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BPaL Treatment: A Ray of Hope for MDR-TB Patients

Zafar Iqbal[1], **Uzma Hidayat**✉

[1]Department of Pulmonology, Medical Teaching Institute, Lady Reading Hospital, Peshawar - Pakistan [2]Programmatic Management of Drug Resistant TB Unit, Lady Reading Hospital, Peshawar - Pakistan

Corresponding Author:
Uzma Hidayat
Programmatic Management of Drug Resistant TB Unit,
Lady Reading Hospital, Peshawar - Pakistan
Email:uzmahidayat4466@gmail.com

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ABSTRACT

BPaL treatment, comprising bedaquiline, pretomanid, and linezolid, offers a promising ray of hope for patients suffering from multidrug-resistant tuberculosis (MDR-TB). This novel combination therapy has demonstrated remarkable efficacy in treating MDR-TB cases, particularly those with limited treatment options due to resistance or intolerance to conventional medications. Through rigorous clinical trials, BPaL has shown significantly higher success rates in achieving culture conversion and favorable outcomes compared to previous regimens, marking a significant advancement in the fight against MDR-TB. With its potential to reduce treatment duration and improve patient outcomes, BPaL represents a critical breakthrough in tuberculosis management, offering new hope for patients grappling with this challenging infectious disease.

Keywords: Drug Resistant TB; MDR-TB; BPal Treatment

Introduction

Multidrug-resistant tuberculosis (MDR-TB) poses a significant challenge in global health, necessitating the development of comprehensive and effective treatment strategies. MDR-TB is defined as tuberculosis (TB) that is resistant to at least isoniazid and rifampicin, the two most potent TB drugs.[1,2] Treatment strategies for MDR-TB have evolved significantly over the years, moving away from longer regimens with potentially toxic drugs to shorter, more tolerable regimens with newer, more effective medications.[3,4] The World Health Organization (WHO) recommends different treatment strategies for treating MDR-TB patients which are longer MDR-TB treatment (LTR) and shorter MDR-TB regimen (STR). Treatment duration of LTR is 18-24 months and STR is 9–12 months.[5,6] Now a days among more cases STR treatment strategies is used. STR has shown high efficacy in observational studies. This regimen typically includes a combination of drugs such as fluoroquinolones, bedaquiline, clofazimine, and second-line injectables. Moreover, individualized treatment regimens are tailored based on drug susceptibility testing results, considering patient-specific factors and potential drug interactions. The aim is to construct a regimen with at least four effective drugs to which the TB strain is susceptible.

In recent years, the BPaL regimen (bedaquiline, pretomanid, and linezolid) has emerged as a promising treatment for MDR-TB, particularly for extensively drug-resistant TB (XDR-TB) and TB that is not responsive to other treatments.[7] The BPaL regimen is a shorter, all-oral regimen that has demonstrated high efficacy in clinical trials. In a pivotal trial known as the Nix-TB trial, the BPaL regimen showed a success rate of approximately 90% in treating highly drug-resistant forms of TB. This regimen's advantage lies in its shorter duration (6 months), reduced pill burden, and the absence of injectable drugs, which significantly improves patient adherence and reduces the risk of side effects. The inclusion of bedaquiline and pretomanid, newer anti-TB drugs with novel mechanisms of action, and the high-dose use of linezolid, an effective drug against TB, contribute to the regimen's efficacy. However, the use of high-dose linezolid has been associated with significant adverse effects, such as peripheral neuropathy and myelosuppression, necessitating careful monitoring and management.[8]

Despite the advancements in treatment strategies for MDR-TB and the introduction of the BPaL regimen, several challenges remain. Access to new and repurposed drugs is limited in many high-burden countries, and the cost of these drugs can be prohibitive. Moreover, the global TB response faces challenges such as diagnostic delays, limited laboratory capacity for drug susceptibility testing, and the need for more robust health systems to support the management of MDR-TB. Additionally, adherence to treatment regimens is crucial for the success of MDR-TB management, and this can be hampered by factors such as drug side effects, the complexity of regimens, and socioeconomic barriers. Thus, while the BPaL regimen and other new treatment strategies offer hope, there is a pressing need for improved access to these treatments, alongside stronger health systems, enhanced patient support, and ongoing research to further refine and improve TB treatment approaches.

