Incidence analysis and prediction of potentially harmful drugs among asthma patients

Victor Pera[1], Peter Rijnbeek[1], Katia Verhamme[1]

[1]Department of Medical Informatics, Erasmus University Medical Center - Rotterdam (Netherlands)

Background

Drugs that can be potentially harmful to patients with specific medical conditions are usually marked as contra-indicated drugs. Accidentally prescribing such a contra-indicated drug while having a better alternative is considered a medication error as described within the Medical Dictionary for Regulatory Activities (MedDRA®) terminology. There are several drugs that can be considered potentially harmful for asthma patients as described in literature (1–5). However, for asthma patients, none of these drugs are considered as strictly contra-indicated by the Global Initiative for Asthma (GINA) guidelines (6). Currently, only beta-blockers and non-steroidal anti-inflammatory drugs (NSAIDs) are considered potentially harmful to a selected group of asthma patients and are not considered as being absolutely contra-indicated by GINA. So far, the incidence of prescribing these potentially harmful drugs for asthma-patients has not been described in literature. The primary objective of this research was to provide a first insight on the incidence-rate of potentially harmful medication to asthma-patients. The secondary objective was to set-up a prediction model, evaluate the discriminative value and get first insights on predictive parameters.

Methods

A retrospective population-based cohort study was conducted using data from the Integrated Primary Care Information (IPCI) database which was mapped to the Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM). The study period was from 1st January 2010 until 31st December 2020. The study-population was defined within ATLAS (7) as patients with a first asthma-diagnosis (index-date), with at least 2 prescriptions of respiratory drugs within 365 days after index-date, having a medical-history of at least 365 days before and 365 days after index-date. Patients with a diagnosis of chronic obstructive pulmonary disease (COPD) any time before or after index-date were excluded. Asthma and COPD were defined based on a selection of SNOMED Clinical Terms as described in a previous study-package (8) for the purpose of a multi-database-study with Observational Health Data Sciences and Informatics (OHDSI) collaborators. The incidence-rate analysis on the following drugs was performed: systemic NSAIDs (excluding cyclooxygenase-2 inhibitors), ophthalmic NSAIDs, systemic non-selective beta-blockers, systemic selective beta-blockers, ophthalmic beta-blockers, parasympathomimetics and benzodiazepine agonists. The incidence-analysis was performed with the CohortIncidence package (9), expressed as the incidence-rate of prescriptions per person year (PY). A logistic regression model to predict prescribing of the potentially harmful drugs was developed based on the Least Absolute Shrinkage and Selection Operator (LASSO) within each cohort by utilizing the PatientLevelPrediction-package with default covariate-settings.(10)

Results

A total of 42,112 people with asthma from the IPCI-database met the inclusion criteria for the study population. The prescription-incidence-rate of the potentially harmful drugs for asthma patients was 9.1/100 PYs (Figure 1). Analysis on the distinct drug-groups revealed that systemic NSAIDs were the most frequently prescribed with an incidence-rate of 7.9/100 PYs. The second most prescribed drug-group was benzodiazepines, having an incidence-rate of 3/100 PYs. Stratified analysis (Figure 1) on sex

