

WG3

Can pyrethroid pesticides cause diabetes?

Martin Rune Hassan Hansen^{1,2}, Flemming Lander³, Erik Jørs³, Anelli Sandbæk², Vivi Schlünssen^{2,4}

DiMoPEX



¹ Department of Cardiology, Aarhus University Hospital, DK

² Department of Public Health, Aarhus University, DK

³ Department of Occupational Medicine, Odense University Hospital, DK

⁴ The National Research Center for the Working Environment, Copenhagen, DK

Address all correspondence to mrha@clin.au.dk

Background

Pyrethroids are a group of pesticides whose principal mode of action is delayed closure of voltage-gated sodium channels in excitable cells. The WHO considers spraying with pyrethroids a cornerstone in the fight against mosquitoes spreading malaria and dengue fever – diseases that are still significant threats to global public health.

There may be a link between long-term pyrethroid exposure and diabetes mellitus. In 2012, we carried out a cross-sectional study among Bolivian spraymen showing a significant positive relation between cumulated exposure to pyrethroids (defined as total number of hours sprayed) and OR of prediabetes: OR above 7 for the most exposed compared to the least exposed (p for trend = 0.014) (1).

Until now, the possible association between pyrethroid exposure and diabetes mellitus has only been investigated in two cross-sectional studies. We propose a new and more robust study on the subject.

Hypotheses

- Long-term exposure to pyrethroids is associated with abnormal glucose regulation.
- There is a positive exposure-response relationship between pyrethroid exposure and average blood glucose concentration.
- Pyrethroids may have a sustained effect on blood glucose levels. Alternatively the effects seen are acute, but are detectable due to repeated exposures.

Exposed individuals

Pyrethroids are used globally, but this project will be carried out in Nepal because pesticide sprayers working in Nepal are expected to have considerably higher exposure levels than Western farmers due to spraying practices and sparse use of personal protective equipment.

The project "Community Based Management of Diabetes in Nepal: A Cluster-Randomized Controlled Trial" is a PhD project at Aarhus University in collaboration with the Nepal Development Society (2). Its goal is to investigate the effect of education by community health volunteers on diabetes mellitus in a population of 2000 men and women aged 25-64 in the semi-urban Lekhnath Municipality in Nepal. We expect around 60% of the population to be exposed to a mixture of pesticides.

Methods and materials

Faze 1a: Baseline study

Blood samples are drawn from all participants and analyzed for hemoglobin A1c - a measure of the average blood glucose level for the last 6-8 weeks.

Exposure to pesticides will be determined in three ways:

- Because pyrethroids have a short half-life in the human organism, chronic exposure has to be determined from a job exposure matrix.7-26.
- Urine samples will be analyzed for metabolites of pyrethroid and organophosphate pesticides to quantify acute exposure.
- The distance from the home of each participant to the nearest field will be calculated using GPS and used as an indirect measure of pesticide exposure.

HbA1c results are analyzed with raw and adjusted linear regression models with both subjective and objective measures of pyrethroid exposure as the exposure of interest.

Faze 1b: Exposure study

The purpose of this sub-study is to determine whether the possible effects of pyrethroids on glucose levels are acute or chronic. In a cross-over design, 50 sprayers are randomized to spraying for 3 hours with permethrin (a pyrethroid) or placebo solutes. Blood glucose levels will be measured before, repeatedly during and after spraying. Data will be analyzed using paired t-tests.

To quantify the levels of pyrethroids in the air while spraying, air samples from the breathing zone of 20 randomly selected workers will be collected.

Faze 2: Follow-up

After approximately 1 year, a follow-up study will be carried out among the participants from faze 1a. As COBIN-D is a cluster-randomized intervention study we will restrict our part of the project to the non-intervention clusters (approximately half of the original population).

The main interest is the impact of average pyrethroid exposure in the one year follow-up period on changes in average blood glucose. Data will be analyzed both assuming constant exposure levels since the baseline study, and taking into account any changes in exposure that may have happened.

Perspectives

If we can confirm that pyrethroid exposure is associated with diabetes mellitus, we will have to re-evaluate how pyrethroids are used in public health programs.

We also plan to establish a bio-bank with the urine and blood samples from the project after ethical approval from the Nepal Health Research Council. To our knowledge, no bio-banks exist in Nepal. The proposed study is a unique opportunity to create a well-defined large cohort in which to study health challenges in a developing country.

Research plan

The project will be carried out from February 2017 to January 2020.

Literature references

1. Hansen MR, Jors E, Lander F, Condarco G, Schlünssen V. Is cumulated pyrethroid exposure associated with prediabetes? A cross-sectional study. *J Agromedicine*. 2014;19(4):417-26.

Free full text available from



goo.gl/uFWp5Z

2. Nepal Development Society. www.nedsnepal.org/activity/