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Study on the Effectiveness and Safety of Linezolid Dose Reduction in Multidrug-Resistant Tuberculosis

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ABSTRACT

Background: The following study discusses how Multidrug-resistant tuberculosis (MDR-TB) poses a significant global health challenge. It has been found that it is mainly in resource-limited environments. Linezolid is an oxazolidinone antibiotic that has shown promise in MDR-TB treatment. However, its extended use is associated with severe adverse effects. Moreover, this study evaluates the effectiveness and safety of a reduced dose of Linezolid. The primary aim was to assess treatment outcomes, sputum culture conversion, and adverse events in patients receiving Linezolid as part of their MDR-TB regimen compared to a control group.

Methods: This randomized controlled trial was conducted in Maharshi Devraha Baba Autonomous State Medical College Deoria and included patients aged 18-64 with extensively drug-resistant (XDR) TB. Participants were assigned to either a linezolid or control group based on drug susceptibility. Linezolid therapy started at 1200 mg/day for 4–6 weeks, then adjusted based on tolerability. The primary endpoint was sputum-culture conversion. Adverse events like anemia and neuropathy were monitored, and statistical analysis was performed using SPSS 27. Safety and microbiological evaluations were conducted throughout the treatment.

Results: The Linezolid group achieved significantly higher treatment success (68% vs. 40%, p=0.007) and a lower failure rate (12% vs. 40%, p=0.009). Faster sputum culture conversion and cavity closure were observed in the Linezolid group. However, adverse effects such as anemia (48% vs. 12%, p=0.002) and optic neuropathy (16% vs. 0%, p=0.037) were more prevalent.

Conclusion: This study concluded that a reduced dose of Linezolid is an effective and safer alternative for treating multidrug-resistant tuberculosis (MDR-TB).

Key-words: Adverse effects, Drug resistance, Linezolid, MDR-TB, *Mycobacterium* TB strains, Tuberculosis treatment

INTRODUCTION

This is a large public health challenge, along with the cumulative incidence of drug-resistant strains and the complexities associated with treatment. According to the latest WHO report, an estimated 10 million people fell ill with TB in 2019, with approximately 465,000 cases of MDR-TB reported worldwide [1].

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The incidence is increasing, mainly in low- and middle-income countries whose healthcare systems cannot implement effective TB control measures.

The growth of widely drug-resistant TB, which is resistant to most anti-TB drugs, including the first-line drugs and most of the second-line drugs, makes the treatment scenario complicated, thus leading to increased morbidity and mortality in the affected populations [2]. Isoniazid and rifampicin, the primary medications for tuberculosis treatment, have extensively recognized limitations. These drugs are effective against *Mycobacterium* TB strains that are vulnerable to standard treatment; however, their activity is significantly reduced in the presence of drug-resistant

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strains. Contributing factors to the growth include inappropriate treatment regimens, poor adherence to therapy, and the use of substandard medications [3].

The WHO has underlined the significance of early drug susceptibility testing, which may lead to the early detection of resistant strains during treatment and may, therefore, enable appropriate tailoring of therapy, thus enhancing the outcome [1]. However, the reality remains that most of the patients are diagnosed late or not diagnosed at all, leading to the further spread of resistant strains within the community [4]. Another theory is that the emergence of drug-resistant TB strains can be traced back to non-functional TB control programs, interruptions in the provision of drugs, and the inappropriate use of antibiotics [3].

Poor case management and treatment defaults have been responsible for historically increasing MDR-TB trends, especially in high-burden regions [5]. Treatment is inherently much more complicated and expensive than for drug-susceptible TB and mostly requires a mixture of second-line drugs that are less effective and more toxic than the first [6]. Rates of success among MDR-TB patients show wide variability. Success rates can be as low as 42.6% for XDR-TB [5]. Hence, urgent work is needed toward effective treatment methods and the design of new treatments.

