Postdoctoral fellowship

Employer:

Centre Hospitalier Universitaire of Toulouse (France)
Service de Pharmacologie Médicale et Clinique

Location:

Service de Pharmacologie Médicale et Clinique -
Unité « Médicaments, Reproduction, Grossesse et Allaitement »

Faculté de Médecine - 37 Allées Jules Guesde - 31000 Toulouse (France)

Research laboratory presentation:

Our research team in Pharmacoepidemiology is located in the department of Clinical Pharmacology, at Toulouse school of Medicine (South-West France). From several years, we have been working on reproductive risks of drugs. In 2004, we have created EFEMERIS database (www.efemeris.fr), the first French database on prescriptions during pregnancy in general population which currently records anonymous data for more than 137,000 pairs mother/ pregnancy outcome. Children from EFEMERIS cohort are followed up until 2 years of age. In 2010 the cohort "POMME 2010" of around 8000 children was also set up. For the children of POMME, drug prescriptions are recorded during prenatal life and during childhood, until 7 years old at the present time. Five years later, "POMME 2015" has been created. The team also performs pharmacoepidemiological studies on national databases such as EGB (Echantillon Generaliste des Beneficiaires), an administrative database which represents a 1/97 sample of the French population. The team is involved in developing new methodological or statistical approaches.

The team is the leader of the French network "REGARDS" (REproduction Gestation And Risk of DrugS) and is a partner of the European Consortium **ConcePTION** (IMI2 call 13 Topic 9), the aim of which is to "Build an ecosystem for better monitoring and communicating safety of medicines use in pregnancy and breastfeeding".

Research project description:

In collaboration with the other members of the team, the post-doctoral fellow will conduct the following project that has been planned for the IMI ConcePTION project and participate to other missions of our group in the ConcePTION consortium:

Methods for controlling by indication for prescriptions: application to medications for neuropathic pain

Rationale of the study (background): One of the major issues that arise when using large administrative health care registries is the absence of indication for drug use. This is a crucial problem for drugs with several indications when the risk for adverse pregnancy outcomes is different according to the underlying maternal disease. This uncertainty is an important limitation for the interpretation of pregnancy medication safety studies. The motivating example for this demonstration projects is drugs for neuropathic pain and dysfunctional (NDP). These medications include gabapentinoids (G), tricyclic antidepressants (TA), dopamine agonists (DA) and analgesics, which are also used for a range of other diseases like epilepsy and mental disorders. The increase in use and lack of data on safety during pregnancy, makes this topic of great public importance.

Aim and impact of the study: The aim of the study is to develop a method to identify drug indication in big electronic data sources in order to evaluate the risk of medications prescribed to pregnant women for NDP.
The first step of the demonstration project is to estimate the prevalence and the incidence of women of childbearing age and pregnant women being dispensed medications for NDP. Then, an algorithm to determine the reason why the medication has been prescribed will be developed and validated with clinician experts by *ad hoc* preliminary study.
Finally, the safety of medications (see *"outcomes"* below) for NDP in pregnancy (for ex G vs TA) will be evaluated in the different groups of pregnant patients (patients with NDP according to their treatment/ non treated NDP/without NDP). The European multicentre design of the demonstration project will allow including a sufficient number of pregnant patients in each group. Special attention will be paid to congenital anomalies, maternal and perinatal outcomes as well as childhood outcomes including growth and (neuro) development.
This demonstration project will provide Health Agencies and Pharmaceutical industry with a regulatory valid algorithm to identify drug indication in administrative health care registries as well as recommendations on management of neuropathic and dysfunctional pain during pregnancy.

Innovative elements of the demonstration study: This project will use a novel approach to account for the underlying indication for use thus limiting the "disease bias" in future medications in pregnancy studies since disease physiopathology could account for some adverse effects in pregnancy outcomes. The ability of the algorithm developed with clinician experts to correctly identify women with NDP will be validated with medical records. The algorithm will take into account essential information, such as the drug name and dosage, the prescriber specialty, patient diagnoses and co-medications so that the basis algorithm can be applied and adapted in the data sources and different indications from different partner countries. For the demonstration project, pain severity will be taken into account through utilization of pain medications as a proxy for pain intensity and the trajectory method, which enables to assess the impact of drugs for NDP in pregnancy according to the profile of exposure. Other potentially confounding factors (such as environmental or genetic factors, comorbidities and co-prescriptions, alcohol or cigarette consumption when available) will be controlled using other methods: propensity scores (probability of exposure to medications for NDP given the observed confounders) and sibling comparison design.

Description of the study, including the methodology employed:

- *Data sources:* Several databases could be used from across Europe, such as healthcare databases from Euromedicat, SNIIRAM and Scandinavian partners. Data concerning prenatal exposure to drugs for NDP will be also gathered among children's disability registries (for example RH31) in Europe
- *Study population:* women of childbearing age, pregnant women and their children followed in time
- *Outcomes:* congenital anomalies, maternal and perinatal outcomes as well as neurodevelopmental risk or childhood outcomes
- *Exposure:* medications for NDP
- *Analysis methods:* algorithm validation, trajectory method, propensity score, sibling comparison

Preferred Experience and Skills:

Academic requirements: PhD or equivalent degree in pharmaco-epidemiology or related fields

Skills and experiences:

- Strong biostatistics skills are mandatory,
- Experience on studies on large databases,
- Previous SAS programming experience.

Language requirements: Fluent English (reading, writing and speaking)

Personal qualities: Strong organizational skills, communication skills, scientific rigor

Employment contract

- For 3 years
- Date of takeover: April 2019
- Salary: according to experience and to hospital research salary scale

Application information

Please, send CV and motivation to Christine Damase-Michel, by email at:

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