A CROSS SECTIONAL STUDY OF NEUROPATHY IN PATIENTS ON ART WITH COMPARISON TO PATIENTS ON BOTH ART WITH ATT

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ABSTRACT

BACKGROUND

It is estimated that there are 35.5 million PLHA worldwide and 1.6 million have received ART. ART is freely available in designated ART centers. The main challenge in prescribing HAART along with ATT is ADRs associated with it affecting patient compliance and treatment outcomes.

MATERIALS AND METHODS

This is a cross sectional study of 100 patients who were on TLE therapy for one year. Of these 100 patients, half were on ART alone (Group-A); half were on ART and ATT both (Group-B). Complete work up as per NACO guideline and nerve conduction study of all patients was performed. Results were analysed in the light of clinical, laboratory test and NCV studies.

RESULTS

Data for neuropathy and other ADRs was collected from 100 patients over a period of one year. It shows gastrointestinal disturbance as the most common adverse event followed by neuropathy. Overall incidence of neuropathy in both groups was 59%. Asymptomatic neuropathy was present in 58% of patients. Commonest symptoms of neuropathy were pain in calf muscle, ankle and sole (83%). Most common sign was reduced distal superficial sensation (88%). Knee jerk was diminished in 84.44% of patients. Commonest type of neuropathy on Nerve Conduction Study was distal axonal neuropathy (94.44%) with NCS showing reduced amplitude of sensory nerve action potential and reduced compound motor action potential. Statistically significant incidence of neuropathy was found among the Group B patients having low CD4 count and advanced HIV infection. Incidence of neuropathy in patients with >11 months exposure to TLE was 69.49% as compared to 30.51% in <11 months group.

CONCLUSION

There is significant additive effect of ATT in development of neuropathy in patients on TLE with advanced HIV infection. It is an independent risk factor for development of neuropathy. The real burden of ADRs due to ART and ATT (anti tubercular treatment) cannot be estimated until voluntary and mandatory reporting system of ADRs work efficiently. A structured surveillance of the pharmacovigilance system can help to overcome these hurdles to ensure compliance with ART regimens.

KEYWORDS

ART, ATT, NACO, Peripheral Neuropathy, Nerve Conduction Study.

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BACKGROUND

Human immunodeficiency virus infection and acquired immune deficiency syndrome is a spectrum of conditions caused by infection with the human immunodeficiency virus (HIV).[1]

ART (antiretroviral therapy) for the treatment of people living with HIV and AIDS (PLHA) under NACO is freely available in designated ART centres and has contributed in prolonged survival. ART works by suppressing the viral load and restoring the immune system. The introduction and availability of highly active anti-retroviral therapy (HAART) involves using translated to significant reduction of AIDS related morbidity and mortality.

HAART involves using at least three different drugs from two different classes. Nevertheless challenges persist as HAART is fraught with high risk of adverse drug reactions (ADRs) and consistent use is required to prevent viral drug resistance and meet treatment goals. High percentage of ADRs deter the patients from taking regular medication and drug withdrawal or discontinuation results in treatment failures.[2]

Lack of adherence to treatment can have grave consequences with implications both for the individual patients and community.[3]

At the patient level non adherence to ART can lead to adverse HIV related outcomes in terms of viral load, CD4 cell

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count, increased opportunistic infections, and progression to AIDS and survival.[4,5]

For the community non-adherence to ART may increase viral resistance to antiretroviral drugs and transmission of drug-resistance to antiretroviral drugs and transmission of drug resistant strains to HIV.[6]

Knowledge of antiretroviral toxicities is a prerequisite for choosing an appropriate regimen among many possible combinations in HAART.

We have high tuberculosis rate in India and the risk increases further in HIV positive patients. It has been suggested that tuberculosis and gastrointestinal diseases might increase in sero positive individual and vice-versa.[7]

Tuberculosis often appears before other opportunistic infections occur in person infected with HIV infection.[8]

Anti-Koch Treatment (ATT) is known to cause neuropathy, the chance of neuropathy increases further in combination with ART. ATT induced peripheral neuropathy was known to be there in pre HIV era. Most common culprit is isoniazid. This study will help to identify the incidence and clinical pattern of type and severity of neuropathy in tertiary care centre.

Aim of The Study

To study of incidence and clinical pattern of types and severity of neuropathy in patients taking antiretroviral therapy- TLE (Tenofovir+ Lamivudine+ Efavirenz) along with ATT (Anti-Tuberculosis Treatment).

MATERIALS AND METHODS

Study Site

Government Bundelkhand Medical College, Sagar (Madhya Pradesh).

Study Duration

July 2017 to July 2018.

Sample Size

100 cases.

Study Design

Cross sectional study.

Inclusion Criteria

1. 20 to 40 year patients.
2. HIV with Tuberculosis patients.

Exclusion Criteria

1. Pregnant women.
2. HIV with diabetic patients.
3. Geriatric patients.
4. Chronic alcoholic.

Source of Data Collection

Required data is acquired from the patient treatment record (white card) and by questioning the patients about the therapy.

This is a cross sectional study of 100 patients who were on TLE for more than one year. Of these 100 patients 50 were on ART alone (Group-A), and 50 were on ART NACO guideline. Nerve conduction study of all these patients was performed. Results were analysed in the light of clinical features, examinations, laboratory tests and nerve conduction study.

