2020 Health Technology Reassessment Report

Safety of Oseltamivir in Children and Adolescents

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Summary

Background

National Evidence-based Healthcare Collaborating Agency conducted a '2020 Public demand survey for reassessment topic' to accommodate the social demand for health technology reassessment. The topic of ‘Tamiflu Capsule’ proposed through the demand survey was finally adopted through the priority selection process of the Health Technology Reassessment Committee.

As a result of the review of the assessment protocol of the 4th Health Technology Reassessment Committee (2020.04.09.~04.17. written review) in 2020, it was determined that the priority of systematic literature review or claim data analysis was not high, so it is intended to provide information on the safety of Tamiflu in children and adolescents at this point through domestic and international evidence arrangement. For the purpose of providing information to the public, it was deliberated not to decide a grade of recommendation on this case.

Through the discussion of the subcommittee on the safety of oseltamivir in children and adolescents, the title of the agenda was changed to ‘Safety of oseltamivir in children and adolescents’ to clarify the evaluation target and scope without specifying the specific product name (Tamiflu capsule).

The 9th Health Technology Reassessment Committee (2020.09.11.) in 2020 finally reviewed the safety evaluation results of oseltamivir in children and adolescents and decided to additionally describe the phrase for public guidance in the report.

Methods

To evaluate the evidence for the safety of oseltamivir at the present time in children and adolescents, previous systematic literature review, overseas health technology assessment reports, and overseas reimbursement status were reviewed. All evaluation methods were finalized after deliberation by the subcommittee in consideration of the research purpose.

The safety subcommittee of oseltamivir in children and adolescents, consisting of a total of 8 members (1 from Department of Family Medicine, 1 from Department of Infectious Disease, 1 from Department of Internal Medicine, 1 from Department of Pediatrics, 1 from Department of Otolaryngology, 1 from Department of Psychiatry, 1 from Department of Pulmonary and Critical Care Medicine, 1 from Department of Evidence-based Medicine, 1 from Department of Pharmacology), evaluated the technology based on the literature and submitted the review results

through the total of 3 subcommittees meetings for about 3 months from June 2020 to August 2020.

The search for previous systematic literature review studies was performed in three overseas databases, and two reviewers independently screened and selected them according to the literature inclusion and exclusion criteria determined through subcommittee discussion. The risk of bias assessment on the literature was conducted independently by two reviewers using the AMSTAR tool and consensus was reached. Qualitative analysis was applied for data analysis.

To find the health technology assessment report (including the accelerated assessment report), the website of agencies for the health technology assessment and the Cochrane Library were searched. In order to confirm the current status of oseltamivir benefit for children and adolescents in major countries, the benefit item and reimbursement coverage of oseltamivir were confirmed mainly on the website of major government agencies.

Results

As a result of assessment based on six systematic reviews that reported the safety results of oseltamivir in children and adolescents, oseltamivir significantly increased the risk of vomiting in children and adolescents, and other side effects were not significantly increased or different compared to placebo. However, outcome indicators of neurological abnormalities were not reported in most of the literature.

Overseas health technology assessment reports and guidelines on antiviral agents for the treatment and prevention of influenza also mentioned that oseltamivir increases the risk of vomiting in children and adolescents, and neurological abnormalities have been reported in children and adolescents. However, it was stated that no correlation with oseltamivir was confirmed.

Conclusion and Suggestion

The subcommittee on the safety of oseltamivir in children and adolescents made the following recommendations based on the current assessment results.

As a result of an extensive review of previous systematic literature reviews, overseas health technology assessment reports, and guidelines, oseltamivir showed a tendency to significantly increase the risk of vomiting in children and adolescents. However, as there is a lack of studies with a high level of evidence to determine the association between oseltamivir administration and neurological

symptoms in children and adolescents, an observational study through a large-scale prospective registry is required. At present, it is difficult to draw conclusions about the safety of oseltamivir in children and adolescents. In addition, it was recommended that children and adolescents not be alone during the period of fever while taking oseltamivir.

The Health Technology Reassessment Committee deliberated that the sub-committee review result on “safety of oseltamivir in children and adolescents” was appropriate, and requested to write a guide for the public in easy-to-understand terms (2020.09.11.)

Guideline for the public

The 10th Health Technology Reassessment Committee reviewed and finally approved the following guideline for the public (2020.10.16.). The text for a public guideline is as follows:

As a result of an extensive review of clinical studies and clinical guidelines reported so far, when oseltamivir (Tamiflu, etc.) was administered to children and adolescents for the treatment of influenza (flu), vomiting symptoms increased, but the association with neurological symptoms such as convulsions and delirium was not confirmed. In conclusion, the subcommittee composed of relevant clinical experts determined that there was no evidence to change the previously proven safety of oseltamivir as an influenza treatment because there is insufficient evidence to determine whether it is a side effect from the drug or a symptom from the flu even though there were reports of neurological symptoms such as convulsions and delirium after taking oseltamivir. It was suggested that a large-scale patient observational study is needed to confirm the association between oseltamivir and neurological symptoms in children and adolescents.

Also, taking into account the contents mentioned in the safety letter and safety leaflet issued by the Ministry of Food and Drug Safety, a guardian is required to prevent children and adolescents from being alone for at least 2 days after taking oseltamivir. If any abnormal symptoms are observed, it is recommended to immediately consult with the attending physician about whether to stop taking the drug.

Keywords

Influenza, Oseltamivir, Tamiflu, Safety