Linezolid is an oxazolidinone drug with a promising potential as a second line of treatment. It has already been effective in the treatment, especially where the other second-line agents fail to show their efficacy [6]. In addition, SR and MA reported the rate of sputum smear conversion and culture conversion in the patients included under the linezolid-containing regimen to be up to 81.8%. All patients enrolled in the regimen achieved successful results [7,8]. Several clinical reports have documented the efficiency of linezolid in the treatment. An SR and MA conducted by Sotgiu et al. revealed that linezolid-including regimens exhibited high sputum smear and culture conversion rates in MDR-TB patients [9]. According to the study, 92.5% of patients achieved sputum smear conversion, and 93.5% achieved culture conversion following treatment with individualized regimens containing linezolid [9]. Moreover, in terms of complete success, treatment was curative in 81.8%, which indicates that linezolid does offer excellent clinical effectiveness, especially where fewer other regimens are available [9]. From the results presented here, therefore, it will be evident that this drug may have an important role to play within the standard or intensive multidrug-resistant regimens.

XDR-T is defined as resistance to the two most important first-line TB drugs, such as isoniazid and rifampicin, or any fluoroquinolone and at least one injectable second-line drug [10,11]. This can provide a synergistic effect with other drugs and can even improve the treatment outcomes of patients suffering from XDR-TB [9,12]. Studies on linezolid's use in combination regimens for XDR-TB have supported its efficacy in difficult-to-treat cases. For instance, a cohort study showed that more than 40% of patients used off-label linezolid; therefore, acceptance of the drug in clinical practice increased [11]. In addition, pharmacogenetic data showed that oxazolidinones such as linezolid are useful in treating mycobacterial infections, even resistant strains [11]. Results, though promising, the challenge is in determining an appropriate combination of drugs and the duration of treatment, which may dramatically affect the patient's outcomes [13].

MATERIALS AND METHODS

Study design- This is a Randomized Controlled Trial conducted in Maharshi Devraha Baba Autonomous State Medical College, Deoria. They were allocated randomly to the linezolid or control group. Patients were assigned to particular chemotherapeutic agents based on drug susceptibility tests (DST) and previous drug history. Each regimen consists of at least 5 drugs, they were selected based on the WHO 5 anti-TB drugs. After 4–6 weeks, they started with a 1200 mg per day linezolid mouth dose and continued on linezolid at 300–600 mg per day based on tolerability and body weight. It was continued till the patients presented two negative sputum cultures consecutively, for 2 months, separated for a month. The adverse events formed due to linezolid in the previous studies which included anemia, peripheral neuropathy, and leukopenia. In this study, side effects were defined as leukocytes <2000 mm^{-3}, hemoglobin <60 $g{\cdot}L^{-1}$, or the symptoms that would result in limited activity or require any treatment or were possible to occur. In case of the occurrence of events considered related to linezolid linezolid dose would be decreased to 300- 600 mg a day. The sputum-culture conversion was the primary end-point. Conversion was thought of if two consecutive cultures were negative 30 days apart. Directly observed therapy (DOT) was given to each patient directly

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throughout the treatment. In the communities, the supervisors were trained and DOT was carried out.

The study got approval from the ethical committee of the hospital. All the patients were provided with informed consent. The study was following the Ethical Committee. Attending physicians collected all the data of the patients and recorded them routinely.

Study patients- Patients of the age range 18-64 years positive to strains of extensively drug-resistant (XDR) and continuously positive strains after administration of chemotherapeutic drugs in the previous ≥12 months were included in the study. All the HIV-positive patients were immediately transferred to the hospital. Patients allergic to linezolid, mental illness, severe liver, blood, kidney, cardiovascular, or other diseases, lactating or pregnant women, HIV positive, and unable to purchase linezolid were excluded from the study.

Study Procedures

Microbiological Evaluation and Outcomes- Specimens of sputum were obtained every 3 months in the morning during the period of treatment. However, the sputum is collected every month before the conversion of the sputum culture. The samples of sputum were tested on fluorescence by smear by Lowenstein-Jensen culture and by BACTEC MGIT 960 system. The guidelines of WHO were used to perform DSTs using the MGIT 960 System on positive cultures with seven drugs isoniazid, streptomycin, rifampin, ofloxacin, ethambutol, capreomycin, and amikacin. All the tests were done at the reference laboratory of TB and quality control was carried out routinely.

