Journal of Biomedical and Pharmaceutical Research
Available Online at www.jbpr.in
CODEN: - JBPRAU (Source: - American Chemical Society)
Index Copernicus Value 2018: 88.52
NLM (National Library of Medicine): ID: (101671502)
Research Article
Volume 7, Issue 6: November-December: 2018, 61-67
ISSN (Online): 2279-0594
ISSN (Print): 2589-8752

STUDY OF THE CLINICAL CHARACTERISTICS OF SECOND-LINE ART PATIENTS AT A TERTIARY INSTITUTION

Dr. Pawan Kakraniya

Assistant Professor Dept. of Gen. Medicine Jawaharlal Nehru Medical College Wardha

Article Info: Received 09 October 2018; Accepted 25 December. 2018
Address for Correspondence: Dr. Pawan Kakraniya Assistant Professor Dept. of Gen. Medicine Jawaharlal Nehru Medical College Wardha
Conflict of interest statement: No conflict of interest

ABSTRACT:
Background: There have been cases of HIV infection and AIDS recorded from almost every nation in the world. Since the discovery of the first case of AIDS, more than 25 million people have died as a result of the pandemic, and 2.5 million children are among the nearly 33.2 million (range 30.6-36.1 million) people living with HIV.
Aims & objectives: The current study aimed to examine the clinical profile and relationship between immunosuppression and patient mortality who were receiving second-line ART.
Material and Methods: The current investigation was an observational, prospective study carried out at the Department of Medicine. The study lasted two years (from Oct 2018 to Oct 2020). Institutional ethical committee's prior approval was obtained for the study and protocol.
Results: A one-year study including 100 patients who began on second line was conducted. Our study's most prevalent age range, which made up 52% of the cohort, was 31 to 40. 76 (76%) of the 100 patients under study were men, and 24 (24%) were women. Hemoglobin% significantly improved from the initial value of 11.98 to the subsequent value of 12. (13.27). The clinical T Staging of patients in our study showed that the number of patients in T1 increased from baseline levels of 62% (62 patients) to 78% (78 patients), while the number of patients in T4 decreased from baseline levels of 16% (16 patients) to 8%.
Conclusion: Following the start of second-line ART, there has been a significant improvement in CD4 count, clinical T staging of patients, and viral load.

Keywords: ART, HIV infection, AIDS pandemic.

INTRODUCTION

There have been cases of HIV infection and AIDS recorded from almost every nation in the world. Since the discovery of the first case of AIDS, more than 25 million people have died as a result of the pandemic, and 2.5 million children are among the almost 33.2 million (range 30.6-36.1 million) individuals living with HIV[1-3]. Assessing the true scope of the HIV epidemic is still challenging. The cornerstone of treating patients with HIV infection is combination antiretroviral therapy (ART), also known as highly active antiretroviral therapy (HAART). The incidence of the majority of AIDS-defining diseases has significantly decreased since the introduction of HAART into mainstream use. The standard of care is now the administration of HAART, which typically consists of a combination of three to four antiretroviral medications. Second-line ART is a blessing for HIV/AIDS patients. In India, there hasn't been much study on second line ART's side effects[4]. The current study aims to examine the clinical profile and relationship between

immunosuppression and patient death who were receiving second-line ART[5].

Aims & objectives: The current study aimed to examine the clinical profile and relationship between immunosuppression and patient mortality who were receiving second-line ART.

MATERIAL AND METHODS

The current investigation was an observational, prospective study carried out at the Department of Medicine. The study lasted two years (from Oct 2018 to Oct 2020). Institutional ethical committee's prior approval was acquired for the study and protocol.

inclusion standards: Patients are moved to second line ART if first line ART fails as defined by NACO and WHO recommendations. Patients who are not registered at an ART center and patients who refuse to consent to the study are excluded.

