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Original Article

COMPARATIVE ANALYSIS OF THE EFFECTIVENESS OF OLD AND NEW TB DRUGS IN THE TREATMENT OF PULMONARY TUBERCULOSIS

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ABSTRACT

Background. The availability of effective drug regimens of Pulmonary tuberculosis (TB) poses a global health challenge. Traditional first-line therapies-isoniazid, rifampicin, pyrazinamide, and ethambutol-remain the cornerstone of TB management due to their accessibility and documented cure rates exceeding 85%. Nevertheless, limitations such as variable drug metabolism, patient non-adherence, and the emergence of multidrug-resistant strains have prompted evaluation of newer treatment combinations to optimize efficacy, safety, and duration. The purpose was to compare the effectiveness of older first-line tuberculosis (TB) drug regimens with newer therapeutic regimens in the treatment of pulmonary tuberculosis.
Research Method. This narrative review synthesizes findings from five peer-reviewed studies comparing the effectiveness and safety profiles of conventional and novel TB drug regimens. The review focused on regimen composition, treatment duration, bacteriological clearance, hepatotoxicity, and patient adherence outcomes.
Findings. The inclusion of pyrazinamide in six-month regimens significantly accelerated bacterial clearance without increasing hepatic toxicity compared to traditional nine-month isoniazid–rifampicin regimens. Additionally, shorter rifampin-based regimens for latent TB demonstrated higher treatment completion rates and fewer adverse effects than isoniazid monotherapy. Emerging regimens, such as fluoroquinolone-based HRM therapies and the novel BPaL combination (bedaquiline, pretomanid, and linezolid), yielded comparable or improved outcomes, with BPaL achieving success rates up to 93% in drug-resistant TB cases.
Conclusion. Current evidence supports the strategic adaptation of TB therapy to balance efficacy, tolerability, and treatment duration. Incorporating newer drug combinations, particularly for drug-resistant TB, enhances adherence and clinical outcomes, underscoring the need for individualized treatment protocols aligned with evolving resistance patterns and patient profiles.

Keywords: Pulmonary Tuberculosis, Drug Regimens, Pyrazinamide, Rifampin, BPal Regimen, Treatment Adherence, Drug-Resistant TB.

BACKGROUND

Tuberculosis (TB) is an airborne infectious disease caused by the bacterium *Mycobacterium tuberculosis*. Tuberculosis (TB) continues to be a significant global health concern, infecting millions of individuals each year and leading to high rates of illness and death, particularly in low- and middle-income countries [1]. The commonly used first-line treatment regimen, which includes isoniazid, rifampicin, pyrazinamide, and ethambutol, has shown strong effectiveness in treating drug-susceptible TB [1]. Research by Denti et al. [3] explains that in many TB-endemic regions, this standard regimen has achieved treatment success rates exceeding 85%. Due to its affordability and widespread availability, this treatment approach remains a fundamental part of global TB control strategies. However, challenges such as differences in how patients metabolize these drugs, inconsistent adherence to treatment, and the increasing presence of drug-resistant TB strains have raised concerns about the long-term sustainability of these regimens [1]–[4].

The use of multiple drugs to treat tuberculosis was designed to enhance the effectiveness of treatment while lowering the chances of relapse, with isoniazid and rifampicin serving as the primary components [5]–[7]. Additional drugs such as streptomycin, ethambutol, and pyrazinamide were added to improve bactericidal activity and ensure that any remaining bacteria were eliminated more effectively. This approach aimed to strike a balance between killing the bacteria quickly and preventing the development of resistance, which can occur when only one or two drugs are used over long periods. Clinical research by the British Thoracic Association demonstrated that the inclusion of pyrazinamide in a six-month regimen led to better outcomes than regimens of longer duration that did not include the drug [5]

Specifically, six-month treatment plans that incorporated pyrazinamide alongside ethambutol or streptomycin resulted in a faster reduction of bacterial presence in the lungs, with 77 percent of patients testing negative in their sputum cultures after two months of treatment, compared to 64 percent for those on nine-month regimens without pyrazinamide [1], [5]. This evidence emphasized pyrazinamide's critical role in sterilizing TB bacteria early in the treatment process, which allowed for the overall treatment duration to be shortened without sacrificing effectiveness. While the addition of pyrazinamide slightly increased the likelihood of side effects not related to liver function, such as skin reactions, the benefits it offered in enhancing treatment outcomes outweighed these mild adverse effects.

