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

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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- The enrollees can be followed up from their enrollment until the insurance plans are no longer valid.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 = ≥ 10 days after the prescription start date
- R4 = 7 days after the prescription end date

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

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

<table>
<thead>
<tr>
<th>Variables</th>
<th>Events(n)</th>
<th>Total person-days</th>
<th>IRR(95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline Period (reference)</td>
<td>46,106</td>
<td>18,012,546</td>
<td>1.00</td>
</tr>
<tr>
<td>R0</td>
<td>326</td>
<td>143,619</td>
<td>1.44 (1.29-1.61)</td>
</tr>
<tr>
<td>R1</td>
<td>3,424</td>
<td>23,860</td>
<td>93.93 (90.08-97.93)</td>
</tr>
<tr>
<td>R2</td>
<td>554</td>
<td>96,093</td>
<td>3.96 (3.63-4.33)</td>
</tr>
<tr>
<td>R3</td>
<td>170</td>
<td>73,822</td>
<td>2.19 (1.81-2.64)</td>
</tr>
<tr>
<td>R4</td>
<td>715</td>
<td>154,154</td>
<td>3.01 (2.78-3.25)</td>
</tr>
</tbody>
</table>

Inclusion criteria

1. those who had ever acute asthma attack during follow-up period
2. those who had ≥3 months follow-up period from follow-up start

Exclusion criteria

1. those with asthma during the first 3 months of their observation period
2. those with chronic obstructive pulmonary disease during the observation period

Exposed cases who had ever NSAIDs prescription in their observation period; n = 9,769.

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.