Patients were enrolled in the study after being informed of the need for investigations and treatment, as well as the side effects of medications and the importance of adhering to prescribed regimens. Before beginning the actual study, the patient and the responsible attendant provided written consent. A comprehensive physical examination was performed, and a detailed history including prior ART regimens the patient was on, length, reason for changing ART, serial CD4 counts, opportunistic infections, diabetes, and hypertension in the past were collected. All patients underwent tests like complete blood counts, RBS, LFTs, RFTs, fasting lipid profiles, CD4 counts, viral load estimations, and chest x-rays. For pertinent patients, USG abdominal, serum lactate levels, biopsy, FNAC of lymph node, CT brain, and LP- CSF were performed as needed. In order to monitor side effects such as acute gastritis, loose stools, rash, dyslipidemia, diabetes mellitus, hyperbilirubinemia, lactic acidosis, and Fanconi syndrome, patients were monitored for a year. They were also monitored to see if their clinical WHO T staging, CD4 count, and viral load response to second line ART changed or improved. In the current study, descriptive and inferential statistical analysis was completed. Results for categorical data are reported in Number (%) whereas results for continuous measurements are presented as Mean SD (Min-Max). repeated actions The significance of study parameters between three or more patient groups has been determined using analysis of variance (RMANOVA), and a p value of less than 0.05 was regarded as statistically significant.

RESULTS

A one-year study involving 100 patients who began on second line was conducted. Our study's most prevalent age range, which made up 52% of the cohort, was 31 to 40. 76 (76%) of the 100 patients under study were men, and 24 (24%) were women.

Table 1: Age distribution of patients studied

Age in years	Number of patients	%
<30	10	10.0
31-40	52	52.0
41-50	26	26.0
51-60	12	12.0
Gender		
Male	76	76.0
Female	24	24.0

Stage 3 was the most prevalent WHO stage at the time of the initial diagnosis, accounting for 52%, and stage 2 made up 22%.

Table 2: Distribution of WHO stage at diagnosis of HIV positive

WHO stage at diagnosis	Number of patients	%
Stage I	8	8.0
Stage II	22	22.0
Stage III	52	52.0
Stage IV	18	18.0

When they were started on second line ART, all 76 of the patients out of 100 had a documented decline in CD4 count, satisfied immunological requirements, and had previously experienced recurrent opportunistic infections while on first line ART. Weight loss, loose stools, fever, and cough with expectoration were all reported by 24 patients, suggesting opportunistic infections.

Table 3: Chief complaints

Chief complaints	Number of patients (n=100)	%
None	76	76.0
H/O loose tools	10	10.0
Multiple painful mouth ulcers	4	4.0
Weight loss	4	4.0
Breathlessness ,cough with sputum	2	2.0
Difficulty in walking	2	2.0
Fever, cough with expectoration	2	2.0

A total of 38 patients had previously received ATT for pulmonary or extrapulmonary tuberculosis, and 4 patients had diabetes, 6 had hypertension. Four patients had Herpes Zoster in the past, six patients had peripheral neuropathy, and two patients had a history of MI.

Table 4: Co morbidities and opportunistic infections in past

Comorbidities/ opportunistic infections	Number of patients (n=100)	%
TB	38	38.0
Hypertension	6	6.0
Peripheral neuropathy	6	6.0
Herpes zoster	4	4.0
DM	4	4.0
IHD	2	2.0

Hemoglobin% significantly improved in our study from baseline (11.98) to 12 months (13.27). ESR decreased, but it was not significantly so. In our investigation, 88 patients with hyperbilirubinemia were seen, 56 with grade 1, 20 with grade 2, and 14 with grade 3. Not one patient experienced grade 4. Each patient had no symptoms. Indirect bilirubin rise was greater (mean of 2.56 mg/dl) than direct bilirubin elevation (mean of 3.27 mg/dl). The changes to SGOT, SGPT, and ALP were minimal. At 6 months and 12 months in our study, there was a mean increase in total cholesterol, LDL, and VLDL. However, there was an increase in triglycerides at 6 months, which decreased at 12 months. At 6 months and 12 months, the HDL level had significantly decreased. In our study, 2 patients who had stopped taking tenofovir for acute renal failure at the end of 3 months also experienced Fanconi's syndrome-like symptoms. In our study, the mean blood sugar increased after 12 months, although this rise was not statistically significant. In our study, the mean CD4 count increased gradually over time from baseline, going from 115 to 324 at 6 months and 451 at 12 months. At baseline, the lowest CD4 count was 22. At 12 months, the highest CD4 count was 786. The CD4 count decreased in 2 patients at 6 months and only slightly increased at 12 months.

