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Therapeutic Options for Melioidosis: A Systematic Review

Therapeutic Options for Melioidosis: A Systematic Review

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Summary

Introduction: Melioidosis is a disease caused by the bacterium Burkholderia pseudomallei, common in tropical regions. It is poorly understood and studied by healthcare professionals, but some antibiotics reduce mortality from infection by 50%. Method: This review aimed to evaluate the quality of the literature on basic information characteristic of melioidosis, comparing diagnostic methods and medications used according to PRISMA guidelines. Inclusion criteria were individuals infected with the bacterium Burkholderia pseudomallei, and exclusion criteria were individuals under 3 years of age and over 70 years of age. Results: Immunochromatography assay results were insensitive. The use of PCR can reduce the time to reach a definitive diagnosis by up to 36 hours. API 20NE and 20E identified 98% and 99% of B. pseudomallei isolates, respectively. AKI, advanced age, or DM did not worsen mortality. Treatment with ceftazidime was associated with good activity compared to conventional therapy. In severe sepsis, meropenem was used to achieve lower mortality rates than ceftazidime.

Hepatic and bacteremic comorbidities had a worse prognosis. Treatment with ceftazidime, meropenem, TMP-SMX plus doxycycline is therapeutic in non-septicemia. Doxycycline alone is not recommended as the treatment of choice. Conclusion: Through comparative research, the culture method remains the method of choice for investigation, despite the longer time it takes to produce results.
Regarding treatment, the medication considered as a first-line option is ceftazidime.
Keywords: melioidosis, Burkholderia pseudomallei, Treatment

Abstract

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1. Introduction

Melioidosis is a disease caused by the bacterium Burkholderia pseudomallei, found in contaminated water and soil. It is typically a disease of tropical countries, with the main country affected being... Thailand. The emergence of Melioidosis in Brazil is an example of the growing recognition of

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The disease is appearing in new areas of the world. Transmission of the disease can occur through percutaneous inoculation. through a penetrating injury or open wound, inhalation during severe weather, or as a result deliberate release or ingestion through contaminated food or water, affecting primarily people in regular contact with soil and water.

Infection with B. pseudomallei has variable clinical manifestations, with varying degrees of severity. ranging from fulminant septic shock to a chronic infection with symptoms present for more than Symptoms last 2 months, occurring in 11% of cases, and can mimic cancer or tuberculosis. Pneumonia is the most common. The presentation of melioidosis is described in slightly more than half of the cases, in its In the acute form, patients present with cough with expectoration, chills, and respiratory distress with... or without shock.

The importance of knowing the signs and symptoms of the disease contributes significantly to seek faster, more specific and sensitive diagnostic methods in Early detection of melioidosis can minimize the course of the disease. Delay in diagnosis It can be fatal, since empirical antibiotic regimens used for bacterial sepsis often... Sometimes, they do not provide adequate coverage for B. pseudomallei.

Regarding therapeutic methods, some antibiotics reduce mortality by 50%. due to infection, therefore, understanding it is of great importance for reducing morbidity and Mortality. Melioidosis has a notoriously prolonged course; a cure is difficult without a course of treatment. Prolonged course of appropriate antibiotics. B. pseudomallei is inherently resistant to penicillin. first-generation ampicillin, second-generation cephalosporins, gentamicin, tobramycin, Streptomycin and polymyxin. Potentially, melioidosis is preventable, however, these have not yet been proven. licensed vaccines developed for immunization against the bacterium B. pseudomallei despite the The existence of research groups with significant progress.

2. Results

Melioidosis is an infectious and endemic disease in tropical countries such as Southeast Asia and northern Australia. Often fatal, it is caused by an environmental Gram-negative bacillus. Burkholderia pseudomallei. The bacillus is identified in the laboratory, moreover, with the increase in International travel and the threat of bioterrorism have made it common for laboratories in certain areas to be involved. Non-endemic areas may also encounter this organism.

Limited experience and a lack of validated diagnostic reagents make Burkholderia pseudomallei is difficult to recognize in the diagnostic microbiology laboratory. Currently, the The most commonly used method for diagnosing melioidosis involves culturing the bacteria. B. pseudomallei using samples such as urine, blood, or sputum. Despite being a With its high specificity, the culture method presents itself as a technique considered...

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Incorporating PCR-based identification can improve the percentages of Recognition, however, requires a more detailed evaluation. An immunosorbent assay linked to An enzyme using a fluorescein isothiocyanate amplification system was developed for To detect Pseudomonas pseudomaleiantigen in urine. At a cutoff point of 1:10, the The sensitivity and specificity of the test were 81% and 96%, respectively.

