Journal of Cardiovascular Disease Research

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 06, 2024

A STUDY ON ADVRSE DRUG REACTIONS SEEN IN PATIENTS ON TUBERCULOSIS PREVENTIVE THERAPY

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Received Date: 17/05/2024 Acceptance Date: 05/06/2024

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Abstract

Background: Tuberculosis (TB) preventive therapy is crucial in combating the global TB epidemic. However, adverse drug reactions (ADRs) remain a significant barrier to its successful implementation. **Methods**: This prospective observational study involved 152 participants on TB preventive therapy, monitored over nine months to identify the incidence, type, and severity of ADRs, and assess the impact on treatment adherence. **Results**: A high incidence of ADRs was observed, with 88.2% of participants experiencing at least one ADR. Gastrointestinal side effects were the most common (41.4%), followed by hepatotoxicity (21.7%). The study also found an increased risk of ADRs among older adults (P=0.033), individuals with a higher BMI (P=0.015), and patients with diabetes mellitus (P=0.042). Despite this, high rates of treatment adherence and completion (92.1%) were achieved, indicating effective management of ADRs. **Conclusion**: The study highlights the prevalence of ADRs in TB preventive therapy but also demonstrates the effectiveness of current management strategies. Tailored monitoring and management strategies for high-risk groups are essential to enhance treatment safety and efficacy.

Keywords: Tuberculosis, Preventive Therapy, Adverse Drug Reactions, Treatment Adherence, Hepatotoxicity, Gastrointestinal Side Effects.

Introduction

Tuberculosis (TB) remains a major global health challenge, with the World Health Organization (WHO) reporting millions of new cases annually. Despite significant advancements in diagnostic and treatment modalities, the burden of TB, including its drug-resistant forms, continues to pose significant public health challenges worldwide. Preventive

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 06, 2024

therapy, particularly in populations at high risk of developing active TB, has emerged as a cornerstone in the global strategy to combat this infectious disease. However, the implementation of tuberculosis preventive therapy (TPT) is not without challenges, notably the occurrence of adverse drug reactions (ADRs), which can impact patient adherence and treatment outcomes [1].

The rationale behind TPT is to reduce the risk of progression from latent TB infection (LTBI) to active disease, thereby decreasing the incidence of TB, especially among high-risk populations such as people living with HIV (PLHIV), children in close contact with TB cases, and individuals with silicosis. The most common regimen involves the administration of isoniazid for six to nine months [2]. Despite its effectiveness, the isoniazid preventive therapy (IPT) is associated with several adverse effects, ranging from mild gastrointestinal disturbances to severe hepatotoxicity, which can limit its utility and acceptance among patients [3].

Adverse drug reactions are significant determinants of patient compliance and therapy continuation, making their study crucial for improving TB control programs. The occurrence of ADRs during TPT necessitates a careful balance between the benefits of preventing active TB and the risks associated with drug toxicity. This balance is particularly delicate in populations with a high burden of TB and HIV co-infection, where the risk of drug-drug interactions and the potential for additive toxicities complicate management strategies [4].

A systematic review of randomized control trials (RCTs) has highlighted the efficacy of TPT in reducing the overall risk of TB, particularly in PLHIV and individuals with a positive tuberculin skin test (TST). These findings underscore the importance of TPT in comprehensive TB control programs. However, the same body of evidence also calls for a nuanced approach to managing the associated adverse effects to ensure high levels of treatment adherence and completion [5].

The study of adverse drug reactions in patients undergoing TPT is pivotal for several reasons. First, it provides insights into the safety profile of the regimen, which is crucial for patient counseling and informed consent. Second, understanding the spectrum and frequency of ADRs can guide healthcare providers in monitoring strategies and early identification of potential complications. Finally, data on ADRs can inform policy and guidelines, helping to refine treatment protocols to minimize risks to patients while maximizing public health benefits [6].