WHO and IUATLD (International Union Against Tuberculosis and Lung Disease) definition of treatment outcomes was done.' The term 'cured' was used for a patient who would have fulfilled program protocol treatment and provided negative cultures consistently over the final 12 months of treatment of TB. Completed treatment refers to a patient who finished the program's prescribed course of therapy, but who did not meet the criteria for being cured since he did not exhibit bacteriological findings. Patients who died for any reason during the course and period of the TB treatment were included in the 'died' category. Treatment failure was defined as any patient with the counts of the five cultures in the final 12 m of therapy positive for two or more or a patient with a single culture in the final three is positive. A patient with any reason leading to interruption of TB treatment for ⩾2 consecutive months was defined as the 'defaulted' patient. Furthermore, treatment success and treatment failure were combined for curing and complete categories and poor treatment outcomes for others.

Imaging evaluation- Computed tomography and chest radiographs were obtained at least once in 3 months during the period of treatment. A radiologist and 2 physicians evaluated all the images.

Safety Evaluation- Baseline and serial safety evaluations were done every week till the linezolid was decreased at 4–6 weeks and after that for every 2 weeks until the linezolid was stopped once a month. The definition of leukopenia was WBC < 4.0×109 L^{-1}. Hemoglobin was defined as mild anemia when it was in the range of 9–12 $g{\cdot}dL^{-1}$. Hemoglobin between 6 and 9 $g{\cdot}dL^{-1}$ was defined as moderate anemia. Hemoglobin <6 $g.dL^{-1}$ was defined as severe anemia. All patients were evaluated by a physician with nerve-conduction studies at entry and, if peripheral neuropathy developed, with consultation of a neurologist. For optic neuropathy surveillance of linezolid, the staff tested patients for vision and color vision. Daily, these adverse effects were recorded and these were evaluated for clinically significant abnormal laboratory results or immediately reportable events.

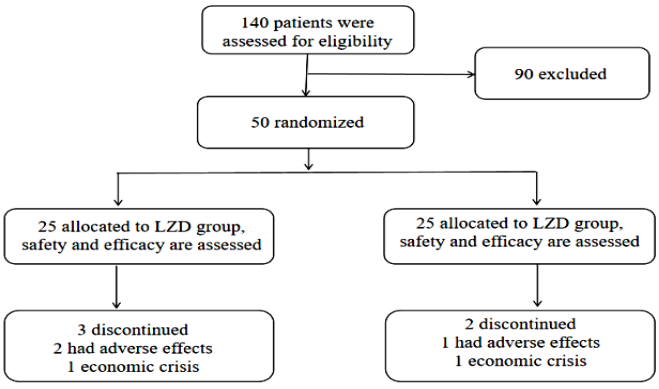

Fig. 1: Study Drug Assignment, Patient Enrollment, Randomization, and Follow-Up. A total of 155 patients were screened for eligibility, with 50 randomized. Three patients discontinued in the linezolid therapy group (two due to adverse effects, one due to economic factors), and two in the control group (one due to adverse effects, one due to economic factors).

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Statistical analysis- This study used the SPSS-27 software, was used for the analysis of statistics. The continuous data was expressed as mean±SD and discrete data was expressed as frequency and its respective percentage. The Pearson Chi-squared tests compared different groups, and Fisher's exact tests compared categorical variables. Statistical significance was considered at $p<0.05$.

RESULTS

Table 1 presents the baseline characteristics of 50 patients, evenly distributed between the Linezolid Therapy Group (n=25) and the Control Group (n=25). The median age was similar across both groups (Linezolid: 45 years, Control: 44 years), with a male predominance of 62%. The mean body mass index (BMI) was comparable (Linezolid: 19.7, Control: 19.5). Common comorbidities included diabetes (18%), chronic obstructive pulmonary disease (10%), bronchiectasis (26%), tuberculous pleurisy (18%), and respiratory failure (18%), with slightly varying prevalence between groups. Decreased albumin levels were observed in 30% of patients. Lung cavities were present in all patients, with 46% having unilateral and 54% bilateral involvement. The majority had a disease duration of at least one year before randomization, with 54% in the 1–5-year range and 46% over five years. Prior treatment followed a similar distribution, with 66% treated for 1–5 years and 34% for over five years. Drug susceptibility testing revealed high resistance rates, with all patients resistant to isoniazid, rifampin, and ofloxacin, and over 70% showing resistance to ethambutol, amikacin, and capreomycin. The background regimen was uniform across groups, comprising prothionamide, pyrazinamide, a fluoroquinolone, and para-aminosalicylic acid, while capreomycin/amikacin (54%), clofazimine (64%), and clarithromycin (50%) were included in varying proportions. Overall, the baseline characteristics were well-balanced between the two groups.

