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Cell-mediated and serology-based tests for Mycobacterium ulcerans disease: A systematic review and meta-analysis. V.3

PLOS Neglected Tropical Diseases

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1 Works for me dx.doi.org/10.17504/protocols.io.bdhti36n

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ABSTRACT

Background:
Buruli ulcer (BU) is a subcutaneous necrotic infection of the skin caused by *Mycobacterium ulcerans (M. ulcerans* disease*)*. It is the third most common human mycobacterial disease after tuberculosis (TB) and leprosy. The available methods for detection of the bacilli in ulcers are microscopic detection, isolation and cultivation of the bacterium, histopathology, and polymerase chain reaction (PCR). These methods, although approved by the World Health Organization (WHO), have infrastructural and resource challenges in medical centres and cell-mediated immunity (CMI) and/or serology-based tests have been suggested as easier and more appropriate for accurate assessment of the disease, especially in remote or underdeveloped areas.

Methods: This study systematically reviewed and conducted a meta-analysis for all research aimed at developing cell-mediated immunity (CMI) and/or serology-based tests for *M. ulcerans* disease. Information for this review was searched through PubMed and Web of Science databases and identified up to June 2019. References from relevant articles and reports from the WHO Annual Meeting of the Global Buruli Ulcer Initiative were also used.

EXTERNAL LINK

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THIS PROTOCOL ACCOMPANIES THE FOLLOWING PUBLICATION

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ATTACHMENTS

Systematic_Review_Protocol_ASM.pdf

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Review question

1 Review question

What attempts have been made to develop cell-mediated and/or serology-based tests for *Mycobacterium ulcerans* disease within at risk population?
Context and rationale
Current methods of diagnosis of the Buruli ulcer disease include, polymerase chain reaction, histopathology and culture of the pathogen. These methods have their infrastructural and resource challenges. Cell-mediated and/or serology-based tests have been suggested as easy and quick to potentially aid diagnosis of the disease.

Searches

2

The following online reference databases were searched for relevant articles: PubMed (1930 to June 2019), Web of Science / ISI Web of Knowledge (1930 to June 2019) and the Buruli ulcer disease database maintained by WHO in Geneva, Switzerland (http://www.who.int/buruli/en).

2.1 Search strategy
This study collated all research attempts made in developing cell-mediated immunity and/or serology-based tests for *M. ulcerans* disease by reviewing all published studies until June 2019 that have reported relevant efforts. The search terms used were: Buruli ulcer and/or *Mycobacterium ulcerans* in combination with the following terms: “cell-mediated screening test”, “serological screening test” and “diagnostic tests”. All searches were with no language restrictions.

2.2 Inclusion criteria:
Study papers that met selection criteria, included

1. Original full text papers and conference abstracts.
2. Studies that had attempted developing protein/antigen preparations either cell-derived or recombinant from M. ulcerans and had utilized them in cell-mediated and/or serology-based test for *M. ulcerans* disease.

Exclusion criteria:
Reviews papers were excluded.

Data extraction

3

The following study information were extracted and assessed;
1. Country and year of study.
2. *M. ulcerans* strains used for antigen preparation.
3. Culture media used for pathogen growth.
4. Method of protein preparation (Heat and/or non-heat treatment of pathogen).
5. Pathogen cell-derived (lysate/culture filtrate) and/or recombinant proteins used as test antigens or stimulant.
6. Immuno-detection method employed (ELISA, western blot, etc.).
7. Samples tested (Blood and/or serum) and were they human or animals?
8. Outcome (Sensitivity and specificity results).
Data collation followed the guidelines for review structure in the PRISMA checklist. The extracted data was cross-checked with a second reviewer and any discrepancies were resolved by a senior author.

Quality assessment of studies

4 The Newcastle-Ottawa Scale (NOS) was used to assess the quality of the included studies. NOS is used to assess the quality of non-randomised studies, and scores as follows: Good quality score: 3 or 4 stars in selection domain and 1 or 2 stars in comparability domain and 2 or 3 stars in outcome/exposure domain. Fair quality score: 2 stars in selection domain and 1 or 2 stars in comparability domain and 2 or 3 stars in outcome/exposure domain. Poor quality score: 0 or 1 star in selection domain or 0 star in comparability domain or 0 or 1 star in outcome/exposure domain.

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Strategy for data synthesis

5 Summary effect was generated using the positivity and negativity outcomes of each selected article in relation to test antigen(s).

Statistical and meta-analyses

6 Studies that provided sufficient information, effect size (diagnostic odd ratio) with standard error (SE) were calculated and assigned weight at 95% confidence interval (CI). STATA statistical tool was then used to conduct a random-effects model meta-analysis to assess study heterogeneity and bias. The meta-analysis results were graphically displayed as forest and funnel plots ($p< 0.05$).

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