Detection of urinary antigen by enzyme immunoassay is a valuable laboratory test. and rapid for early diagnosis of acute melioidosis. Non-pathogenic Burkholderia thailandensis, It is used as a model for Burkholderia pseudomallei due to its genetic similarities, in addition to Your safety during experimental handling.

In one study, recombinant flagellin protein fragments were constructed from B. thailandensis E264 (FLAG300 - best performance in melioidosis diagnosis with sensitivity) 82.7% and specificity of 94.6%, FLAG600, FLAG900 and FLAGFL) and fragments as antigen to detect melioidosis antibodies by an indirect enzyme-linked immunosorbent assay (indirect ELISA). Serum samples consisted of serodiagnostic melioidosis sera (N 1ÿ4 52), septicemic sera caused by other bacteria (N 1/4 16) and sera from healthy donors (N 1/4 40).

Several sets of PCR primers have been developed in recent years for the Detection of Burkholderia pseudomallei. All primer sets, 16S rRNA gene, gene rRNA spacer and LPS were compared, in addition to being tested by PCR amplification. from the same DNA samples extracted from blood samples of 46 patients from the northeast of Thailand, of which 29 had melioidosis based on blood culture as the gold standard. The low The sensitivity of the PCR test was most likely due to the small number of bacteria in the samples. samples. In addition, one set of primers failed to detect all strains of B. pseudomallei. To make PCR for melioidosis more practical, this involves concentration steps. Bacterial factors should be added. Finally, mixed infection in patients in endemic areas may This could be the cause of controversial false-positive PCR results and should be investigated further.

Regarding therapeutic methods for melioidosis, the regimen with antimicrobials This includes the use of intravenous drugs for at least 10 days, followed by oral drugs for at least 10 days. minus 12 weeks. The standard oral regimen based on experimental evidence is sulfamethoxazole + trimatoprim (SMX-TMP) plus doxycycline. This regimen is used in Thailand and recommended in [country name]. Australia, but it is associated with side effects and poor patient adherence.

A prospective, open-label, randomized, comparative treatment study was conducted. to compare the therapeutic efficacy of the conventional four-drug combination of chloramphenicol, trimethoprim-sulfamethoxazole and doxycycline, with the use of doxycycline alone in the oral treatment of melioidosis maintenance. Adult Thai patients with melioidosis confirmed by examination of

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Culture participants were randomized to receive treatment for 12 weeks after intravenous treatment of severe illness. Therefore, doxycycline monotherapy is not recommended as a first-line treatment. Oral treatment of melioidosis.

In cases of sepsis, melioidosis is difficult to cure. A review of experience with meropenem in the treatment of severe melioidosis in 63 patients over a 6-year period, results showed similar to those of patients treated with ceftazidime. Mortality among Of the patients treated with meropenem, 19% had a possible fever. medication associated with the use of meropenem. However, meropenem 1g or 25mg/kg every 8 Administering intravenously for 14 days is an alternative to ceftazidime and imipenem in treatment. melioidosis. The use of meropenem may be associated with better outcomes in patients with sepsis associated with melioidosis.

An open-label, matched, randomized, controlled study of high-dose parenteral ceftazidime. 120 mg/kg/day versus amoxicillin and clavulanate 160 mg/kg/day for the treatment of severe melioidosis. It was conducted in Ubon Ratchatani in northeastern Thailand. The overall mortality rate was 47%. Similar for both treatment groups. The overall rate of treatment failure or death due to Uncontrolled melioidosis was significantly higher for the amoxicillin/clavulanate group. that for the ceftazidime group. The clinical and bacteriological responses for patients treated with Success rates were similar in both groups, and both treatments were well tolerated. Parenteral amoxicillin/clavulanate is a safe and effective initial treatment, but ceftazidime Parenteral therapy remains the treatment of choice for severe melioidosis.

An open-label randomized study was conducted to compare ceftazidime 120 mg/kg/day with Conventional therapy includes chloramphenicol 100mg/kg/day, doxycycline 4mg/kg/day, and trimethoprim. 10 mg/kg/day and sulfamethoxazole 50 mg/kg/day in the treatment of severe melioidosis. Treatment with Ceftazidime was associated with a 50% lower overall mortality rate than conventional treatment.

A prospective, randomized treatment study was conducted in northeastern Thailand. to compare ceftazidime and imipenem in severe melioidosis over 6 hours after the first dose. antibiotic dose. Patients treated with ceftazidime experienced systemic endorphin toxin. significantly higher than patients treated with imipenem after the first dose of antibiotic.