Table 1: Baseline characteristics of patients

Characteristics	Linezolid Therapy Group	Control Group	Total
Subjects (n)	25	25	50
Age (years)	45 (19–64)	44 (18–63)	44 (18–64)
Male sex (n, %)	16 (64.0)	15 (60.0)	31 (62.0)
Body mass index (kg/m²)	19.7 (12–30)	19.5 (12–29)	19.6 (12–30)
With comorbidity (n, %)			
Diabetes	5 (20.0)	4 (16.0)	9 (18.0)
Chronic obstructive pulmonary disease	2 (8.0)	3 (12.0)	5 (10.0)
Bronchiectasis	6 (24.0)	7 (28.0)	13 (26.0)
Tuberculous pleurisy	4 (16.0)	5 (20.0)	9 (18.0)
Respiratory failure	5 (20.0)	4 (16.0)	9 (18.0)
Decreased albumin	8 (32.0)	7 (28.0)	15 (30.0)
Lung cavities (n, %)			
Unilateral	12 (48.0)	11 (44.0)	23 (46.0)
Bilateral	13 (52.0)	14 (56.0)	27 (54.0)
Course of disease (n, %)			
≥1 yr <5 yrs before randomization	14 (56.0)	13 (52.0)	27 (54.0)
≥5 years before randomization	11 (44.0)	12 (48.0)	23 (46.0)
Previous treatment (n, %)			

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≥1 yr <5 yrs before randomization	16 (64.0)	17 (68.0)	33 (66.0)
≥5 years before randomization	9 (36.0)	8 (32.0)	17 (34.0)
Susceptibility test results resistance (n, %)			
Streptomycin	22 (88.0)	23 (92.0)	45 (90.0)
Isoniazid	25 (100)	25 (100)	50 (100)
Rifampin	25 (100)	25 (100)	50 (100)
Ethambutol	21 (84.0)	23 (92.0)	44 (88.0)
Ofloxacin	25 (100)	25 (100)	50 (100)
Amikacin	20 (80.0)	19 (76.0)	39 (78.0)
Capreomycin	19 (76.0)	18 (72.0)	37 (74.0)
Background regimen (n, %)			
Prothionamide, pyrazinamide, moxifloxacin or gatifloxacin or levofloxacin, para-aminosalicylic acid	25 (100)	25 (100)	50 (100)
Capreomycin or amikacin	14 (56.0)	13 (52.0)	27 (54.0)
Clofazamine	17 (68.0)	15 (60.0)	32 (64.0)
Clarithromycin	13 (52.0)	12 (48.0)	25 (50.0)

Table 2 presents the treatment outcomes for the Linezolid and Control groups, each comprising 25 patients. Treatment success was significantly higher in the Linezolid group (68%) compared to the Control group (40%) (p=0.007), with a higher cure rate (48% vs. 24%, p=0.032). Treatment completion rates were similar between groups (20% vs. 16%, p=0.606). Poor treatment outcomes were more frequent in the Control group (60%) than in the Linezolid group (32%) (p=0.007). Although mortality rates were comparable (Linezolid: 8%, Control: 12%, p=0.606), treatment failure was significantly lower in the Linezolid group (12%) compared to the Control group (40%) (p=0.009). Both groups had low and similar default rates (12% vs. 8%, p=0.606). These findings suggest that Linezolid therapy led to significantly better treatment success rates and lower failure rates than the control group.

Table 2: Treatment outcomes for both group

Treatment Outcomes	Linezolid Group (n=25)	Control Group (n=25)	Chi-squared	p-value
Treatment success (n, %)	17 (68.0)	10 (40.0)	6.125	0.007
Cure (n, %)	12 (48.0)	6 (24.0)	4.578	0.032
Treatment completion (n, %)	5 (20.0)	4 (16.0)	0.267	0.606
Poor treatment outcomes (n, %)	8 (32.0)	15 (60.0)	6.125	0.007
Death (n, %)	2 (8.0)	3 (12.0)	0.267	0.606
Failure (n, %)	3 (12.0)	10 (40.0)	6.908	0.009
Default (n, %)	3 (12.0)	2 (8.0)	0.267	0.606