RESULTS

Pharmacovigilance is defined as the science and activities relating to the detection, assessment, understanding, reporting and prevention of adverse effects or any other drug-related problem.[9]

The association between HIV and Tuberculosis is bidirectional. HIV infection increases the risk of both primary and reactivation tuberculosis and this risk increase tremendously with advanced HIV disease.[10]

ADRs in developing countries differ from those of developed world because of high prevalence of conditions such as malnutrition, anaemia, tuberculosis, and patients presenting with advanced HIV disease.[11]

Present study showed that prevalence of neuropathy is much higher in patients above the age of 40 years. High prevalence of neuropathy was also observed in taller patients with height of >160 cms. No significant difference was observed in prevalence of neuropathy in males as compared to females. Most common adverse event was gastrointestinal disturbance followed by neuropathy (table 1).

GI Side Effects	64
Rash	24
Peripheral Neuropathy	59
Raised Liver Enzymes	6
Lactic Acidosis	1

Table 1. Incidence of Adverse Effects

The overall prevalence of neuropathy in this study in both groups was 59%, suggesting peripheral neuropathy is a frequent side effect of TLE based therapy. Clinical profile of neuropathy in this study shows significant no. of patients with asymptomatic neuropathy (58%) that shows the burden of this adverse effect is quite higher than observed in day to day ART clinics.

The commonest symptom of neuropathy in our study was pain is calf muscles, ankle or sole (83%). This finding suggests that the major complaint that brings attention of patients of neuropathy is pain.

The most common sign encountered on neurological examination was reduced distal superficial sensations, found in 88% of patients. No. of patients with reduced knee jerk on neurological examination was also high (84.44%). This finding is helpful to decide the clinical screening test in early identification.

We observed statistically significant increase in prevalence of neuropathy was found among the group taking both ATT and ART (group B) as compared to group taking ART alone (group A), showing additive effect of

isoniazid in development of neuropathy with antiretroviral TLE therapy. (Table 2).

Study Group	No.
Group A (n=50)	20
Group B (n=50)	39
Total (n=100)	59
Chi Square Value 14.92.' p' =0.0001	
Table 2. Patients with Neuropathy in Both Groups	

In this study, out of total 59 patients who were diagnosed to have neuropathy, 54 patients were found to have positive NCS results. Commonest type of neuropathy on nerve conduction study was Distal Sensory Axonal Neuropathy (94.44%) (Table 3) with NCS showing reduced amplitude of Sensory nerve action potential (SNAP) and reduced compound motor action potential (CMAP).

Type	No.	%
Distal Sensory Axonal Neuropathy	51	94.44%
Multifocal-Sensory, Motor-Axonal Loss	2	3.70%
Demyelinating Type Polyradiculopathy	1	1.85%
Table 3. Result of Nerve Conduction Test (n=54)		

It has been observed that prevalence of neuropathy with CD4 count<150 was 38 patients out of 49 patients and with CD4 count >150 was 21 patients out of 51 patients.

CD4 Count	Total No. of Patients	Patients with Neuropathy
<150	49	38
>150	51	21
Total	100	59
Chi Square Value: 13.669; p Value: 0.0002		
Table 4. Neuropathy in Relation to CD4 Count		

Prevalence of neuropathy in patient with >11 months exposure to TLE Therapy was 69.49% compared to 30.51% in <11 months group signifying the effect of duration of TLE Therapy on development of peripheral neuropathy (table 5).

Duration of Treatment	Total Patients	Patients with Neuropathy
>11 Months	55	41
<11 Months	45	18
Total	100	59
Chi Square Value: 12.21; p Value: 0.0005		
Table 5. Neuropathy in Relation to Duration of Treatment		

DISCUSSION

Since the efficacy and safety for any drug regimen is the major concern in chronic disease like HIV and Tuberculosis, we attempted to ensure the same in the present study. In present study out of total 100 patients 59 were diagnosed to have neuropathy. Distal symmetrical polyneuropathy related to HIV is one of the most common neurological complications of HIV. Two potentially neurotoxic mechanisms have been proposed to play a crucial role in the pathogenesis of neuropathy: neurotoxicity resulting from the virus and its products; as well as neurotoxic effects of medications used in the treatment of HIV.[12,13]

In present study prevalence of neuropathy with low CD 4 count was high (38 out of 49 patients). There are several studies suggesting that a lower CD4 nadir represents a risk factor for HIV neuropathy.[14,15]

In present study prevalence of neuropathy is high among the group taking ATT and ART (Group- B). HIV infection itself results in an increased rate of serious adverse events in patients on TB treatment and ART may further increase this.[16] A retrospective cohart study in south Africa patients on rifampicin based TB treatment found increased serious adverse effects, primarily peripheral neuropathy and increased vomiting, in HIV infected compared with uninfected patients.[17] The same result was found in study of HIV associated sensory neuropathy probably because of combined toxicity of both drugs.[18]

CONCLUSION

TLE induced neuropathy is becoming an important complication of HAART therapy. Early identification and management of this complication is critical. The significant additive effect of isoniazid in development of neuropathy in patients on TLE Therapy with an advanced HIV infection is an independent risk factor for development of neuropathy. The risk of developing peripheral neuropathy can be minimized by timely initiation of ATT and ART therapy. Further research is needed to develop additional option for neuropathy prevention and treatment. It can be managed in an individualized manner using a wide range of agents for pain control. Researchers are also working on future therapies that may enable nerve regeneration and reversal of existing damage.

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