ROUTINE USED OF ACETAMINOPHEN FOLLOWING CHILDHOOD IMMUNIZATION

HEALTH TECHNOLOGY ASSESSMENT SECTION
MEDICAL DEVELOPMENT DIVISION
MINISTRY OF HEALTH MALAYSIA

019/2010

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Please contact: htamalaysia@moh.gov.my, if you would like further information.

Health Technology Assessment Section (MaHTAS),
Medical Development Division
Ministry of Health Malaysia
Level 4, Block E1, Precinct 1
Government Office Complex
62590 Putrajaya

Tel: 603 88831246

Fax: 603 8883 1230

Available at the following website: http://www.moh.gov.my
Prepared by:

Puan Maharita Ab Rahman
Pharmacist
Health Technology Assessment Section (MaHTAS)
Ministry of Health

Reviewed by:
Datin Dr Rugayah Bakri
Deputy Director
Health Technology Assessment Section (MaHTAS)
Ministry of Health Malaysia

Dr. Junainah Sabirin
Senior Principal Assistant Director
Health Technology Assessment Section (MaHTAS)
Ministry of Health

DISCLOSURE

The author of this report has no competing interest in this subject and the preparation of this report is totally funded by the Ministry of Health, Malaysia

EXECUTIVE SUMMARY

Introduction

Acetaminophen is very widely used as an antipyretic as well as analgesics because of its high efficacy and good safety profile. It is used to relieve mild to moderate pain from headaches, muscle aches, menstrual periods, colds and sore throats, toothaches, backaches, and reactions to vaccinations, and to reduce fever.[1]

Acetaminophen is considered as safer antipyretic for children compared to other drugs. After receiving immunizations, fever is part of the body's normal inflammatory process. In many cases, acetaminophen is administered to relieve possible risk of high fever or febrile convulsions in children after routine infant vaccinations.

The technology review was requested by a Family Medicine Specialist from Klinik Kesihatan Bandar Alor Setar, following a finding from a new study which showed that the use of acetaminophen after vaccination may reduce the immunogenicity of the vaccine.

Objective/Aim

The objective of this technology review was to assess the safety, efficacy or effectiveness and cost-effectiveness of routine used of acetaminophen following childhood immunization.

Results and Conclusions

There was only one good level of evidence to show that routine prophylactic use of acetaminophen after vaccination was effective to reduce fever. However, this trial also showed that the routine prophylactic use of acetaminophen may reduce the antibody response. No study was retrieved on the cost-effectiveness.

Methods

Electronic databases were searched, included PubMed, Ovid Medline (R) from 1990-2006 (EBM Reviews – Cochrane Databases of Systematic Reviews), National Horizon Scanning, INAHTA and FDA, NIOSH website, for published reports. There was no limit in the search. Additional articles were identified from reviewing the bibliographies of retrieved articles.

The search strategy used the terms which were either used singly or in various combinations; "acetaminophen", "vaccine", "acetaminophen reduce the immunogenicity", "acetaminophen reduce the efficacy of vaccine", "cost effectiveness of acetaminophen" and "management of fever in children"

ROUTINE USED OF ACETAMINOPHEN FOLLOWING CHILDHOOD IMMUNIZATION

1. INTRODUCTION

Acetaminophen is very widely used as an antipyretic (fever reducer) as well as analgesic (pain reliever) because of its high efficacy and good safety profile. It is used to relieve mild to moderate pain from headaches, muscle aches, menstrual periods, cold and sore throats, toothaches, backaches, and reactions to vaccinations and to reduce fever.[1]

The acetaminophen comes as a tablet, chewable tablet, capsule, suspension or solution (liquid), drops (concentrated liquid), extended-release (long-acting) tablet, and orally disintegrating tablet (tablet that dissolves quickly in the mouth), to take by mouth, with or without food. Acetaminophen also comes as a suppository to be used rectally.[1] The recommended dose of acetaminophen for children is 12 to 15 mg/kg every 6 hours and in suppository form, the dose is 80-325 mg every 4 to 6 hours depending on age and weight.[2]

Acetaminophen is considered as a safer antipyretic for children compared to other drugs. After receiving immunizations, fever is part of the body's normal inflammatory process. In many cases, acetaminophen is a drug of choice to relieve possible risk of high grade fever or febrile convulsions in children after routine infant vaccinations.

According to *Petunjuk Kesihatan 2007* annual report, the number of children (0-2 years old) involved in vaccination programme in 2008 were about 936,786.[3]

The technology review was requested by a Family Medicine Specialist from Klinik Kesihatan Bandar Alor Setar, following a finding from a new study which showed that the use of acetaminophen after vaccination may reduce the immunogenicity of the vaccine.

2. OBJECTIVE /AIM

The objective of this technology review is to assess the safety, efficacy or effectiveness and cost-effectiveness of routine used of acetaminophen following childhood immunization.