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Table 3 summarizes the adverse events observed in both the Linezolid and Control groups, each comprising 25 patients. Anaemia was significantly more common in the Linezolid group (48%) compared to the Control group (12%) (p=0.002), as was nausea/vomiting (44% vs. 12%, p=0.008). Optic neuropathy was reported in 16% of patients in the Linezolid group but was absent in the Control group (p=0.037). Other adverse events, such as thrombocytopenia, leukopenia, peripheral neuropathy, and liver injury, occurred at slightly higher rates in the Linezolid group, but the differences were not statistically significant. Tinnitus or hearing loss, rash or pruritus, arrhythmia, and hypokalaemia were observed at similar frequencies in both groups. Overall, the Linezolid group experienced a higher incidence of certain adverse effects, particularly anaemia, nausea/vomiting, and optic neuropathy, which were statistically significant compared to the control group.

Table 3: Adverse events for both group

Adverse Event	Linezolid Group (n=25)	Control Group (n=25)	Chi-squared	p-value
Anaemia (n, %)	12 (48.0)	3 (12.0)	9.375	0.002
Thrombocytopenia (n, %)	3 (12.0)	1 (4.0)	0.923	0.337
Leukopenia (n, %)	4 (16.0)	2 (8.0)	0.727	0.394
Nausea/vomiting (n, %)	11 (44.0)	3 (12.0)	7.143	0.008
Peripheral neuropathy (n, %)	6 (24.0)	2 (8.0)	2.667	0.102
Optic neuropathy (n, %)	4 (16.0)	0 (0)	4.348	0.037
Liver injury (n, %)	5 (20.0)	6 (24.0)	0.114	0.736
Tinnitus or hearing loss (n, %)	3 (12.0)	4 (16.0)	0.167	0.683
Rash or pruritus (n, %)	2 (8.0)	2 (8.0)	0	1
Arrhythmia (n, %)	2 (8.0)	2 (8.0)	0	1
Hypokalaemia (n, %)	1 (4.0)	2 (8.0)	0.351	0.554

Table 4 presents the ratio of patients with a positive and negative culture in sputum over time for both the Linezolid Therapy and Control groups. At the start of treatment (0 months), both groups had a ratio of 1, indicating all patients had a positive sputum culture. By 3 months, the ratio dropped more sharply in the Linezolid group (0.66) compared to the Control group (1), suggesting a faster decline in bacterial presence. The trend continued at 6 months, where the ratio further decreased to 0.4 in the Linezolid group, while it remained higher at 0.66 in the Control group. From 9 months onward, the Linezolid group showed a consistently lower ratio (0.2–0.3), indicating a sustained reduction in bacterial presence, whereas the Control group had a slower decline, with a ratio remaining around 0.6 until 21 months and slightly decreasing to 0.58 at 24 months. This suggests that the Linezolid therapy led to a faster and more effective clearance of bacterial infection in sputum cultures compared to the Control group.

Table 4: Ratio of patients with a positive and negative culture in sputum.

Time (Months)	Linezolid Therapy Group (n=33)	Control Group (n=32)
0	1	1
3	1	0.66
6	0.4	0.66

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9	0.2	0.6
12	0.2	0.6
15	0.2	0.6
18	0.3	0.6
21	0.25	0.6
24	0.2	0.58

Table 5 presents the ratio of patients over time with cavity closure in the lungs for both the Linezolid Therapy and Control groups. At the beginning of treatment (0 months), both groups had a ratio of 1, indicating no cavity closure. By 3 months, the ratio decreased slightly to 0.8 in both groups, suggesting an initial similar response. However, from 6 months onward, the Linezolid group demonstrated a more pronounced reduction in cavity presence, with the ratio decreasing to 0.53, compared to 0.78 in the Control group. By 9 months, the disparity widened further, with the Linezolid group showing a ratio of 0.28 versus 0.6 in the Control group. Between 12 and 24 months, the Linezolid group continued to show a more significant decline, stabilizing at 0.3 by 24 months, whereas the Control group had a slower reduction, remaining at 0.65. These findings suggest that patients in the Linezolid Therapy group experienced faster cavity closure compared to those in the Control group, highlighting the potential effectiveness of Linezolid in promoting lung healing.