Yet, long-duration monotherapy, such as the commonly used nine-month isoniazid preventive therapy (IPT) for managing latent tuberculosis infection (LTBI), has shown

notable limitations, particularly in terms of patient compliance and the risk of liver toxicity [8]. Many patients struggle to complete the full course of treatment, which reduces its overall effectiveness and increases the risk of developing active TB [8]. A large-scale international study found that a shorter four-month regimen using rifampin was just as effective as the traditional nine-month isoniazid regimen in preventing the progression from latent to active TB, while also achieving better patient completion rates and significantly lowering the risk of hepatotoxic effects [8]. These results have led to growing interest in adopting shorter and safer treatment alternatives for latent TB, questioning the continued dominance of isoniazid-based protocols that have long been the standard in preventive strategies.

In recent years, there has been growing interest in exploring new tuberculosis treatment options that aim to improve the speed of bacterial clearance during the initial phase, shorten the duration of therapy, and increase patient adherence [3]. One promising strategy involves replacing traditional companion drugs such as pyrazinamide and ethambutol with moxifloxacin in the early stage of treatment. Clinical studies have indicated that a regimen consisting of isoniazid, rifampicin, and moxifloxacin (HRM) delivers treatment results that are on par with the standard combination of isoniazid, rifampicin, pyrazinamide, and ethambutol (HRZE) [3], [7], [9]. In addition to maintaining similar effectiveness, the HRM regimen may lead to fewer side effects and higher sputum conversion rates, which are important indicators of early treatment success.

Although these alternative regimens are still under clinical investigation and have yet to be officially adopted in treatment guidelines, they offer an important option for patients who cannot tolerate pyrazinamide or ethambutol due to adverse reactions or underlying health issues [3], [10], [11]. For individuals in these categories, the use of fluoroquinolone-based therapies such as HRM could help ensure successful treatment while reducing the likelihood of complications. These findings have encouraged a reexamination of long-established TB protocols and have opened the door for safer and more flexible approaches that align better with patient needs and improve overall treatment completion rates [3].

Treating patients with highly drug-resistant tuberculosis presents unique challenges, as traditional first-line drugs often fail to produce effective results in these cases [12]. This has led researchers to develop new treatment strategies that are more suitable for resistant strains of TB. One of the most notable breakthroughs came from the ZeNix trial, which tested a combination of bedaquiline, pretomanid, and linezolid, known as the BPaL regimen [12]. The results showed that this three-drug regimen was able to achieve successful treatment outcomes in 84 to 93 percent of participants, even when different doses and treatment

durations of linezolid were used [12]. These outcomes were especially encouraging given the complex nature of drug-resistant TB and the limited options available for such cases [4], [12].

One of the most important insights from the trial was the discovery that lowering the dose of linezolid to 600 mg over a period of 26 weeks significantly reduced the risk of serious side effects, such as nerve damage and suppression of bone marrow, without compromising the treatment's effectiveness. This finding is critical because it highlights how adjusting the dosage of certain drugs can help strike a balance between safety and efficacy. As a result, the BPaL regimen is seen as a major advancement in the treatment of resistant TB, offering a shorter and more tolerable option that still maintains strong therapeutic performance [12]. This shift represents a move toward more targeted and efficient treatment strategies for one of the most difficult forms of tuberculosis to cure.

When comparing treatments for drug-susceptible and drug-resistant tuberculosis, the differences in therapeutic approaches become increasingly evident. Standard first-line regimens, although still widely used, are being questioned due to challenges such as inconsistent drug absorption, patient-specific metabolic responses, potential toxicity, and the emergence of drug-resistant strains [1], [5]. These issues have been well-documented in both pharmacokinetic studies and clinical trials, leading to a growing awareness that traditional approaches may not be sufficient for all patient groups. While these older regimens have played a critical role in global TB control, their limitations call for a reevaluation, especially in light of current clinical demands and shifting resistance patterns.

