INPLASY PROTOCOL

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None declared.

Antigen detection methods of Opisthorchis viverrini in human: Systematic review and Meta-analysis

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Review question / Objective: Research question - Among all of the available antigen methods for Opisthorchis viverrini in human, which one is the most accurate result. Objectives - General objective. To meta-analyze the accuracy of Opisthorchis viverrini antigen detection methods in human. Specific objectives -To compare the overall detection accuracy of Opisthorchis viverrini antigen in humans among FECT and other antigen detection methods -To systematically review Opisthorchis viverrini antigen methods in human -To investigate the effect of bias on the Opisthorchis viverrini antigen detection results in terms of participant selection, index test, reference standard, and flow and timing -To investigate the heterogeneity of the Opisthorchis viverrini antigen detection methods in human.

Eligibility criteria: Inclusion criteria 1.1 Research articles related to antigen detection method of Opisthorchis viverrini in humans. 1.2 Research articles in the databases between 2000 - 2021. 2. Exclusion criteriaResearch articles which do not use Formalin Ethyl acetate Concentration Technique (FECT) as the reference standard.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 20 May 2022 and was last updated on 20 May 2022 (registration number INPLASY202250123).

INTRODUCTION

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among FECT and other antigen detection methods -To systematically review Opisthorchis viverrini antigen methods in human -To investigate the effect of bias on the Opisthorchis viverrini antigen detection results in terms of participant selection, index test, reference standard, and flow and timing -To investigate the heterogeneity of the Opisthorchis viverrini antigen detection methods in human.

Condition being studied: Opisthorchis viverrini at adult stage resides in the bile duct of Opisthorchiasis patients. O. viverrini has lobe-shaped ovaries sizing about ⅔ of the anterior segment, with a long uterus coiled in the middle from the ventral sucker to the ovaries. Moreover, there are also testicles. It is able to make a reproduction within itself and produces eggs mixed with feces starting at the 4th week of the adult stage. If infected patients have unsanitary disposal of excreta nearby water source or there is not adequate sanitation facilities, Opisthorchis eggs will go to water. Egg shape is oval and has an embryo of miracidium developed inside, covered with a clear shoulder and a knop opposite the lid. Miracidium will not hatch from the egg until being eaten by snails. Bithynia snails are first-intermediate hosts. After snails eat miracidium, it will grow and change its shape to sporocyst, rediae and cercariae. Then cercariae will shed out of snails, swim and reside beneath Cyprinid fish scales and inside fish: freshwater fish such as red cheek barb, hampala barb etc. After cercariae goes inside freshwater fish, it will shake off its tail and go to encyst. It will grow and change its shape to metacercariae which is an infective stage. If people consume undercooked freshwater fish that have metacercariae, people will get infected and O. viverrini will reside in bile duct until becoming adult stage which takes about 4 weeks after consuming food contaminated with metacercariae. Generally, Opisthorchiasis symptom expression starts at middle-age of patients. Classification of patients with Opisthorchiasis can be categorized as asymptomatic patients, mild, moderate, and severe symptom patients. Asymptomatic patients are patients with

less amount of O. viverrini which is about 100 - 200 adult worms. Patients with mild symptoms present abdominal distension, dyspepsia at times but do not show right upper quadrant pain and never have jaundice which found 1,000 - 9,999 O. viverrini eggs per 1 gram of fecal in this patient category. Patients with mild symptoms can be treated effectively by praziquantel. Moderate symptom patients present cholangitis disease causing jaundice, low fever, right upper quadrant pain, hepatic enlargement, and these symptoms are intermittent. There are about 10,000 - 30,000 O. viverrini eggs per 1 gram of fecal found in moderate symptoms patients. The last category is severe symptom patients which is the final stage of this disease. There are enormous numbers of O. viverrini inside the bile ducts of the liver. Patients with severe symptoms present lack of appetite, fatigue, larger liver, jaundice, pale color of facal, failure of liver and kidney; moreover, there are complications such as cholangitis, cirrhosis, cholangiocarcinoma. Patients without proper treatment normally collapse and die.

