Risk of asthma attacks is increased in association with non-steroidal anti-inflammatory drugs adjusting for season effects

Takashi Ando, Yoshinori Takeuchi, Chieko Ishiguro, Yoshiaki Uyama

Office of Medical Informatics and Epidemiology, Pharmaceuticals and Medical Devices Agency (PMDA) – Tokyo, JAPAN

Objectives

- ✓ **Acute asthma attacks (AAAs)** is a well-known adverse event associated with the use of **non-steroidal anti-inflammatory drugs (NSAIDs)**, but few studies have evaluated using a quantitative epidemiological approach.
- ✓ Seasonal effect is an important risk factor for the incidence of asthma, but the attribution to the association between NSAIDs use and AAAs is not also fully known.
- ✓ **A self-controlled case series study (SCCS)** using Japanese claims database was conducted to evaluate the risk of **AAAs** associated with the prescription of NSAIDs considering with seasonal effects.

Methods

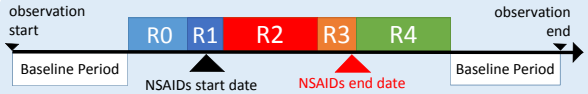
Data Source

- ✓ A commercial database comprising monthly administrative claims data from between January 1st 2012 and December 31st 2013 provided from the Japan Medical Data Center Co. Ltd (Tokyo, Japan) .
- ✓ The database covered insurance claims for employed workers and their immediate families in Japan; approximately 1.6 million patients.
- ✓ The enrollees can be followed up from their enrollment until the insurance plans are no longer valid.
- ✓ The database included information on patient characteristics (encrypted personal identifiers, age, and gender), prescribed or dispensed medications, procedures, and diagnoses.

Study population

- ✓ The study population for the SCCS comprised "cases", referring to patients who had experienced an AAA (defined as the combination of an inhalation procedure and the prescription of any inhaled β2-agonist) during the observation period.
- ✓ We divided the observation periods of exposed cases who had been prescribed any of the NSAIDs into five risk periods (R0, R1, R2, R3, and R4) based on a timing of period relating to the NSAID prescription start date and baseline periods.
  - ✓ Since some previous studies indicated that including the non-exposed case in the study population of SCCS lead to better adjustment for time-varying confounding, we include not only exposed cases but also non-exposed cases as their entire observational periods were treated as baseline periods.

Definitions of exposure and analytical periods



- R0 = 7 days before prescription start date
- R1 = the prescription start date
- R2 = 1–9 days after the prescription start date
- R3 = > 9 days after the prescription start date
- R4 = 7 days after the prescription end date

Figure 1. Definition of risk periods and baseline periods

Estimation of the incidence rate ratio

- ✓ The incidence rate ratio (IRR) and 95% confidence intervals (CI) of AAAs were calculated for each risk periods compared with baseline periods using conditional Poisson regression models.
- ✓ We included seasonal effects as a time-dependent variable with the four categories.
  - ◆ spring (March to May), summer (June to August), autumn (September to November), and winter (December to February).

Results

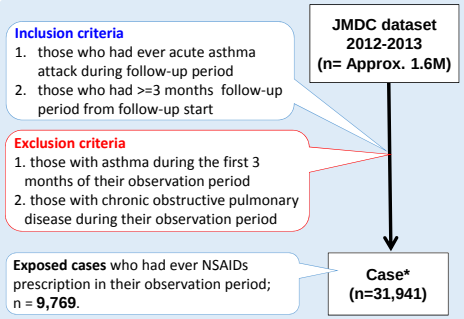


Figure 2. Enrollment of analysis population

Table. Results of conditional Poisson regression analysis of AAAs for NSAIDs

Variables	Events(n)	Total person-days	IRR(95%CI)
Periods			
Baseline Period (reference)	46,106	18,012,546	1.00
R0	326	143,619	1.44 (1.29-1.61)
R1	3,424	23,860	93.93 (90.08-97.93)
R2	554	96,093	3.96 (3.63-4.33)
R3	170	73,822	2.19 (1.81-2.64)
R4	715	154,154	3.01 (2.78-3.25)
Seasons			
Summer (reference)	11,350	5,256,067	1.00
Autumn	18,431	5,241,192	1.61 (1.57-1.64)
Winter	9,709	3,607,909	1.21 (1.18-1.24)
Spring	11,805	4,398,926	1.23 (1.20-1.26)

Study population

- ✓ After application of both the inclusion and exclusion criteria, there were 31,941 cases included in analysis.
- ✓ This population comprised nearly equal proportion of men and women (50.8%, 49.2%, respectively), and consisted mainly of patients aged below 60 years (>95% of the sample). The median of age was 8.6 years old, although that of 9,769 exposed cases was 32.9 years old.

IRR estimates for NSAIDs

- ✓ All risk periods had a significantly higher risk of asthma attacks than the baseline period. Specifically, the highest risk was observed in R1 (IRR = 93.93 [95% CI: 90.08–97.93]).
- ✓ Smaller than the effect of NSAIDs, but significant effects of seasonal factors were also observed, especially in autumn (IRR = 1.61 [95% CI: 1.57–1.64]), when compared with summer in which the risk of asthma onset is considered to be lowest.

Conclusions

- ✓ The increased risk of AAAs was associated with NSAID prescriptions during entire risk periods after taking seasonal effects into account.
- ✓ The remarkable high risk was obtained at the R1 (the prescription start date) but it could be overestimated due to the reverse causation (the asthmatic attack observed in R1 might occurred prior to the administration of NSAIDs).

Disclosure Takashi Ando and the other authors: Nothing to disclose.