Table 5: Outcome and side effects noted in patients

Outcome	Number of patients (n=100)	%
Alive on ART	88	88
Deaths	12	12
Complications/ side effects		
IRIS	12	12
Patients on ART but not improved	4	4
Patients with lactic acidosis	2	2
Fanconi syndrome	2	2
Vomiting Grade 4	2	2
Hyperbilirubenia	88	88
Dyslipidemia	88	88
Diarrhea/ vomiting grade 1	96	96

The clinical T Staging of patients in our study showed that the number of patients in T1 increased from baseline levels of 62% (62 patients) to 78% (78 patients), while the number of patients in T4 decreased from baseline levels of 16% (16 patients) to 8%.

Table 6: Comparison of T staging from baseline to 12 months

T STAGING	BASELINE	3 MONTHS	6 MONTHS	12 MONTHS
T1	62	80	80	78
T2	8	2	0	0
T3	14	6	0	2
T4	16	6	14	8

DISCUSSION

Viral load and resistance testing have increased our understanding of viral dynamics, and it is now clear that combination therapy using the most effective and potent agents will reduce viral replication to the lowest level possible while lowering the likelihood of the emergence of resistance[6-8]. In our study, the mean CD4 count increased gradually over time from baseline, going from 115 to 324 at 6 months and 451 at 12 months. At baseline, the lowest CD4 count was 22. At 12 months, the highest CD4 count was 786. The CD4 count decreased in 2 individuals at 6 months and only slightly increased at 12 months (both of them had a CD4 Count always below 100). At six months, plasma viremia had dramatically decreased, and 40% of patients had no detectable target. According to a research by Pujades-Rodrguez et al., the CD4 count increased from a median of 99 at baseline to 90 at 6 months and 135 at 12 months in 370 patients who were converted to second line ART. They came to the conclusion that people who had a WHO stage 4 diagnosis at the start of ART and a low CD4 count (50 cells/microlitre) had a greater death rate. On second-line therapy, there was a higher mortality rate in relation to severe immunosuppression. Similar results were seen in the current investigation. In our trial, 12 patients passed away—six at the end of the first three months and six at the end of the sixth month of follow-up[9,10]. Patients who passed away had a baseline CD4 count of 66.67% (8 patients) or less, 16.67% (2 patients) between 100 and 200 cells/microlitre, and 16.67% (2 patients) between 200 and 250 cells/microlitre. Our investigation came to the conclusion that patients with low CD4 counts (less than 100 cells) at baseline had a significant mortality rate. At the time of their deaths, 50% (6 patients) of the patients were in the T4 stage. 33% (4 patients) and 16.67% (2 patients) of the patients were staged as T1. Patients having a WHO T4 stage at baseline had a significant death rate. Eight out of 69 patients who started on second line ART died in a study by Bankim Mankad et al[11]. According to a study on fatalities, a late