METHODS

Search strategy: 1. Searching strategy
This study is a systematic review and meta-analysis by searching various databases. The researcher searched for information during November - December 2021.
1.1 International published literature via databases: MEDLINE, EMBASE, Google scholar, PubMed, Scopus, Scient direct
1.2 Thai-Journal Citation Index Centre, Online Computer Library Center, Inc. (www.worldcat.org) for theses and dissertations: including Thai Thesis Database
Keyword for searching uses PICO strategy composing of
P: ("Opisthorchiasis" or "Opisthorchis viverrini") and I: ("Antigen detection" or "ELISA" or "monoclonal antibody" or "enzyme-linked immunosorbent assay" or "excretory-secretory antigen" or "crude antigen" or "somatic antigen" or "tegument antigen" or "egg antigen" or "sperm

antigen") and C: ("FECT" or "Formalin ethyl acetate") and O: ("Sensitivity" or "Specificity")

2 Inclusion criteria

2.1 Research articles related to antigen detection method of Opisthorchis viverrini in humans.

2.2 Research articles in the databases between 2000 - 2021

3. Exclusion criteria

Research articles that do not use the Formalin Ethyl acetate Concentration Technique (FECT) as the reference standard.

Participant or population: Any participants suspecting to have Opisthorchiasis infected by Opisthorchis viverrini worldwide.

Intervention: None.

Comparator: Gold standard method, Formalin ethyl acetate (FECT).

Study designs to be included: Experiment, Cross sectional.

Eligibility criteria: Inclusion criteria 1.1 Research articles related to antigen detection method of Opisthorchis viverrini in humans. 1.2 Research articles in the databases between 2000 - 2021. 2. Exclusion criteriaResearch articles which do not use Formalin Ethyl acetate Concentration Technique (FECT) as the reference standard.

Information sources: Electronic databases 1. International published literature via databases: MEDLINE, EMBASE, Google scholar, PubMed, Scopus, Scient direct 2. Thai-Journal Citation Index Centre, Online Computer Library Center, Inc. (www.worldcat.org) for theses and dissertations: including Thai Thesis Database.

Main outcome(s): 1. Since there are evaluating processes of each research paper, it promotes the understanding of qualities and limitations of studies about antigen detection methods in O. viverrini in humans. 2. Meta-analysis will increase statistical power; therefore, they narrow confidence intervals and enhance accuracy. 3. Utilize and implement benefits of the studies in order to early detection of the disease in a timely manner. Moreover, it assists policymakers in designing and assigning efficient public health policies.

Quality assessment / Risk of bias analysis: Quality assessment of research articles Two independent individuals evaluate risk of bias by using a modified QUADAS-2 tool (7). There are 4 domains to be considered in this assessment. 1) Patient selection 2) Index test 3) Reference standard 4) Flow and timing.

Strategy of data synthesis: Data analysis STATA BE 17 is the program used in this study. Sensitivity and specificity were the measurements of diagnostic accuracy of the antigen detection method of Opisthorchis viverrini in this study. The analyzed results are illustrated as a pooled estimate, forest plot graph showing sensitivity, specificity as average, 95% confidence interval- CI, percentage of inconsistency index (I2) measuring heterogeneity of each included study. Analysis of I2. is presented as a percentage; the higher of the I2 value, the more heterogeneity it is represented. The interpretation of I2 is that I2 equals or less than 25% meaning low heterogeneity, value at 50% meaning moderate heterogeneity and value more than 75% meaning high heterogeneity. Publication bias is analyzed by the result of Deek's test in funnel plot. When the Deek's test result is more than 0.1, the publication bias does not exist.

Subgroup analysis: None.

Sensitivity analysis: Using average sensitivity and specificity data from forest plot to analyze the accuracy of the antigen detection of Opisthorchis viverrini.

Language: No, searching in English and Thai.

Country(ies) involved: Thailand.

Keywords: Antigen detection methods of Opisthorchis viverrini in human; Systematic review; Meta-analysis.

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