High compliance of six-month INH preventive therapy in HIV patients: A stepping stone for the future

Gyanshankar Mishra
Associate Professor, Dept. of Respiratory Medicine, Indira Gandhi Government Medical College, Nagpur, Maharashtra, India

Abstract
Introduction: Tuberculosis (TB) continues to be the leading cause of morbidity and mortality among human immunodeficiency virus (HIV) infected individuals. Isoniazid preventive therapy (IPT) is one of the widely recommended interventions aimed to reduce the burden of TB (Tuberculosis) in people living with HIV.

Methodology: A Retrospective analysis from clinical records, of all diagnosed HIV patients registered at ART (Anti-Retroviral Therapy) center of a tertiary care health institute & initiated on six-month IPT (INH Preventive Therapy) during the period of November 2017 to December 2018 was conducted.

Results: A total of 575 HIV patients (554 (96%) adults and 21(4%) pediatric patients) were initiated on six-month IPT. These included 298 (52%) males and 277 (48%) female patients. 435 (76%) patients completed full six months of therapy. 15(2%) stopped treatment prior to completion of six months. 120(21%) patients were on regular therapy at the time of study. 5 patients were taking the IPT irreguarly at the time of study. Among the 15 HIV patients who stopped IPT prior to completion of therapy duration, reasons for stopping IPT were adverse drug reactions (ADRs) in 8 (53%) patients, refusal in 4 (27%) patients and increased pill burden in 3 (20%) patients. The compliance rate of IPT in HIV patients was 97%.

Discussion: IPT Compliance is a potentially important factor in the disease course of HIV and hence an important determinant of survival rates in these patients. Appropriate monitoring and counselling may further increase the compliance rate of IPT among HIV patients.

Conclusion: HIV patients initiated on IPT have a good compliance rate for completion of regular six-month IPT.

Introduction
Worldwide, TB is one of the top 10 causes of death and the leading cause from a single infectious agent (above HIV/AIDS). Tuberculosis (TB) continues to be the leading cause of morbidity and mortality among human immunodeficiency virus (HIV) infected individuals. In 2017, TB caused an estimated 3 million deaths from TB among HIV-positive people [1]. Isoniazid preventive therapy (IPT) is one of the widely recommended interventions aimed to reduce the burden of TB (Tuberculosis) in people living with HIV [2]. IPT entails the administration of Isoniazid (INH) to individuals with latent TB infection so as to prevent progression to active TB disease [3]. Treatment compliance is the extent to which a patient’s behavior matches the prescriber’s advice and it is a major determinant of a therapy’s success [4]. With this background, we aimed to study the compliance of IPT among HIV patients.

Materials and Methods
A retrospective analysis from clinical records, of all diagnosed HIV patients registered at ART (Anti-Retroviral Therapy) center of a tertiary care health institute during the period of November 2017 to December 2018 was conducted. INH preventive therapy (IPT)
All HIV patients registered at ART center of tertiary care health institute during the study period were first screened for active tuberculosis. After active tuberculosis disease was ruled out, the patients were initiated on IPT. INH was administered in a dose of 300 mg for all adult patients and 10 mg/kg for pediatric patients (children more than 12 months of age) for a standard duration of 6 months as per the RNTCP guidelines. Supplemental pyridoxin (50 mg/day for adults and 25 mg/day for children) was co administered along with INH throughout the study period. The medications had to be collected every month by the patient from the ART center for six months. All HIV patients initiated on six months IPT during the study period were included in the study.

Compliance
All HIV patients who were initiated on IPT and either completed full six months of IPT or were on regular IPT at the time of the study were considered as compliant patients. All HIV patients who were initiated on IPT and either stopped IPT prior to completion of full six months of IPT or

*Corresponding Author: Gyanshankar Mishra, Associate Professor, Dept. of Respiratory Medicine, A Indira Gandhi Government Medical College, Nagpur, Maharashtra, India
Email: gpmishra81@gmail.com
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were taking IPT irregularly at the time of the study were considered as non-compliant patients.
Patient compliance was measured as follows:

\[
\text{Compliance rate of IPT among HIV patients} = \frac{\text{Total number of compliant patients}}{\text{Total number of patients initiated on IPT}} \times 100
\]

**Results**

A total of 575 HIV patients were initiated on six months IPT. Six months IPT Compliance among all HIV Patients initiated on IPT is shown in Fig. 1. Overall there were 555 compliant patients and thus the compliance rate of IPT among HIV patients was found to be 97%.