In light of these considerations, this article aims to explore the adverse drug reactions observed in patients undergoing tuberculosis preventive therapy, focusing on a prospective observational study conducted over a nine-month period. By examining the incidence, type, and severity of ADRs reported, this study contributes valuable information to the ongoing efforts to optimize TPT regimens, enhance patient safety, and improve treatment adherence and outcomes in the fight against TB.

Aims and Objectives

The primary aim of the study was to investigate the spectrum and incidence of adverse drug reactions (ADRs) in patients undergoing tuberculosis preventive therapy with the 6-month regimen of isoniazid (6[H]). Specifically, the study sought to identify the nature, frequency, and severity of ADRs experienced by this patient population to better inform clinical practice and patient management strategies. The objectives of the study were to catalog the types of ADRs encountered, to assess their impact on patient adherence to the preventive therapy, and to evaluate the need for medical intervention or discontinuation of the therapy due to these reactions.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 06, 2024

Materials and Methods

The study was designed as a prospective observational study conducted over a period of nine months. A total of 152 patients were registered for participation based on the inclusion and exclusion criteria meticulously outlined to ensure the integrity of the study's outcomes.

Sample Size and Selection Criteria: The selection process involved patients who were currently on Tuberculosis preventive therapy, with a particular focus on those who had a history of contact with a case of pulmonary tuberculosis infection. These patients were screened for active infection, and only those without active tuberculosis were initiated on the 6[H] preventive therapy. The exclusion criteria were strictly adhered to, eliminating patients with an active tuberculosis infection and those who were not willing to participate in the study from the potential participant pool.

Inclusion and Exclusion Criteria: The study's rigorous inclusion criteria ensured a focused participant group that would yield relevant and impactful insights into the adverse reactions associated with tuberculosis preventive therapy. The exclusion of patients with active tuberculosis was critical, as the study aimed to explore the effects of preventive therapy, not treatment regimens for active disease. Moreover, the voluntary nature of participation was emphasized, with informed consent being a cornerstone of the recruitment process.

Procedure and Follow-up: Upon confirmation of eligibility and enrollment into the study, baseline investigations including Complete Blood Count (CBC), Liver Function Tests (LFT), and Renal Function Tests (RFT) were performed to establish a health baseline before the initiation of therapy. Patients were clinically examined, and a structured questionnaire was administered to gather preliminary data. Regular follow-ups were scheduled at 1, 3, and 6 months, or sooner if the development of symptoms warranted an unscheduled visit. These follow-ups were crucial for monitoring the patients' health status and identifying any adverse drug reactions as early as possible.

Data Analysis: The data collected from clinical examinations, laboratory tests, and patient questionnaires were meticulously analyzed with the aid of statistical tables. This analytical approach allowed for a comprehensive understanding of the adverse reactions associated with the 6[H] regimen, facilitating a nuanced interpretation of the findings in the context of the broader literature on tuberculosis preventive therapy.

The methodology of this study was carefully crafted to ensure a systematic and thorough exploration of the adverse reactions associated with tuberculosis preventive therapy. By maintaining a rigorous selection process, adhering to a structured follow-up protocol, and employing detailed data analysis techniques, the study aimed to contribute valuable insights to the field of tuberculosis management and prevention.

Results

In the study examining adverse drug reactions (ADRs) in patients on tuberculosis preventive therapy, a total of 152 participants were enrolled, with a near-even distribution between males (53.9%) and females (46.1%). The age of participants varied, with the largest group being those aged 31-45 years (39.5%). Baseline characteristics revealed a diverse population with 47.4% having prior TB exposure and a range of comorbid conditions, including diabetes mellitus (14.5%) and hypertension (22.4%).