In contrast, more recent treatment options that involve either fluoroquinolones or newly developed drugs like bedaquiline and pretomanid present alternative paths that may improve both the effectiveness and safety of TB therapy [3], [12]–[14]. These innovative regimens are essential for patients who do not respond well to conventional treatments or who experience severe side effects from first-line drugs. Clinical evidence has shown that these newer combinations can maintain strong bactericidal activity while reducing the risk of complications, which makes them valuable additions to the TB treatment landscape [3], [12]. As a result, the development and implementation of such alternatives mark a significant step forward in tailoring TB care to meet the needs of diverse patient populations.

The aim of this research was to analyze and compare the clinical effectiveness, safety profiles, and treatment outcomes of conventional first-line TB drug regimens with newer and emerging therapeutic combinations used in pulmonary tuberculosis management. This research contributes to the understanding of how traditional first-line TB regimens compare

with newer therapeutic combinations in terms of effectiveness, safety, and treatment duration. By synthesizing evidence from recent studies, the research provides updated insights that support more informed clinical decision-making and guide the development of optimized, patient-centered TB treatment strategies.

RESEARCH METHOD

This study employed a qualitative narrative review method to gather, interpret, and critically assess a wide range of scientific evidence related to therapeutic regimens for pulmonary tuberculosis. The review incorporated five peer-reviewed studies encompassing diverse forms of evidence, including clinical pharmacokinetic research, randomized trials evaluating standard first-line therapies, investigations on preventive treatment regimens for latent TB infection, and recent findings involving innovative multi-drug combinations. These studies examined both the established first-line regimen isoniazid, rifampicin, pyrazinamide, and ethambutol as well as newer therapeutic alternatives designed to enhance bacteriological clearance, shorten treatment duration, or address drug-resistant TB. Through this methodological approach, the study provides a comprehensive and coherent understanding of treatment effectiveness, safety profiles, and the evolving strategies shaping current TB management across varied clinical contexts.[1], [3], [5], [8], [12]

Data extraction was carried out by reviewing each study's purpose, method, patient characteristics, treatment regimens, and main outcomes, such as sputum conversion, treatment completion, relapse rates, and adverse events. The studies used in this review were taken from Scopus-indexed international journals [1], [12], [15] to ensure strong scientific quality and reliable evidence. International articles were chosen because they provide larger sample sizes, wider population coverage, and more complete evaluation of both old and new TB regimens. This allows for better comparison of treatment effectiveness. These studies came from different settings, including high TB-burden countries in Africa and Asia, multinational trials on latent TB treatment, and studies evaluating new regimens for drug-resistant TB [15]. Using evidence from various countries is appropriate because TB treatment standards are based on WHO guidelines, which are also used in Indonesia. Therefore, the findings from international studies can still be compared with the national TB treatment program (HRZE regimen and MDR-TB protocols). By using studies from different global contexts, this review was able to identify common patterns such as which regimens improve bacterial clearance or adherence and differences that arise due to local health

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systems or resistance levels. These comparisons provide a clearer understanding of how international findings may support or improve national TB treatment strategies.

The analytical process followed a thematic synthesis approach to analyze the collected literature, focusing on common patterns related to treatment effectiveness, safety concerns, and issues with patient adherence, while also taking into account the pharmacological processes behind these outcomes.[16], [17] Instead of using aggregated statistical data, the review applied a qualitative approach to better understand how different treatment regimens perform in various populations and healthcare environments. This method allowed the study to connect different strands of evidence and offer a detailed view of the practical use of tuberculosis therapies, the difficulties that continue to arise in clinical settings, and the potential directions for improving future treatment practices.

FINDINGS

The analysis of findings from the five selected studies shows a noticeable shift in the approach to treating pulmonary tuberculosis, moving gradually from conventional long-term regimens to newer therapies that are more specific, shorter in duration, and potentially easier for patients to tolerate.