showed that the incidence-rate of prescribed drugs was higher in women (12/100 PYs) than men (7/100 PYs). The incidence-rate was also the highest among the elderly, being 25/100 PYs for the age-group 80-89 years and 20/100 PYs for the age-group 70-79 years (Figure 2). For the prediction model, the area under the receiver operating curves (AUROCs) with 95% confidence interval (95% CI) was 0.71 (95% CI: 0.70-0.72). The strongest positive predictors were age groups from 30-54 years, having predictive values ranging from 0.30-0.53. Presence of the CHA_2DS_2-VASc score-variable was also a strong predictor with a value of 0.37. Hypertensive disorder and mood disorder showed predictive values of respectively 0.24 and 0.23. Antidepressants and analgesics had a predictive value of 0.19 and 0.17 respectively.
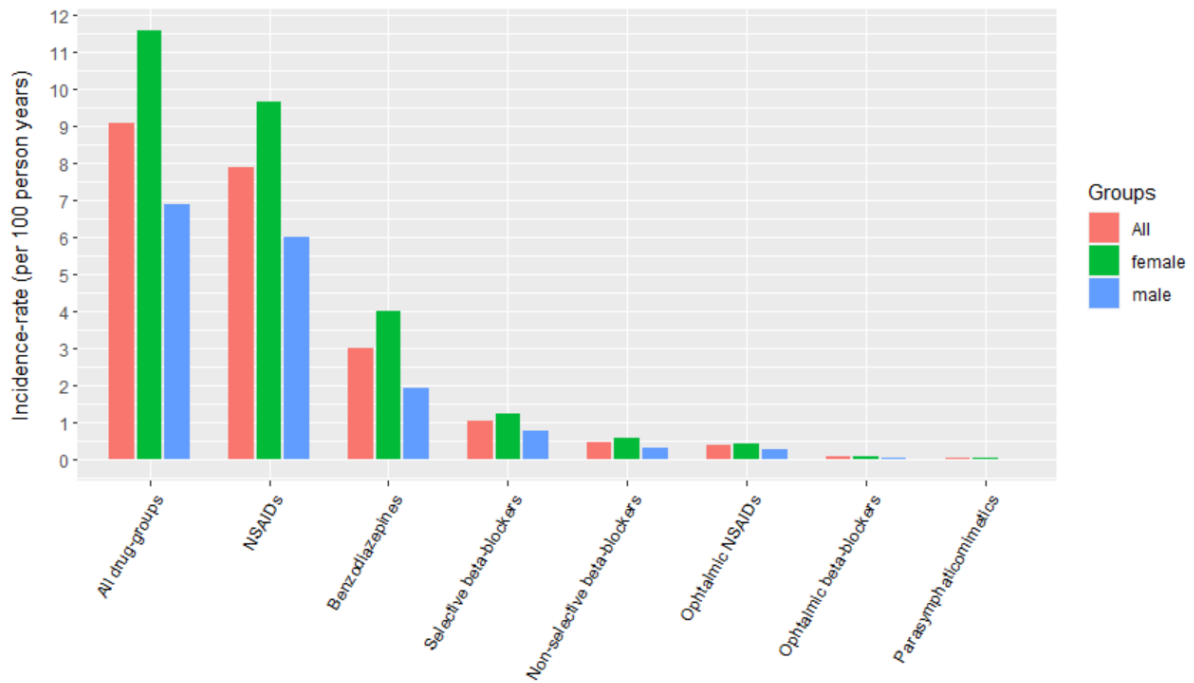

Figure 1. Incidence-rate for all drug-groups among the asthma-population stratified by sex. NSAID = Non-steroidal anti-inflammatory drug
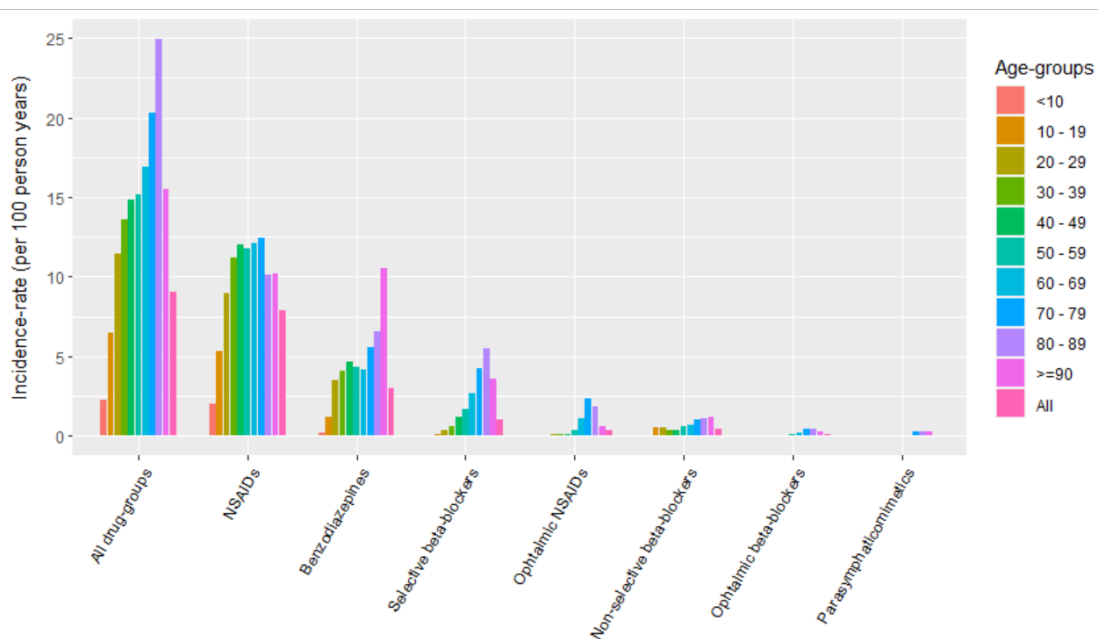

Figure 2. Incidence-rate for all drug-groups among the asthma-population stratified by age-groups. NSAID = Non-steroidal anti-inflammatory drug

Conclusion

Prescribing potentially harmful drugs for asthma-patients occurred frequently, and mainly considered of NSAIDs. The incidence rate was the highest among the elderly populations and women. The prediction model showed acceptable discriminative value, but requires further optimization. The prediction model indicates that select age-groups, co-morbidities and drugs have predictive properties for receiving a prescription of a potentially harmful drug among asthma-patients.

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