switch to 2nd Line ART at CD4 100 cells/mm3 may not achieve the anticipated therapeutic outcomes. In our study, 4% of the patients (2 patients) did not improve after receiving second-line ART; both patients were in the same T-Staging (T3 and T4) at baseline and at follow-up. At baseline, both of these patients had WHO - T3, T4 and a low CD4 count of 100 cells/microlitre. In our study, 12% (6 patients) of those receiving second-line ART experienced the development of second-line IRIS in the form of new opportunistic infections (OIs), of which 83.33% (5 patients) had TBM and 16.67% (1 patient) had bacterial meningitis[12]. At six months, all of them had higher CD4 counts than at baseline, and their viral loads were all lower. 11 patients in a study by Ana Canestri, et al., who successfully used ART to decrease plasma viremia, experienced acute and subacute neurological problems. In a research by C. Torti et al., 1,072 (44.6%) and 174 (7.2%) of the patients, respectively, had grade III and IV hyperbilirubinemia. A increased likelihood of developing grade III hyperbilirubinemia was linked to higher CD4+ T-cell counts, aberrant baseline bilirubinemia, and co-administration of ritonavir. Contrarily, clinical class C, non-nucleoside reverse transcriptase co-administration, and female gender appeared to be protective factors. A higher probability of grade IV hyperbilirubinemia was linked to higher baseline bilirubinemia and ritonavir usage. There was no link between grade III hyperbilirubinemia and severe hepatotoxicity. The major effectiveness endpoint (plasma HIV RNA decrease determined by time-averaged difference (TAD)) for Johnson M et al trial's was identical for ATV/RTV and LPV/RTV at 48 weeks (TAD 0.13; 97.5% confidence interval, -0.12 to 0.39). ATV/RTV and LPV/RTV had equivalent mean decreases from baseline at 1.93 and 1.87 log10 copies/ml, respectively. For the combinations ATV/RTV and LPV/RTV, the mean CD4 cell count increases were 110 and 121 106 cells/l, respectively. At 6 months and 12 months in our study, there was a mean increase in total cholesterol, LDL, and VLDL[12]. However, there was an increase in triglycerides at 6 months, which decreased at 12 months. At 6 months and 12 months, the HDL level had significantly decreased. All PI-treated groups had elevated plasma cholesterol levels, according to Pe'riard D et al., but ritonavir had the greatest effect (p 0.001), followed by indinavir (p 0.03), and nelfinavir (1.260.2 mmol/L, n=21, P=0.01). Ritonavir administration, but not indinavir or nelfinavir, was linked to a significant increase in plasma triglyceride levels (p=0.002). Plasma HDL cholesterol concentrations remained constant. Saquinavir combined with ritonavir or nelfinavir did not cause plasma lipid levels to rise any higher. After starting second line ART, none of the patients in our study experienced lipodystrophy. At 12 months, the mean blood sugar increased, although it was not statistically significant. The cumulative incidence of new-onset hyperglycemia, hypercholesterolemia, hypertriglyceridemia, and lipodystrophy was 5%, 24%, 19%, and 13%, respectively, in a study by Tsioridas S, et al. The majority of these incidents happened after the start of PI therapy. Lipodystrophy, hyperglycemia, hypercholesterolemia, and hypertriglyceridemia were all independently linked to protease inhibitors. In our study, 3 months after beginning second line ART, one patient experienced Fanconi's syndrome. Proximal renal tubular acidosis and a spike in serum creatinine of up to 3 were both noted in the patient. Other medications were continued while tenofovir was stopped. Following the withdrawal of tenofovir, the patient got better. According to a study by A. Karras et al. reported 3 instances of renal damage brought on by the antiviral medication tenofovir. Observed conditions included renal failure, proximal tubular dysfunction, and nephrogenic diabetes insipidus. Renal biopsy results in 2 individuals showed severe tubular necrosis with distinctive nuclear alterations. Patients on TDF-containing HAART regimens with either rtv/LPV or rtv/ATZ did not have greater declines in renal function during the first year of observation compared to those on TDF-containing HAART regimens without these agents or other protease inhibitors, according to a study by K. Buchacz et al. At 9 months of follow-up in our study, one patient experienced

lactic acidosis. After tenofovir withdrawal, the patient's symptoms of nausea, vomiting, and easy fatigue improved. A lab test revealed a lactate level of 52.7 mg/dl and a pH of 6.9.

12 patients with HIV infection who were using nucleoside analogues for their condition had an inexplicable metabolic acidosis, according to a study by Falco V et al. One patient receiving the combination of tenofovir and didanosine was reported to have died from lactic acidosis in a research by Guo Y et al. Didanosine levels and the likelihood of hyperlactatemia are both increased by tenofovir. When a patient meets the clinical and laboratory requirements for starting ART on a national level, first-line ART is the first regimen that is recommended for the patient. (Two medication classes—two NRTIs and one NNRTI—are used as the first line of treatment. After first-line therapy has failed, the second regimen, known as second-line ART, is used[12-15]. According to the most recent NACO treatment recommendations, second-line ART should only be used when protease inhibitor (PI) therapy is indicated. Two NRTI-class medications support the recommendation for ritonavir-boosted protease inhibitors (bPIs). It is important to make a careful distinction between switching prescribed ARVs and changing the entire ART regimen.