Table 1. Completion Rates of Tuberculosis Treatments Across Selected Studies

Study	Regimen Type	Treatment Duration	Completion Rate	Key Insights
Denti et al. (2015)	Isoniazid, rifampicin, pyrazinamide, ethambutol (first-line, drug-susceptible TB)	6 months	~85% (varied by PK profile and patient adherence)	Completion affected by genetic variability (NAT2) impacting drug levels; monitoring could improve adherence.
British Thoracic Association (1981)	6-month SHRZG (with pyrazinamide) vs. 9-month EHR regimens (culture-positive TB)	6 months vs. 9 months	Higher for 6-month regimen (>80% vs. ~70% for 9-month)	Shorter duration improved completion and culture conversion without increasing relapse rates.
Menzies et al. (2018)	4-month rifampin (LTBI) vs. 9-month isoniazid (LTBI)	4 months vs. 9 months	15% higher completion for rifampin (approx. 90% vs. 75%)	Shorter preventive therapy led to better adherence and fewer severe side effects, especially hepatotoxicity.
Shang et al. (2021)	HRM (isoniazid, rifampicin, moxifloxacin) vs. HRZE (standard regimen for new TB cases)	6 months	Comparable (~85–90%)	HRM associated with fewer adverse events, potentially supporting completion, but long-term data lacking.

Conradie et al. (2022)	BPaL regimen (bedaquiline, pretomanid, linezolid) for XDR, pre-XDR, and rifampin-resistant TB	6 months (26 weeks linezolid)	~84–93% (dose-dependent)	600 mg linezolid dose supported higher completion by reducing severe side effects like neuropathy and myelosuppression.

According to table 1, the study also found that rifampin caused fewer serious side effects compared to isoniazid, especially when it came to liver problems. Severe side effects, rated as grade 3 to 5, were more than 1% lower in the rifampin group [8]. Even though this study looked at preventive treatment and not active TB, the findings show a common issue: using isoniazid for a long time can make it harder for patients to stick with the treatment. This is important for active TB treatment too, where similar problems might happen if isoniazid is used for an extended period. These results suggest that shorter and safer treatment options should continue to be explored for both prevention and treatment of TB.

Table 2. Comparison of Treatment Regimens

Source	**Regiments Studied**	**Population Context**	**Efficacy (Main Findings)**	**Safety Outcomes**
Denti et al. (2015)	Isoniazid, pyrazinamide, ethambutol (with rifampicin)	Newly diagnosed TB (Tanzania)	88% success rate; PK variability affected exposure	PK influenced by NAT2 genotype, age; minimal effect of HIV status
British Thoracic Association (1981)	6-month SHRZG (streptomycin, pyrazinamide) and EHRZ6 vs. 9-month EHR9	Culture-positive pulmonary TB	Faster culture conversion (77% vs. 64% at 2 months); comparable relapse control	Slightly increased dermatologic events in pyrazinamide regimens; no extra hepatitis
Menzies et al. (2018)	4-month rifampin vs. 9-month isoniazid (LTBI prevention)	Adults with latent TB	Non-inferior prevention; 15% higher completion with rifampin	Hepatotoxicity 1.2% lower with rifampin; fewer severe adverse events
Shang et al. (2021)	HRM (isoniazid, rifampicin, moxifloxacin) vs. HRZE	Newly diagnosed pulmonary TB	Comparable efficacy; potential for faster sputum conversion	Lower incidence of adverse effects; long-term outcomes pending
Conradie et al. (2022)	BPaL (bedaquiline, pretomanid, linezolid – various doses)	XDR, pre-XDR, rifampin-resistant TB	84–93% favorable outcomes; 600 mg linezolid optimal balance	Neuropathy and myelosuppression dose-dependent; reduced at 600 mg

Table 2 offers a clear comparison of five important studies that looked at different ways to treat tuberculosis in various patient groups and healthcare settings. It shows the types of treatment used, starting from the standard combination of isoniazid, rifampicin, pyrazinamide, and ethambutol, to newer options like moxifloxacin or the BPaL combination that includes bedaquiline, pretomanid, and linezolid. The table outlines important results, such as how quickly patients' sputum tests turned negative and how well the treatments

worked overall, along with common side effects like liver damage, skin problems, and nerve issues. This summary highlights that while traditional treatments remain effective for most regular TB cases, there is growing hope in newer, faster, and more effective treatments for more complex cases. At the same time, it reminds us that the best treatment is not just the most effective one, but also the one that patients can safely tolerate.