The Challenge of MDR-TB

Treating MDR-TB is complicated, time-consuming, and associated with numerous adverse effects. Standard treatment regimens involve a combination of second-line drugs, some of which are less effective, more toxic, and require prolonged treatment durations, often exceeding two years. The cure rates for MDR-TB using these regimens remain distressingly low, hovering around 56%, leaving a significant proportion of patients with unresolved disease.

The Emergence of BPaL Treatment

BPaL treatment is a novel and highly promising regimen for MDR-TB. The name "BPaL" stands for three of its key components: bedaquiline, pretomanid, and linezolid. These drugs, in combination, have shown remarkable efficacy in early clinical trials and have since garnered significant attention in the global fight against MDR-TB.

1. **Bedaquiline (Bdq):** Bedaquiline is a first-in-class drug specifically developed for TB. It targets the ATP synthase enzyme of Mycobacterium tuberculosis, effectively disrupting the bacterium's energy production. Its inclusion in the BPaL regimen has provided a more potent and less toxic alternative to traditional second-line drugs.
2. **Pretomanid (PTD):** Pretomanid is another recent addition to the TB drug arsenal. It has demonstrated excellent bactericidal activity against both drug-sensitive and drug-resistant TB strains. Pretomanid's ability to penetrate tissues and effectively target persisters makes it a critical component of the BPaL regimen.
3. **Linezolid (Lzd):** Linezolid, a well-known antibiotic, plays a crucial role in the BPaL regimen by inhibiting bacterial protein synthesis. It helps prevent the emergence of resistance to bedaquiline and pretomanid, making the combination more effective and sustainable.

Advantages of BPaL Treatment

The BPaL regimen offers several key advantages that make it a beacon of hope for MDR-TB patients and healthcare providers alike.

1. **High Efficacy:** Clinical trials have demonstrated exceptional cure rates with BPaL treatment, surpassing 90% in some studies. This remarkable success rate offers new hope for MDR-TB patients who have struggled with limited treatment options and poor outcomes.
2. **Shorter Treatment Duration:** Unlike traditional MDR-TB regimens, BPaL treatment typically lasts for only six to nine months. This significantly reduces the treatment burden on patients and healthcare systems, increasing treatment completion rates.
3. **Improved Tolerability:** BPaL drugs are generally better tolerated than some of the older, more toxic second-line drugs, reducing the likelihood of treatment interruptions and adverse effects.
4. **Reduced Risk of Resistance:** The combination of bedaquiline, pretomanid, and linezolid reduces the risk of developing resistance, which has been a significant concern with MDR-TB treatment.

Challenges and Concerns

While BPaL treatment holds great promise, it is not without challenges and concerns that need to be addressed.

1. **Limited Access:** Access to BPaL treatment remains limited in many parts of the world, primarily due to high costs and regulatory barriers. Ensuring equitable access to this life-saving regimen is essential.
2. **Adverse Effects:** Linezolid, one of the components of BPaL, can cause serious side effects, such as peripheral neuropathy and bone marrow suppression. Monitoring and managing these side effects are critical during treatment.
3. **Drug Interactions:** BPaL drugs may interact with other medications, making it essential for healthcare providers to carefully assess potential drug interactions and adjust treatment plans accordingly.
4. **Long-Term Safety:** The long-term safety profile of BPaL treatment is not fully understood, and ongoing research is needed to monitor patients for potential late-onset adverse effects.

Conclusion

The advent of BPaL treatment represents a significant breakthrough in the fight against MDR-TB, offering new hope to patients and healthcare providers grappling with this devastating disease. Its high efficacy, shorter treatment duration, and improved tolerability make it a compelling option for MDR-TB management. However, addressing the challenges of limited access, adverse effects, drug interactions, and long-term safety is crucial to ensure that the benefits of BPaL treatment reach all those in need. As we continue to expand our understanding of this innovative regimen, we must work collectively to make BPaL treatment more accessible and safer for MDR-TB patients worldwide.

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