Diabetes mellitus and environmental exposure are important risk factors for the acquisition of melioidosis. A study analyzed the effectiveness of a multifaceted prevention program for melioidosis. melioidosis. The intervention was a behavioral support group session to help patients. Diabetics are encouraged to adopt recommended behaviors, including wearing rubber boots and drinking alcohol. Boiled water. Two primary outcomes were hospitalizations involving illnesses. infectious diseases and melioidosis confirmed by culture. Within the protocol analysis, patients who

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Those who received a behavioral support group session had lower incidence rates of Hospitalizations involving infectious diseases.

3. Method

3.1 Research Project

The aim of this review was to assess the quality of the literature on the subject. basic characteristics of melioidosis and Burkholderia pseudomallei, the causative bacterium, reaching thus to the conclusion of the most effective treatments and their consequences in humans according to the PRISMA guidelines. This approach rigorously examined and interpreted the findings of Research studies on Therapeutic Options for Melioidosis. It is recognized that this method may to produce a new and integrative interpretation of the findings from individual studies.

3.2 Strategy Number

Four databases were comprehensively searched: SciELO, PubMed. Ministry of Health, Google Scholar. The search strategy was applied similarly. all databases were searched, and a set of search keywords was identified and used. for the scope of the literature. The search algorithms included: Burkholderia pseudomallei, Infections Bacterial, Endemic Diseases, Underreporting. The Boolean operators 'or' and 'and' were used for Distinguish between synonyms and combine search terms. The search was restricted to studies written in [Language filters] and [additional filters used]. The reference lists of the publications that Studies that met the inclusion criteria were manually reviewed to identify studies. Additional information was not identified in the electronic search. The last search was conducted in early February. 2026.

3.3 Screening procedures

An initial review involved screening titles and abstracts of potential studies. identified in the original search. The full texts of potentially eligible studies were retrieved and independently reviewed by two reviewers (KTDSL and SAC) in accordance with Inclusion and exclusion criteria. Disagreements were resolved through discussion and with the Third-party reviewer involvement (HDNV).

3.4 Inclusion and exclusion criteria

Any relevant articles that reported on burkholderia were included in the analysis. pseudomallei] in [people infected with this bacterium who are between 10 and 70 years old]. All articles with any design (randomized controlled trials, non-controlled studies) Randomized controlled trials (case-control studies) and cross-sectional studies were included. The articles were Excluded if appropriate information was not reported.

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Two authors [KTDSL and SAC] independently selected and evaluated the literature.
All included articles were evaluated using the PRISMA guidelines. Any discrepancies...
The data extraction and quality classification issues were resolved through group discussions.

3.5 Data extraction and evaluation of the quality of the individual study

The data were extracted from the articles included in this systematic review using tables of Extraction. The data were collected by 1st Author, Title, Year of Publication, Country, Type of Study. Number of Participants, Intervention, Comparison, Results of Interest, Conclusion. Disagreements in Evaluation and data extraction were resolved by consensus among all authors.

4. Discussion

After a systematic and comprehensive review of 17 articles on therapeutic options and In diagnostic studies for melioidosis, it was observed that determining the etiological agent of melioidosis... The bacterium Burkholderia pseudomallei is not complicated in endemic countries. However, this disease It needs to be better known to facilitate its diagnosis and treatment in non-endemic countries, in in relation to the context of international travel.

According to the study by LOWE, P.; ENGLER, C.; NORTON, R, comparing the systems Manual identification of API 20NE and 20E with the automated Vitek 1 and 2 systems. The failure of Vitek 2's failure to correctly identify B. pseudomallei was largely due to differences in Biochemical reactions obtained in comparison with the expected values in the database.

Regarding the study by INGLIS, TJJ et al., which states the incorporation of identification. based on PCR, a scheme that can further improve recognition percentages of The causative agent of melioidosis, however, requires a more detailed evaluation, as experiences... Limited resources and a lack of validated diagnostic reagents make an experienced team mandatory. The study by KUNAKORN, M. et al., reports that the addition of bacterial concentration steps is... necessary to increase the sensitivity of PCR and make the test more practical, which can benefit endemic regions, which still show many false-positive PCR results due to Mixed infections require further investigation.

A very important laboratory test is the enzyme immunoassay detection test for urinary antigen, according to the study by DESAKORN, V. et al., as it presents a cutoff titer of 1:10, with high sensitivity (81%), high specificity (96%) and fast results, which is extremely valuable. for early diagnosis of the disease.