Even though there have been major improvements in TB treatment, putting new therapies into practice is still difficult in many places. Getting approval from regulators, dealing with high costs, and adjusting health systems are major obstacles, especially in countries with limited resources. Because of this, older treatment regimens are still very important. However, they can be improved by closely monitoring how the drugs move in the body, giving patients better nutrition, and helping them stay on track with their treatment [1]. At the same time, carefully introducing newer regimens for patients with drug-resistant or complicated cases can slowly help move TB care toward shorter, safer, and more effective treatments

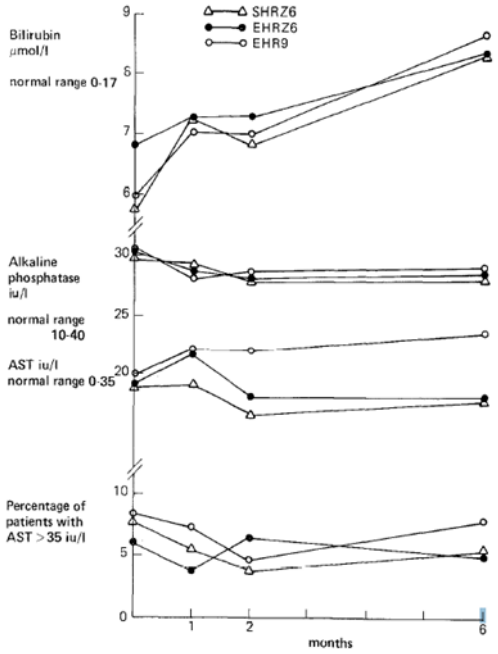

Figure 1. Mean Liver Function Markers Across Three TB Regimens [8,12]

Figure 1 illustrates the mean serum levels of bilirubin, alkaline phosphatase, and aspartate aminotransferase (AST) measured at baseline and at months 1, 2, and 6 across the three treatment regimens: SHRZG, EHRZ6, and EHR9. Throughout the six-month observation period, all three biochemical markers remained within the central laboratory's normal reference ranges, with only a modest rise in bilirubin levels (an average increase of 2 μmol/L) that was statistically significant but clinically negligible. Importantly, the

proportion of patients with elevated AST values did not differ between the pyrazinamide-containing regimens (SHRZG and EHRZ6) and the pyrazinamide-free regimen (EHR9).

These findings confirm that the inclusion of pyrazinamide during the initial two months of therapy did not exacerbate hepatic toxicity when compared to the standard nine-month regimen. By demonstrating that liver function markers remained largely stable across all treatment groups, Figure 1 supports the broader conclusion from the British Thoracic Association (1981) trial that six-month pyrazinamide-containing regimens can accelerate bacterial clearance without introducing additional risk of drug-induced hepatitis.

DISCUSSIONS

Traditional drug combinations such as isoniazid, rifampicin, pyrazinamide, and ethambutol continue to be widely used and are proven to be highly effective in treating drug-susceptible TB, with several studies reporting treatment success rates of over 85% in various patient groups. These regimens have been essential to global TB control efforts because of their strong ability to kill bacteria and prevent relapse [1].

Despite their continued relevance, the effectiveness of these classical treatments is being challenged by concerns about how consistently the drugs behave in the body. Pharmacokinetic differences, especially involving isoniazid and pyrazinamide, have been associated with variations in drug absorption and metabolism, which can lead to uneven therapeutic exposure across patients and increase the risk of treatment failure or resistance [1]. These findings highlight the need for a more personalized approach in TB treatment, where dosing and drug selection are adjusted based on individual health conditions and genetic factors that influence how drugs are processed in the body. Monitoring these variables more closely may improve treatment outcomes, particularly among vulnerable populations who are at higher risk of complications.