CONCLUSION

Following the start of second-line ART, there has been a significant improvement in CD4 count, clinical T staging of patients, and viral load. Increased mortality on second line ART was related to WHO T4 stage at baseline and severe immunosuppression (CD4 Count 100 cells/microlitre). Failure to respond to second line ART was linked to low CD4 count (100 cells/microlitre at baseline) and WHO - T3, T4 at baseline.

REFERENCES

1. Caraël Michel, Piot Peter. Epidemiology of HIV infection. In: Jonathan Cohen, William G. Powderly, Steven M Opal, editors. Infectious Diseases, 3rd ed. Mosby. 2010(2): p1498
2. UNAIDS/WHO: AIDS epidemic update, Geneva, UNAIDS, 2007
3. Walker N, Grassly N C, Garnett G P, Stanecki K A. Estimating the global burden of HIV/AIDS: what do we really know about the HIV pandemic? Lancet 2004; 336:2180-2225
4. Anthony S Fauci, H Clifford Lane. Human Immunodeficiency virus Disease:AIDS and Related Disorders. In: Anthony S Fauci, Eugene Braunwald, Dennis L Kasper, Stephen L Hauser, Dan L Longo, Larry Jameson J et al., editors. Harrison's Principles of Internal Medicine. 18th ed. New York. McGraw Hill; 2012(1):p1506-1588
5. Sharon Safrin. Antiviral agents. In: Bertram G Katzung, editor. Basic and Clinical Pharmacology. 10th ed. New York. McGraw Hill; 2007; 2007:49:p790-819
6. Pujades-Rodríguez, Mar; O'Brien, Daniel; Humblet, Pierre; Calmy, Alexandra, Second-line antiretroviral therapy in resource-limited settings: the experience of Medecins Sans Frontieres AIDS; 2008(22):11:1305-1312
7. Bankim Mankad, Hemang Purohit, Asha Shah, Manoj Shevkani, Burzin Kavina. Our experience in second line Anti Retroviral Therapy (ART) At State Aids Clinical Expert Panel (SACEP) Clinic, Centre of Excellence (CoE), Art Centre, B. J.Medical College, Civil Hospital, Ahmedabad. Retrovirology 2010:7:53
8. C. Torti, G. Lapadula, A. Antinori, T. Quirino, R. Maserati, F. Castelnuovo, et al. Hyperbilirubinemia during Atazanavir Treatment in 2,404 Patients in the Italian Atazanavir Expanded Access Program and MASTER Cohorts. Infection 2009; 37: 244–249.
9. Johnson M, Grinsztejn B, Rodriguez C. Atazanavir plus ritonavir or saquinavir, and lopinavir/ritonavir in patients experiencing multiple virological failures. AIDS 2005; 19: 685–694
10. Pe´riard D, Telenti A, Sudre P. Atherogenic dyslipidemia in HIVinfected individuals treated with protease inhibitors. The Swiss Cohort Study. Circulation 1999; 100:700–5

11. Tsioridas S, Mantzoros C, Hammer S. Effects of protease inhibitors on hyperglycemia, hyperlipidemia, and lipodystrophy: a 5-year cohort study. Arch Intern Med. 2000;160:2050–2056.
12. A. Karras, M. Lafaurie, A. Furco. Tenofovir-related nephrotoxicity in human immunodeficiency virus-infected patients: three cases of renal failure, fanconi syndrome, and nephrogenic diabetes insipidus. Clinical Infectious Diseases 2003:36:1070–1073
13. K. Buchacz, B. Young, R. K. Baker. Renal function in patients receiving tenofovir with ritonavir/lopinavir or ritonavir/atazanavir in the HIV Outpatient Study (HOPS) cohort. Journal of Acquired Immune Deficiency Syndromes 2006:43:5:626-628
14. Vicente Falcól, Dolors Rodríguezl, Esteban Ribera. Severe Nucleoside-Associated Lactic Acidosis in Human Immunodeficiency Virus–Infected Patients: Report of 12 Cases and Review of the Literature. Clin Infect Dis.2002;34(6):838-846
15. Guo Y, Fung H B Fatal lactic acidosis associated with coadministration of didanosine and tenofovir disoproxil fumarate. Pharmacotherapy 2004:24(8): 1089-94.