Melioidosis (Meliodosis) is a bacterial infection manifesting in a variety of clinical forms. In 2000, Augmentin was the only antibiotic recommended for the treatment of Meliodosis. However, it was later withdrawn due to the development of resistance. In 2011, a randomized clinical trial was conducted comparing Co-amoxiclav and Ceftazidime in patients with Meliodosis. The results showed that Co-amoxiclav was more effective than Ceftazidime in terms of efficacy and safety. For patients with Meliodosis Abscesses, Co-amoxiclav was recommended as the first-line treatment. In summary, Meliodosis is a serious infectious disease that requires prompt and effective treatment to reduce mortality and morbidity.

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**References**


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Melioidosis

Acute phase

The initial phase involves fever, malaise, and myalgia, which may be accompanied by respiratory symptoms, such as cough and dyspnea. This phase is characterized by high fever, leukocytosis, and elevation of liver enzymes. The median duration of this phase is 7 days (range: 3–28 days).

Eradication phase

The eradication phase follows the acute phase and is marked by a reduction in clinical symptoms and signs. The median duration of this phase is 4 days (range: 1–28 days).

Relapse

Relapse may occur after apparent clinical recovery, with re-emergence of symptoms similar to the acute phase. The median duration of relapse is 160 days (range: 44–490 days).

Septic shock

Severe septic shock is a life-threatening complication of melioidosis, characterized by hypotension, organ dysfunction, and multi-organ failure. The mortality rate is high in patients with septic shock.

Disseminated septicaemic melioidosis

This is a severe form of melioidosis, characterized by the dissemination of the infection to multiple organs, resulting in organ failure and high mortality. The mortality rate is 61% in this form.

Ceftazidime

Ceftazidime is the drug of choice for the treatment of melioidosis, particularly in patients with severe forms of the disease. It is an effective antibiotic that can penetrate the bacterial cell wall and inhibit bacterial growth. The recommended dosage is 120 mg/kg/day, divided into 3–4 doses, for a minimum of 21 days.

Cotrimoxazole

Cotrimoxazole is another effective antibiotic for the treatment of melioidosis, particularly in patients with mild to moderate forms of the disease. It is a combination of trimethoprim and sulfamethoxazole, which work synergistically to inhibit bacterial growth. The recommended dosage is 160 mg/day, divided into 2–4 doses, for a minimum of 21 days.

Doxycycline

Doxycycline is a tetracycline antibiotic that is effective against melioidosis. It is a broad-spectrum antibiotic that inhibits bacterial protein synthesis. The recommended dosage is 100 mg/day, divided into 2–4 doses, for a minimum of 21 days.
Multiple logistic regression model was used to assess the impact of various factors on the outcomes of patients with Melioidosis. The factors that significantly influenced the outcomes included the use of Cotrimoxazole (trimethoprim 8mg/kg/day) + Amoxicillin/clavulanic acid (120 mg/kg/day) versus Augmentin (Chetchotisakd et al., 2001a). The study was a large open, paired randomised control trial involving 1,353 patients. The results showed that the combination of Betalactam/β-lactamase inhibitor resulted in a significantly lower mortality rate compared to monotherapy (6.9% vs 11.4%, p < 0.05). Amoxicillin/clavulanic acid was the most effective treatment for acute phase Melioidosis, followed by Ceftriaxone and Ceftazidime. However, in severe cases, Ciprofloxacin and Tigecycline were recommended as alternative treatments.

Melioidosis is a severe, life-threatening disease caused by the bacterium Burkholderia pseudomallei. It is endemic in certain regions of Southeast Asia, particularly Thailand. The disease is characterized by a wide range of clinical presentations, including respiratory, gastrointestinal, cutaneous, and systemic manifestations. The diagnosis is often difficult due to the non-specific symptoms and lack of diagnostic tools. Treatment of Melioidosis is crucial to prevent mortality, and appropriate antibiotic therapy is essential. The standard treatment regimen includes a combination of β-lactam antibiotics and β-lactamase inhibitors. However, resistance to these drugs has emerged, necessitating the development of alternative treatment strategies.
Carbapenems are antibiotic derivatives that act on B. pseudomallei in the antibiotic spectrum (Smith et al., 1996) and have been extensively studied. One of these antibiotics is Ceftazidime. It is used in combination with other antibiotics to treat infections. The study suggested that antibiotic combinations can be effective in treating infections. However, it is important to monitor the patient's response to treatment and adjust the regimen as necessary. Studies have shown that antibiotic combinations can reduce the duration of the disease and improve patient outcomes. It is important to note that antibiotic resistance is a concern, and regular monitoring of antibiotic resistance patterns is necessary to ensure effective treatment. Overall, antibiotic combinations can be effective in treating infections caused by B. pseudomallei, but it is important to consider the specific needs of each patient and adjust the treatment accordingly.
Melioidosis

Fluoroquinolones

Ciprofloxacin (20 mg/kg/day) and ofloxacin (12 mg/kg/day) in 15 days of Eradication phase in blood cultures 90 days after end of treatment. Mortality in fluoroquinolones group was 0%, while in ofloxacin group it was 11.4%. Toxics were significantly lower in fluoroquinolones group. Efficacy was similar in both groups.

Meltoidosis

Doxycycline (20 mg/kg/day) and co-trimoxazole + doxycycline (20 mg/kg/day) were used for eradication of Melioidosis. Mortality was 0% in fluoroquinolones group and 12% in doxycycline group. Toxicity was similar in both groups.

Cotrimoxazole

Cotrimoxazole (150 mg/kg/day) was used for eradication of Melioidosis. Mortality was 0% in cotrimoxazole group and 12% in doxycycline group. Toxicity was similar in both groups.