Findings from clinical trials have shown that six-month treatment regimens containing pyrazinamide result in faster bacterial clearance from the lungs when compared to longer nine-month regimens based only on isoniazid and rifampicin [5]. Specifically, after two months of treatment, 77% of patients receiving pyrazinamide-containing regimens had negative sputum cultures, compared to only 64% in the group treated without pyrazinamide [5]. This improvement in early treatment response highlights the added value of including pyrazinamide during the intensive phase of therapy, especially in efforts to shorten overall treatment duration without compromising efficacy.

Importantly, the inclusion of pyrazinamide in shorter regimens did not lead to a higher incidence of hepatitis, which is a common concern with TB medications, although there was an increase in mild side effects such as skin-related reactions. These findings emphasize the strong sterilizing properties of pyrazinamide, which make it a key component in achieving early bacterial clearance. However, the presence of even mild side effects may influence patient comfort and willingness to complete the full course of therapy, which is crucial in preventing relapse or resistance. Therefore, while the benefits of pyrazinamide are clear, its use must be balanced with considerations of individual patient tolerance to maintain both the effectiveness and feasibility of the regimen in everyday clinical settings [5].

The study by Menzies et al. (2018) gives useful information about how well people can stick with and tolerate long-term preventive treatments for latent tuberculosis infection (LTBI). The researchers compared two options: a four-month treatment using rifampin and a longer nine-month treatment using isoniazid. Both were equally good at stopping LTBI from turning into active tuberculosis, but more people were able to finish the shorter rifampin treatment. In fact, the completion rate for rifampin was about 15% higher, showing that shorter treatments can help patients stay on track more easily and reduce the chances of dropping out [8].

New treatment strategies are being developed to make the early phase of tuberculosis therapy more effective and easier for patients to handle. One example is the HRM regimen, which combines isoniazid, rifampicin, and moxifloxacin, as tested by Shang et al. (2021). This approach replaces pyrazinamide and ethambutol with moxifloxacin. The study found that this new combination worked just as well in curing TB as the standard HRZE regimen, but it showed some benefits in helping patients clear the bacteria from their lungs faster and reducing uncomfortable side effects [3].

The study also found that rifampin caused fewer serious side effects compared to isoniazid, especially when it came to liver problems. Severe side effects, rated as grade 3 to 5, were more than 1% lower in the rifampin group (Menzies et al., 2018). Even though this study looked at preventive treatment and not active TB, the findings show a common issue: using isoniazid for a long time can make it harder for patients to stick with the treatment. This is important for active TB treatment too, where similar problems might happen if isoniazid is used for a long period. These results suggest that shorter and safer treatment options should continue to be explored for both prevention and treatment of TB.

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The reason moxifloxacin may be effective is that it can kill TB bacteria both inside and outside of cells, which makes it a strong candidate to support or replace existing drugs. However, while the short-term results are encouraging, more studies are still needed to understand how well this regimen works in the long run. Researchers must also look more closely at the risk of relapse and any possible long-term side effects before this combination can be widely recommended for standard treatment [3]

One of the most important breakthroughs in tuberculosis treatment comes from the ZeNix trial, which tested the BPaL regimen using bedaquiline, pretomanid, and linezolid in patients with hard-to-treat TB, including those with extensively drug-resistant (XDR) and pre-XDR TB [12]. The trial studied four different dosing strategies and found that 84% to 93% of participants had successful treatment results, showing that the regimen worked well even in very severe cases. This approach marks a clear shift from older treatments and offers hope for patients who previously had limited options.

The version of the treatment that worked best used 600 mg of linezolid for 26 weeks. This dosage helped reduce the rate of nerve damage (peripheral neuropathy) to just 13%, much lower than the 38% seen with a 1200 mg dose, without sacrificing treatment success, which still stayed above 90% [12]. These findings show how important it is to not only discover new drugs but also carefully adjust their dosages to avoid harmful side effects. This balance between safety and effectiveness will be key in improving TB treatment moving forward [12].