Fig. 2 shows reasons for stopping IPT among 15 HIV patients who stopped IPT prior to completion of therapy duration. Among them Adverse Drug Reactions (ADR) was the leading cause of stopping IPT. The various ADRs leading to stopping of IPT in HIV patients are detailed in table 1.

![Fig. 1: Reasons for stopping IPT before completing therapy duration in PLHIV](image1.png)

![Fig. 2: Six months IPT compliance among all HIV patients initiated on IPT](image2.png)

**Table 1: ADRs as a cause of stopping IPT in HIV patients**

<table>
<thead>
<tr>
<th>ADR</th>
<th>Number of HIV Patients who stopped IPT due to ADR (%)</th>
</tr>
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<tbody>
<tr>
<td>Peripheral Neuropathy</td>
<td>3 (37.5%)</td>
</tr>
<tr>
<td>Skin Rash</td>
<td>3 (37.5%)</td>
</tr>
<tr>
<td>Giddiness</td>
<td>2 (25%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>8 (100%)</strong></td>
</tr>
</tbody>
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**Discussion**

To the best of our knowledge, the current study is the first study in Indian population to study the compliance of IPT among people living with HIV (PLHIV) under programmatic condition and analyze the possible reasons for non-compliance in them. The current study showed the compliance rate of IPT to be 97% among PLHIV initiated on IPT. Ayele et al., in their meta-analysis found about 15 to 42% percent non-compliance to IPT, a finding much higher than the current study where the non-compliance rate was merely 3%. However unlike the studies included in meta-analysis, the current study mentioned the reasons for non-compliance [5]. The study demonstrates that under programmatic conditions high compliance rate can be achieved for IPT.

In a study by Khongphathanayothin et al., out of the 799 HIV patients in whom IPT therapy was initiated, 633(79.2%) patients completed six-months of IPT and 551(69%) patients completed nine months IPT [6]. Thus maintaining high compliance rate with increased duration of IPT is challenging. The current study helps address this concern by identifying factors which potentially contribute to non-compliance. ADRs, initial refusal and increased pill burden were the reasons for non-compliance to IPT among HIV patients in our study. These factors need to be addressed. Considering the ongoing anti retroviral therapy, pill burden is an important parameter that will only increase with any additional therapy offered to these patients. Pill burden, existing ADRs to ongoing therapy along with pre conceived notions about any additional therapy being offered to these patients may be the factors that contribute to refusals for IPT among these patients. A good initial targeted counseling along with psychological support throughout the treatment duration may help further improve the compliance rates of IPT. Morisky scale is one such simple questionnaire-based screening tool that may be used in future interventions targeted towards these patients [7]. Identification of potential non-compliant patients at the initiation of therapy help the healthcare workers provide a targeted approach to these patients who are potentially at a risk of non-compliance to the newly offered therapy.

The good compliance rate of IPT among PLHIV in the current study may be a stepping-stone for future IPT regime with an increased duration of therapy, where patient compliance is currently being viewed as a potential detrimental factor towards regular completion of the long duration IPT regime. The study paves the way forward for potential implementation of 36 months IPT regime in PLHIV as is currently recommended by the WHO [8].

**Conclusion**

HIV patients initiated on IPT have a good compliance rate for completion of regular six-month IPT. However, if the current recommendation of increased duration of IPT is to be implemented, the factors leading to non-compliance of IPT needs to be addressed as they may be potentially magnified with increased duration IPT regimes. High compliance of
current six-month IPT may thus be considered a stepping stone for future IPT regimes.

**Conflict of interest**
None.

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**References**

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