Another possible diagnostic method is through indirect ELISA, as analyzed in the study of WAJANAROGANA, S. et al., in which non-pathogenic Burkholderia thailandensis was used, bacteria that are safe to handle and have genetic similarities to Burkholderia pseudomallei, by which recombinant flagellin protein fragments from B. thailandensis were constructed and used.

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E264 as an antigen in an indirect ELISA, and with FLAG300 at a serum titer of 1600, it showed Sensitivity of 82.7% and specificity of 94.6%.

Despite the results presented, according to the study by SIRISINHA, S. et al., the The culture method is still the preferred method due to its low cost, reliability, and simplicity. which has the disadvantage of delaying diagnosis, which can be accelerated through Combining culture with other diagnostic methods reduces the time needed to obtain results. definitive for 18 to 36 hours. According to SIMPSON, AJ et al., the routine use of different methods Blood culture - in broth (conventional), in a perforated plate and centrifuged lysis (Isolator 10TM) – They contribute to the early diagnosis of septicemic melioidosis.

Regarding the treatment of melioidosis, the study by WHITE, NJ et al., reveals that... Compare ceftadize and conventional therapy (chloramphenicol + doxycycline + trimethoprim + (sulfamethoxazole) when treating severe melioidosis, patients treated with ceftadiazole presented a lower mortality rate than those using conventional therapy, and that from that time onwards (1989) should be considered as the treatment of choice, and also suggests that amoxicillin + Clavulanate would be a less toxic alternative, but according to the study by SUPUTTAMONGKOL, Y. et al., therapy with amoxicillin + clavulanate presents therapeutic failure. significant when compared to ceftadiazole, and therefore ceftadiazole remains the treatment. of choice in severe melioidosis.

According to the study by CHENG, AC et al, treatment with meropenem presented The response is similar when compared to ceftazidime, therefore it can be used as an alternative to... ceftadiazole and imipenem in treating melioidosis, in addition to showing better results in patients with melioidosis associated with severe sepsis. Furthermore, the study by SIMPSON, AJH et al., to Compare the release of endotoxins in severe melioidosis 6 hours after antibiotic administration. (ceftadizoline or imipenem), reports that ceftadizoline exhibits a greater release of these endotoxins, but which do not have a significant impact on the survival of patients with this condition. treatment.

The effectiveness of conventional therapy (chloramphenicol + doxycycline + trimethoprim + sulfamethoxazole) to doxycycline alone in the maintenance treatment of melioidosis, in the study by CHAOWAGUL, W. et al, in which patients using doxycycline alone They became refractory and, therefore, it cannot be recommended as the oral treatment of choice in maintenance of melioidosis.

The standard regimen was also compared according to experimental evidence to trimethoprim-sulfamethoxazole (TMP-SMX) + doxycycline and TMP-SMX + placebo in the study of CHETCHOTISAKD, P. et al., in which it was found that TMP-SMX + placebo is not inferior in Oral treatment for melioidosis and presents a lower rate of adverse effects compared to TMP-

Year VI, v.1 2026 | Submission: 02/07/2026 | Accepted: 09/02/2026 | Publication: 11/02/2026 SMX + doxycycline, thus being a better alternative in oral therapy.

Diabetes is considered the most important risk factor for melioidosis, in addition to... exposure to infections and, because of this, it would be necessary to conduct prevention programs for melioidosis in diabetic patients. However, according to the study by SUNTORNSUT, P. et al., despite a reduction observed in hospitalizations related to others Infections, no clear benefits were seen for melioidosis.

Due to it being a topic that is rarely discussed in the academic and professional context of the field of health, mainly because it is not endemic in Latin America, we find few articles in The platforms researched. However, it is important to consider individual travel to the most... affected and a possible infection. Furthermore, the studies found were mostly affected. too old. However, little has been found on this subject in specific groups. such as pregnant women, children, and people with comorbidities such as diabetes, hypertension, and heart failure. renal, among others.

Final Considerations

Melioidosis is a disease with high mortality and is endemic in several countries. tropical. The findings reported in this review are of great importance, as they describe the time and the The specificity of diagnostic methods and medications, as well as their most appropriate doses for each disease pattern, such as severe melioidosis and melioidosis associated with sepsis, is important. There are more studies reporting patient comorbidities, such as hypertension, diabetes, and disease. renal factors, which can interfere with the progression of the disease. We therefore hope that this review will encourage... more studies on this subject, which is still little discussed, will help... healthcare professionals can identify patients infected with the virus more quickly and clearly. Burkholderia pseudomallei, reducing the mortality rate of the disease.

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