascular Epidemiology

Epidemiological studies in Malaysia and Sweden on associations between smoking, silica exposure and the risk of developing rheumatoid arthritis

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av

Abqariyah Yahya

Huvudhandledare:
Professor Lars Alfredsson
Karolinska Institutet
Institutionen för Miljömedicin

Bhändledare:
PhD, forskarassistent, Camilla Bengtsson
Karolinska Institutet
Institutionen för Miljömedicin

Professor Lars Klareskog
Karolinska universitetssjukhuset,
Karolinska Institutet
Institutionen för medicin, Solna

Docent Per T Larsson
Karolinska universitetssjukhuset,
Karolinska Institutet
Institutionen för medicin, Huddinge

Fakultetsopponent:
Professor Anne-Marie Landtblom
Linköping Universitet
Institutionen för klinisk och experimentell medicin

Betygsnämnd:
Professor Claes-Göran Östenson
Karolinska Institutet
Institutionen för molekylär medicin och kirurgi

Docent Jette Möller
Karolinska Institutet
Institutionen för folkhälsovetenskap

Docent Ulla Lindqvist
Uppsala Universitet
Institutionen för medicinska vetenskaper

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ABSTRACT

Rheumatoid arthritis (RA) is a chronic, inflammatory disease, frequently associated with joint destruction. Knowledge regarding the aetiology of RA is mainly generated on Caucasian populations. Less is known about RA in other populations with different genetic backgrounds and lifestyles. The aim of this thesis was to contribute to a better knowledge regarding the aetiology of RA in other populations, particularly Asian populations, by studying the association between airborne exposures and RA risk, here smoking and occupational exposure to silica. We studied the risk of developing RA by different subtypes of the disease, defined by the presence or absence of antibodies to citrullinated protein antigens (ACPA+ RA and ACPA- RA).

This thesis is mainly based on data from the Malaysian Epidemiological Investigation of Rheumatoid Arthritis (MyEIRA), Paper I, II and IV. MyEIRA is a population-based case-control study where cases and controls provided extensive information on lifestyle as well as occupational exposures. Cases and controls also provided blood samples for serological and genetic analysis. In Paper III, data from the Swedish Epidemiological Investigation of Rheumatoid Arthritis (EIRA) population-based case control study was used. Information regarding the environmental exposures was gathered by means of a questionnaire. Cases and controls provided blood samples for genetic and serological analysis.

Our results in the MyEIRA study indicate that smokers had an increased risk of developing ACPA+ RA, but not ACPA- RA, compared with never-smokers. A significant dose-response relationship between cumulative dose of smoking (expressed by pack-years) and risk of ACPA+ RA was observed. A significant interaction was noted between smoking and the HLA-DRB1 shared epitope (SE) alleles in the risk of developing ACPA+ RA. We also found that the most common SE allele in the Asian population, HLA-DRB1*0405, also showed signs of interaction with smoking with regard to risk of ACPA+ RA.

We further studied the relationship between occupational exposure to silica, i.e. another airborne exposure, and the risk of developing RA in the Swedish EIRA study. Men that had been exposed to silica in their work were observed to have a moderately increased risk of ACPA+ RA but not ACPA- RA compared to men without such exposure. A significant interaction between silica exposure and current smoking was observed with regard to the risk of developing ACPA+ RA. The findings from MyEIRA were similar to those from EIRA; thus occupational exposure to silica was associated with an increased risk of developing ACPA+ RA, but not ACPA- RA. Furthermore, there were signs of interaction between silica and smoking with regard to risk of ACPA+ RA, even though small numbers hampered a firm conclusion.

In conclusion, this study shows that airborne environmental exposures are strongly associated with risk for RA in Malaysia. The results should have impact on efforts to prevent RA in this large part of the world, as well as for further comparative studies aimed at understanding the aetiology of RA in different populations.

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