3. TECHNICAL FEATURES

Acetaminophen is a synthetic, non-opiate, centrally acting analgesic derived from *p*-aminophenol. The full chemical name is N-acetyl-*p*-aminophenol.[4] Acetaminophen will inhibits cyclooxygenase, to inhibit the formation and release of prostaglandins. It is absorbed in the gastrointestinal tract, reaching peak plasma concentrations within 30

minutes. The time to maximal temperature reduction is approximately 2 hours after ingestion.[2]

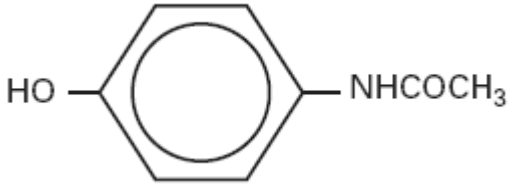

Figure 1: Chemical Structure of Acetaminophen

3.1. Mechanism of Action

The exact mechanism of action of acetaminophen is unknown. Researchers still could not find what the exact mechanism which provide the acetaminophen with ability of reducing fever and relieving pain. Basically the acetaminophen relieves pain by elevating the pain threshold, that is, by requiring a greater amount of pain to develop before a person feels it. It reduces fever through its action on the heat-regulating centre of the brain. Specifically, it tells the center to lower the body's temperature when the temperature is elevated.[2]

4. Methodology

4.1. Searching

Electronic databases were searched, included PubMed, Ovid Medline (R) from 1990-2006 (EBM Reviews – Cochrane Databases of Systematic Reviews), National Horizon Scanning, INAHTA and FDA, NIOSH website, for published reports. There was no limit in the search. Additional articles were identified from reviewing the bibliographies of retrieved articles.

The search strategy used the terms which were either used singly or in various combinations; “acetaminophen”, “vaccine”, “acetaminophen reduce the immunogenicity”, “acetaminophen reduce the efficacy of vaccine”, “cost effectiveness of acetaminophen” and “management of fever in children”

4.2. Selection

All published articles related to the efficacy or cost-effectiveness and safety of routine used of acetaminophen following childhood immunization were included.

5. RESULTS AND DISCUSSION

Only one study was retrieved from the scientific databases which were considered relevant to the issue regarding routine used of acetaminophen following childhood immunization.

5.1. EFFICACY OR EFFECTIVENESS

Only one study was included in this technology review regarding the issue of acetaminophen reducing the immunogenicity of vaccination

Prof Prymula R *et al*. conducted a randomised controlled trial to assess the respond of acetaminophen towards febrile reactions and to assess the immunogenicity of vaccines with the used of acetaminophen. The study involved 459 healthy infants from 10 centres in Czech Republic. Those infants were randomly assigned with a computer-generated randomisation list into two groups. First group received three prophylactic acetaminophen doses every 6-8 hours in the first 24 hours, and the second group without prophylactic acetaminophen (control group) after each vaccination with a ten-valent pneumococcal non-typeable *Haemophilus influenzae* protein D-conjugate vaccine (PHiD-CV) co-administered with the hexavalent diphtheria-tetanus-3-component acellular pertussis-hepatitis B-inactivated poliovirus types 1, 2, and 3-*H influenzae* type b (DTPa-HBV-IPV/Hib) and oral human rotavirus vaccines. At the end of the study they found that most infants had fever after primary vaccination and booster. Apparently, fever reactions in the group that received acetaminophen was decreased compared to control group; 42% versus 66% in primary vaccination and 36% versus 58% in booster group.[5] Level I

From the same study, the authors analysed Antibody Geometric Mean Concentrations (GMCs) Test data. They found that there was a significant decrease in the prophylactic acetaminophen group compared to the control group after primary vaccination for all ten pneumococcal vaccine serotypes, protein D, antipolyribosyl-ribitol phosphate, antidiphtheria, antitetanus, and antipertactin. Meanwhile after boosting, lower antibody GMCs persisted in the prophylactic acetaminophen group for antitetanus, protein D, and all pneumococcal serotypes. The authors concluded that, even though the febrile reactions are significantly decreased, prophylactic administration of antipyretic drugs at the time of vaccination should not be routinely recommended since antibody responses to several vaccine antigens were reduced. [5 Level I]

5.2. SAFETY

Acetaminophen, a non-opiod analgesic without anti-inflammatory effects, was first used in medicine in 1893, but became very widely used after approval by the FDA in 1951. It was approved as over-the-counter drug in 1960. It is used to treat both acute and chronic pain including mild to moderate pain or to reduce fevers. It is considered a drug of choice in patients who are aspirin intolerant, have ulcers, or difficulty in blood clotting. Generally it is well tolerated in order to treat many conditions such as headache, muscle aches, arthritis, toothaches, backache, colds and fevers.[6]

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5.3. COST- EFFECTIVENESS

There was no retrievable evidence from the scientific database on the cost-effectiveness of using acetaminophen following children immunization. However the market price for syrup Acetaminophen within Ministry of Health facilities is; Acetaminophen Syrup 120mg/5ml (60ml) = RM1.77

6. CONCLUSION

6.1. EFFICACY OR EFFECTIVENESS

There was only one good level of evidence to show that routine prophylactic use of acetaminophen after vaccination was effective to reduce fever. However, this trial also showed that the routine prophylactic use of acetaminophen may reduce the antibody response.

6.2. SAFETY

There were many retrievable studies on safety issue of acetaminophen. The adverse effects are well known especially drug-induced hepatotoxicity and overdose when use in large amount. The acetaminophen got FDA approval since 1951 including approval as over the counter (OTC) drug in 1960.

6.3. COST- EFFECTIVENESS

There was no retrievable evidence on cost-effectiveness of routine used of acetaminophen following childhood immunization.

7. REFERENCES

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8. APPENDIX

9.1 Appendix 1

DESIGNATION OF LEVELS OF EVIDENCE

I Evidence obtained from at least one properly designed randomized controlled trial.

II-I Evidence obtained from well-designed controlled trials without randomization.

II-2 Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one centre or research group.

II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.

III Opinions or respected authorities, based on clinical experience; descriptive studies and case reports; or reports of expert committees.

SOURCE: US/CANADIAN PREVENTIVE SERVICES TASK FORCE (Harris 2001)