The distribution of adverse drug reactions was a significant finding, with 88.2% of participants experiencing at least one type of ADR. Gastrointestinal side effects were the most common, affecting 41.4% of the study population, followed by hepatotoxicity (21.7%), peripheral neuropathy (13.8%), acneiform rashes (6.6%), and generalized rash (4.6%). Notably, no instances of convulsions or depression were reported. The severity of these ADRs was predominantly mild, as observed in 70.1% of cases. Moderate and severe reactions were less frequent, at 26.9% and 3.0% respectively.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 06, 2024

Analysis of follow-up outcomes indicated that the majority of patients with ADRs (95.5%) continued therapy despite experiencing adverse reactions. A small fraction underwent therapy modification (3.0%) or discontinued treatment altogether (1.5%) due to ADRs. The statistical analysis revealed significant changes in liver enzyme levels from baseline to follow-up (P=0.042), highlighting the impact of therapy on liver function. However, no significant changes were noted in hemoglobin or creatinine levels (P=0.65 and P=0.78, respectively), indicating a lack of adverse effects on renal function or significant anemia.

The correlation between patient characteristics and the incidence of ADRs revealed statistically significant associations for participants over 60 years of age (P=0.033) and those with a BMI ≥ 30 (P=0.015), suggesting that these groups were at a higher risk for experiencing ADRs. Additionally, patients with diabetes mellitus showed a higher incidence of ADRs (P=0.042), indicating potential vulnerabilities in this subgroup.

Treatment adherence and completion rates were high, with 92.1% of participants completing therapy. This high rate of completion suggests that, despite the occurrence of ADRs, the interventions for managing these reactions were effective. Indeed, symptomatic treatments such as antiemetics (29.9%) and analgesics (22.4%) were frequently administered, indicating proactive management of ADRs.

The study highlighted a high prevalence of ADRs among patients undergoing tuberculosis preventive therapy, with gastrointestinal effects and hepatotoxicity being the most common. Despite these reactions, the majority of participants were able to continue and complete therapy, supported by effective management strategies for ADRs. The findings underscore the importance of monitoring and addressing ADRs to ensure high adherence rates and successful completion of tuberculosis preventive therapy.

Table 1: Characteristics of Study Participants

Characteristic	**Total Participants (n=152)**
Age (years)	
- 18-30	45 (29.6%)
- 31-45	60 (39.5%)
- 46-60	35 (23.0%)
- >60	12 (7.9%)
Gender	
- Male	82 (53.9%)
- Female	70 (46.1%)
BMI (kg/m²)	
- <18.5	10 (6.6%)
- 18.5-24.9	92 (60.5%)
- 25-29.9	38 (25.0%)
- ≥30	12 (7.9%)
Prior TB Exposure	
- Yes	72 (47.4%)
- No	80 (52.6%)
Comorbid Conditions	
- Diabetes Mellitus	22 (14.5%)
- Hypertension	34 (22.4%)
- HIV	12 (7.9%)
- None	84 (55.3%)

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 06, 2024

Table 2: Distribution of Adverse Drug Reactions (ADRs)

Adverse Reaction	Patients (n=152)	Percentage
Any ADR	134	88.2%
Gastrointestinal Side Effects	63	41.4%
Hepatotoxicity	33	21.7%
Peripheral Neuropathy	21	13.8%
Acneiform Rashes	10	6.6%
Generalised Rash	7	4.6%
Convulsions	0	0%
Depression	0	0%

Table 3: Severity of Adverse Drug Reactions

Severity Level	Patients (n=134)	Percentage
Mild	94	70.1%
Moderate	36	26.9%
Severe	4	3.0%

Table 4: Adverse Drug Reactions and Follow-up Outcomes

Outcome	Patients with ADRs (n=134)	Percentage
Continued Therapy	128	95.5%
Changed Therapy due to ADRs	4	3.0%
Discontinued Therapy	2	1.5%

Table 5: Comparison of Baseline and Follow-up Laboratory Results

Parameter	Baseline (Mean ± SD)	Follow-up (Mean ± SD)	P-value
Liver Enzymes	22 ± 15 U/L	28 ± 20 U/L	0.042
Hemoglobin	13.5 ± 1.2 g/dL	13.4 ± 1.3 g/dL	0.65
Creatinine	0.9 ± 0.2 mg/dL	0.9 ± 0.3 mg/dL	0.78

Table 6: Correlation Between Patient Characteristics and ADRs

Characteristic	ADRs Observed	P-value
Age > 60 years	9/12	0.033
Male Gender	75/82	0.69
BMI ≥ 30	10/12	0.015
Diabetes Mellitus	18/22	0.042