Table 5: Ratio of patients with time to cavity closure

Time (Months)	Linezolid Therapy Group (n=33)	Control Group (n=32)
0	1	1
3	0.8	0.8
6	0.53	0.78
9	0.28	0.6
12	0.33	0.68
15	0.4	0.7
18	0.35	0.68
21	0.33	0.65
24	0.3	0.65

Fig. 2 illustrates the time to onset of Linezolid-related adverse events in days. Among the recorded adverse events, optic neuropathy had the shortest onset time, occurring within just 2 days of treatment initiation. Thrombocytopenia and peripheral neuropathy followed closely, both emerging within 4 days. Leukopenia appeared slightly later, at around 5 days. Anaemia and nausea/vomiting took the longest to develop, occurring at 12 and 15 days, respectively. These findings suggest that while some adverse effects of Linezolid appear rapidly, others take longer to manifest, indicating the need for close monitoring, particularly in the early stages of treatment.

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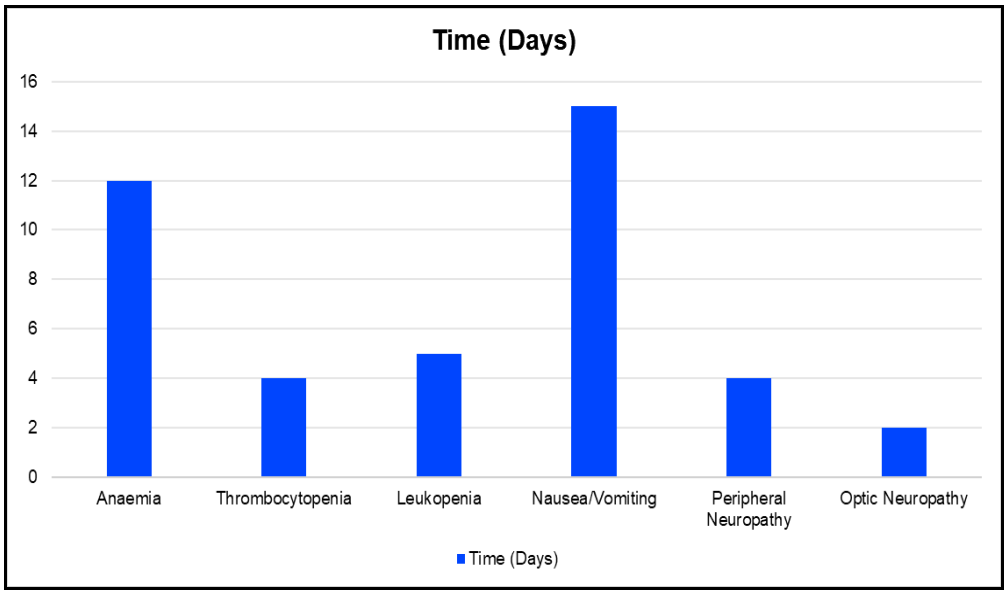

Fig 2: Time to linezolid-related adverse events.

DISCUSSION

The use of therapy has included increased use of oxazolidinone and linezolid, as the antibiotic inhibits bacterial protein synthesis. Studies now focus on results for reduced dosing of linezolid as compared to the standard dosing regimens, which suggest the use of a reduced dose of the drug without losing therapeutic effectiveness but by minimizing side effects, particularly hematologic toxicity.

One major study by Sotgiu *et al*. was an SR and MA that concentrated on the effectiveness and safety of linezolid-containing regimens for multi-drug resistance-TB and XDR-TB. The meta-analysis showed that there were insignificant differences in efficacy between daily linezolid dosages of 600 mg versus higher doses [14]. ADR was reported in 58.9% of patients, and major adverse events occurred in 68.4% of those cases. Most of the adverse events were related to anaemia, peripheral neuropathy, gastrointestinal disorders, optic neuritis, and thrombocytopenia. It is important to note that when the daily dose of linezolid was more than 600 mg, the rate of adverse events was significantly higher, indicating a need for reduced dosing that may produce an improved safety profile without compromising effectiveness [14].

However, standard-dose linezolid (usually 600 mg twice daily) has been shown to result in a higher rate of adverse effects, mainly hematologic toxicities, such as thrombocytopenia and anaemia. The problem with standard dosing is that though it may provide good efficacy, the side effects can cause the treatment to be discontinued or doses to be reduced, complicating the management. The results by Sotgiu et al. support the notion that reduced-dose treatment might be a good alternative with which to balance efficacy and lower the risk of serious adverse effects [14].