Based on the overall comparison of available studies, traditional tuberculosis treatments are still effective for cases where the bacteria are not resistant to drugs. However, these older regimens often face serious challenges, such as patients not completing their treatment, unpredictable drug absorption in the body, and an increase in bacteria that are no longer responsive to standard medications. These issues can reduce the success of therapy, especially in communities where TB remains widespread and healthcare systems are under pressure. Despite their limitations, first-line drugs like isoniazid and rifampicin continue to

be widely used because they are accessible, familiar to clinicians, and supported by established treatment protocols.

At the same time, newer treatment options, such as regimens that include fluoroquinolones or other recently developed drugs, have shown similar or even better results in fighting TB, particularly in patients with certain types of resistance or intolerance to older medications. These newer combinations may cause fewer side effects and lead to better adherence. However, their availability is often limited in countries with high TB burdens due to high costs, regulatory barriers, and the need for close medical monitoring to ensure safety. As a result, while these novel therapies offer hope for the future, many health systems are not yet ready to replace traditional treatments on a wide scale. Their successful use will depend not only on clinical evidence but also on addressing practical barriers related to healthcare infrastructure and affordability.

One of the core arguments that emerges across different studies is how long the treatment lasts. Research has consistently shown that shorter treatment plans can lead to better patient adherence and fewer side effects, while still being effective in curing the disease. For example, using rifampin for a shorter period to treat latent tuberculosis infection (LTBI) was found to be as effective as longer regimens and was easier for patients to complete [8]. Similarly, the BPaL regimen for drug-resistant TB has shown that a shorter treatment duration can still achieve high success rates, even in patients with severe forms of the disease [12]. These results suggest that shorter therapies may help solve some of the challenges with long and difficult TB treatments.

Because of these results, many experts are now calling for a new approach that prioritizes making treatments shorter wherever it is safe and possible. However, this shift must be done with caution. Not all patients may be suitable for shorter treatment, and doctors need to make sure they monitor for safety during the process. While shorter therapies seem promising, they should be matched carefully to each patient's condition and level of drug resistance. As evidence grows, this principle of minimizing treatment duration could become a central part of how TB is managed in the future, provided that healthcare providers ensure safety and proper follow-up throughout [8], [12]

One important aspect to consider in tuberculosis treatment is how different drug regimens come with different side effect profiles. Older medications like isoniazid have long been known to cause liver toxicity, which can be dangerous if not monitored closely [5]. Similarly, pyrazinamide has been linked to skin problems and changes in metabolism that may lead to complications during treatment [8]. On the other hand, newer treatments,

especially those that include linezolid, bring their own challenges, such as nerve damage and a reduction in blood cell production, which can be serious if not detected early [12]. Due to these risks, it is crucial to closely monitor patients during treatment and consider adopting a more personalized approach. Tools like biomarkers or genetic testing may help doctors choose the most suitable therapy for each patient based on their specific health conditions and risks.

This study has several limitations. First, as a narrative review based on only five peer-reviewed studies, the findings may not fully represent the broader evidence base. Second, the included studies differ in design, sample size, population characteristics, and treatment settings, which may limit comparability. Third, the review does not include meta-analysis or quantitative pooling, reducing the ability to measure effect sizes across regimens. Fourth, potential publication bias may influence the available evidence, as studies with positive outcomes are more likely to be published. Finally, newer regimens such as BPaL involve limited long-term safety data, which restricts conclusions regarding sustained treatment effectiveness and adverse effects

CONCLUSION

This narrative review highlights that while traditional first-line regimens remain highly effective for drug-susceptible pulmonary tuberculosis, evolving challenges such as drug resistance, hepatotoxicity, and poor adherence necessitate the adoption of optimized therapeutic approaches. Incorporating pyrazinamide into shorter six-month regimens enhances bacterial clearance without increasing toxicity, and newer rifampin-based regimens improve patient adherence and safety profiles. Moreover, innovative combinations such as fluoroquinolone-based HRM therapies and the BPaL regimen demonstrate remarkable efficacy, particularly against drug-resistant strains. Therefore, individualized treatment strategies that integrate both conventional and emerging therapies are essential to achieving global TB control goals by improving cure rates, minimizing adverse effects, and reducing treatment duration.

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