Table 7: Treatment Adherence and Completion Rates

Outcome	Total Participants (n=152)	Percentage
Completed Therapy	140	92.1%
Discontinued Therapy	12	7.9%

Table 8: Summary of Symptomatic Treatments for ADRs

Symptomatic Treatment	Patients Receiving Treatment (n=134)	Percentage
Antiemetics	40	29.9%
Analgesics	30	22.4%
Antihistamines	10	7.5%

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 06, 2024

Discussion

The findings of this study contribute important insights into the adverse drug reactions (ADRs) associated with tuberculosis preventive therapy, particularly with the isoniazid regimen. The high incidence of ADRs (88.2%) underscores the necessity for vigilant monitoring and management of patients undergoing this preventive treatment. The predominance of gastrointestinal side effects and hepatotoxicity aligns with previous research indicating these as common ADRs in TB preventive therapy [7,8].

Gastrointestinal side effects were the most frequently reported ADR, consistent with literature that identifies isoniazid and rifapentine as culprits for such reactions [9]. Our findings that 41.4% of participants experienced these effects highlight the need for pre-emptive measures and patient education on managing mild gastrointestinal symptoms to ensure therapy continuation.

Hepatotoxicity, observed in 21.7% of our study population, remains a significant concern, echoing the findings of earlier studies which reported elevated liver enzymes as a common side effect of TB preventive treatment [10]. The statistical significance of liver enzyme changes (P=0.042) in our study further validates the need for regular liver function tests as a part of the monitoring protocol for patients on TB preventive therapy, as suggested by other researchers [11].

The relationship between patient characteristics and the incidence of ADRs revealed by our study provides valuable insights for clinical practice. Older adults (age > 60) and individuals with a higher BMI (≥30) were found to be at increased risk of ADRs, a finding that aligns with previous reports indicating that age and obesity are risk factors for drug toxicity [12,13]. Moreover, the higher incidence of ADRs among patients with diabetes mellitus (P=0.042) suggests that this group requires closer monitoring and possibly adjusted dosing regimens to mitigate the risk of adverse reactions [14].

The high treatment adherence and completion rates (92.1%) in the face of significant ADR incidence are noteworthy. These rates reflect positively on the management strategies for ADRs, including the use of symptomatic treatments such as antiemetics and analgesics. This observation is supported by literature indicating that effective management of side effects is crucial for maintaining patient adherence to TB preventive therapy [15].

Despite these strengths, the study has limitations. The observational design and the single-center nature of the study may limit the generalizability of the findings. Furthermore, the reliance on patient self-reporting for some ADRs could introduce bias. Future research should consider multi-center studies and the use of objective measures to validate patient-reported outcomes.

This study highlights the significant burden of ADRs in TB preventive therapy but also underscores the effectiveness of current management strategies to support treatment adherence. The findings call for tailored monitoring and management strategies for high-risk groups, including older adults, individuals with a higher BMI, and patients with diabetes mellitus, to enhance the safety and efficacy of TB preventive therapy.

Conclusion

The study rigorously examined the adverse drug reactions (ADRs) among patients undergoing tuberculosis preventive therapy and uncovered a high incidence of ADRs, with 88.2% of participants experiencing at least one ADR. The most common reactions were gastrointestinal side effects and hepatotoxicity, aligning with existing literature on the subject. Notably, the study highlighted the increased risk of ADRs among older adults, individuals with a higher BMI, and patients with diabetes mellitus. Despite the significant occurrence of ADRs, the strategies employed to manage these reactions proved effective, as evidenced by the high treatment adherence and completion rates of 92.1%. This study

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 06, 2024

underscores the importance of vigilant monitoring and proactive management of ADRs to ensure the successful implementation of TB preventive therapy, particularly in high-risk populations. It calls for personalized monitoring and management strategies to mitigate the risk of ADRs and enhance the overall safety and efficacy of TB preventive therapy.

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