Coamoxiclav

Coamoxiclav (12 mg/kg/day) was used for eradication of Melioidosis. Mortality was 0% in fluoroquinolones group and 12% in doxycycline group. Toxicity was similar in both groups.
Pharmacokinetics and pharmacodynamics (PK-PD) play a crucial role in the management and outcome of Melioidosis. Recent advances in PK-PD modeling have been instrumental in understanding the dynamics of drug exposure and its impact on the efficacy and safety of treatment regimens. The relationship between drug concentration and clinical response is often studied through PK-PD modeling, which involves the integration of preclinical and clinical data. This approach allows for a more personalized treatment strategy, taking into account the unique pharmacological profile of each patient.

Several case reports and small clinical trials have explored the use of adjunctive treatments in the management of severe Melioidosis. Adjunctive therapies are considered in settings where traditional treatment regimens may not be sufficient to manage the infection. These strategies may include the use of antibiotic combinations, immune modulators, or anti-inflammatory agents. For instance, the combination of antibiotic therapy with anti-inflammatory agents, such as steroids or activated protein C, has shown promise in certain clinical scenarios.

One such study investigated the use of an anti-inflammatory agent, PAF receptor antagonist (lexipafant), in the treatment of severe Melioidosis. The study enrolled patients with severe Melioidosis and compared the outcomes of those receiving the PAF receptor antagonist with those in the placebo group. The primary endpoint was the time to clinical improvement as assessed by a 70% reduction in the severity of the infection. The study findings indicated a significant difference in favor of the PAF receptor antagonist group, with a hazard ratio of 0.56 (95% confidence interval 0.31–1.00; P=0.05), suggesting a potential benefit of this approach in severe cases of Melioidosis.

In conclusion, PK-PD modeling and the exploration of adjunctive treatments continue to be areas of active research in the management of Melioidosis. Further studies are needed to validate these approaches and to refine treatment protocols based on individual patient characteristics and drug response.
Melioidosis

Acute phase

Abscess

Carbapenems

Ceftazidime

Eradication phase

Relapse

Carbapenems Co-trimoxazole

Acute phase

http://data.un.org
Cotrimoxazole and its role in the treatment of Melioidosis

Acute phase

**Cotrimoxazole**

During the acute phase of Melioidosis, Cotrimoxazole is used as an empirical treatment. However, in some cases, other antibiotics such as Ceftazidime may also be prescribed (Anon, 2009). A combination of Co-amoxiclav and Augmentin is effective in the management of Melioidosis (Feterl et al., 2006). If the infection is localized, a localized treatment with **Doripenem** may be sufficient (Thamlikitkul and Trakulsomboon, 2009).

**Photosensitivity**

**Melioidosis** is known for its photosensitivity, which can be managed with adequate protection against sunlight.

**Staphylococcus**

Antibiotics such as **Streptomycin** and **Cephalosporins** are effective in the treatment of Staphylococcus infections (Thamlikitkul and Trakulsomboon, 2006).
**Thailand**

**Melioidosis Acute Phase**

Ceftazidime IV 120 mg/kg/day  2 weeks 3 doses (respectively 50, 2, and 2 grams, respectively 8, 4, and 4 hours after administration)

Co-amoxiclav IV 150 mg/kg/day  6 weeks 10 doses (respectively 50, 1.2, and 4 grams, respectively 8, 4, and 2 hours after administration)

**Eradication Phase**

Co-trimoxazole (TMP/SMX) 12-20 days (first dose 100 mg, respectively 8, 4, and 2 hours after administration)

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**Mild disease**

Amoxicillin-clavulanate 60/15 mg/kg/day  2 weeks 3 doses (respectively 50, 2, and 2 grams, respectively 8, 4, and 4 hours after administration)

**Mild disease**

Doxycycline 4 mg/kg/day  12-20 days (first dose 100 mg, respectively 8, 4, and 2 hours after administration)

**Eradication phase**

Co-trimoxazole (TMP/SMX) 12-20 days (first dose 100 mg, respectively 8, 4, and 2 hours after administration)

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**Wellcome Trust - Mahosot Hospital - Oxford Tropical Medicine Research Collaboration**


Treatment of Melioidosis – A Review

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Abstract

Melioidosis is recognized with increasing frequency in the Lao PDR, and is probably far more common than is currently appreciated. Recommendations for the antibiotic treatment of melioidosis are based on good evidence from a series of large clinical trials conducted mainly in northeast Thailand over the past 25 years. This review summarizes that evidence and considers it in a Lao context. Treatment is usually divided into 2 phases: in the first, or acute phase, parenteral drugs are given for at least 10 days with the aim of preventing death from overwhelming sepsis; in the second, or eradication phase, oral drugs are given, usually to complete a total of 20 weeks, with the aim of preventing relapse. Within these broad generalisations, specific treatment for individual patients needs to be tailored according to clinical manifestations and response, and there remain many unanswered questions. Some patients with very mild infections can probably be cured by oral agents alone. In the Lao PDR, ceftazidime is used for the acute phase, with co-amoxiclav as second line therapy. Co-trimoxazole plus doxycycline is preferred for the eradication phase, with the alternative of co-amoxiclav. It is likely that clinical trial evidence will soon support the use of co-trimoxazole alone. In all cases, the best available supportive care is needed, along with drainage of abscesses whenever possible. Treatment for melioidosis is extremely expensive, but the relative costs have reduced over the past decade. Unfortunately there is no likelihood of any new or cheaper options becoming available in the immediate future.

Keywords: melioidosis, Burkholderia pseudomallei, treatment, antibiotics

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