Additionally, clinical results of the use of linezolid in reduced doses fit with the conclusions drawn from various other studies in the literature assessing the use of linezolid as an adjunctive agent for other anti-TB drugs. For instance, a multi-centre study documented promising efficacy in treating complicated resistance at reduced doses for the combination regimen that included linezolid, besides other drugs from the category of second-line agents. This fact establishes that its benefits in the therapy can be preserved while risking fewer adverse effects by using linezolid in lesser dosages [15].

Retrospective assessments further confirm the safety and tolerability of linezolid at reduced dosages. For example, in a retrospective study, it was found that the patients treated with lower doses of linezolid had fewer events of adverse reactions as compared to those treated on standard dosing, and therefore, less dosed is justified in clinical practices [15]. In addition, the pharmacokinetics profile of linezolid, its oral bioavailability is 100%, renders flexible dosing regimens and can be individualized to a patient without compromising therapeutic effectiveness [16].

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There has been much interest in lower doses of linezolid, especially in treatment because of their possible impact on bacterial clearance and time to sputum conversion, as well as the overall rate of treatment success. Some new studies have pointed out that lowered doses of linezolid would retain efficacy without adverse effects such as hematologic toxicity, an important issue associated with standard dosing regimens [16].

One of the major findings concerning the efficacy of lower doses of linezolid is its effect on bacterial clearance and sputum conversion times. De Lorenzo *et al.* demonstrated that most patients receiving linezolid-containing regimens achieved sputum smear conversion in a median time of 43.5 days and culture conversion in 61 days [17]. This is comparable to the results of studies done using linezolid at conventional dosing, whose majority state similar or even longer times to conversion. For example, in some other studies, the median time to culture conversion ranged between 60 and 195 days, depending on the type of patient population and drug regimen. This implies that lower doses can be used appropriately to facilitate adequate bacterial clearance while not delaying conversion [18].

Regarding efficacy, the above meta-analysis was also able to show that of the patients, 81.8% showed successful outcomes among those treated using linezolid-containing regimens, which would be like the success rates described for standard dosing regimens [17]. For instance, MDR-TB regimens that the WHO recommends generally have success rates ranging from 60% to 80%, depending on the combination of drugs used and the population of patients. The similar success rates achieved with reduced-dose linezolid indicate that it could be a potential substitute for standard dosing, especially for patients who are at higher risk for adverse effects [19].

As observed, these findings are compared to the WHO-recommended regimens. However, it must be noted that the standard regimen usually consists of a combination of second-line drugs, including fluoroquinolones and injectable agents, in addition to first-line agents [19]. Individualized treatment plans based on drug susceptibility testing and the characteristics of the patient have been stressed in the WHO guidelines. Although standard regimens have been effective, the development of drug-resistant strains demands research into alternative dosing strategies, for example, reduced-dose linezolid, to improve safety and tolerability without sacrificing the outcome of the treatment [19].

Moreover, a lower linezolid dose has been known to be significantly associated with the reduction of most adverse events as well as hematologic toxicities, most notably thrombocytopenia and anaemia, typical at higher linezolid doses [20]. This is well noted in those patients being subjected to treatment who have extensively drug-resistant tuberculosis that has had excessive drug exposure that makes them easily prone to reactions from treatment regimens. It makes lower-dose linezolid an attractive alternative in the management of drug-resistant tuberculosis since it assures retaining efficacy without elevating the risk of adverse effects [21].

CONCLUSIONS

This study concluded that a reduced dose of Linezolid is an effective and safer alternative for treating multidrug-resistant tuberculosis (MDR-TB). Key findings indicate that the Linezolid group had significantly higher treatment success (68%) compared to the control group (40%), with a lower failure rate (12% vs. 40%). Additionally, the Linezolid group exhibited a faster sputum culture conversion rate and cavity closure, suggesting enhanced bacterial clearance. However, adverse events such as anemia, nausea, and optic neuropathy were more frequent in the Linezolid group, highlighting the need for careful monitoring. Despite these side effects, reduced dosing minimized toxicity while maintaining therapeutic efficacy. Given the global challenge of MDR-TB and limited treatment options, this study supports the integration of Linezolid into individualized regimens, particularly in resource-limited settings. Future research should focus on optimizing dosing strategies to improve safety and treatment outcomes further.

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