Neuropathy complication of antiretroviral therapy in HIV/AIDS patients

by Desiana Radithia

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Neuropathy complication of antiretroviral therapy in HIV/AIDS patients

Saka Winias | **Desiana Radithia** | **Diah Savitri Ernawati**

Department of Oral Medicine, Faculty of Dental Medicine, Universitas Airlangga, Surabaya, Indonesia

Correspondence
Saka Winias, Department of Oral Medicine, Faculty of Dental Medicine, Universitas Airlangga, Surabaya, Indonesia.
Email: saka.winias@fkg.unair.ac.id

Abstract

Objectives: Significant pain from HIV-associated sensory neuropathy (HIV-SN) affects 40% of HIV-infected individuals treated with antiretroviral therapy (ART). The most salient symptom of the neuropathy is pain, which frequently is moderate-to-severe intensity, associated with reduced activities and physical function, sleep disruption, increased severity of depression, and anxiety. Yet, evidence for managing painful HIV-SN is poor. The purpose of this study was to verify by scientific evidence the neuropathy complication in HIV/AIDS patients to develop effective pain management strategies.

Methods: Design: Systematic review. Data sources: PubMed (MEDLINE), Cochrane, www.controlled-trials.com. Selection criteria: the filter "English" was used, time-framed searched was 2009–2019, randomized controlled trials (RCT). Keywords were verified in MeSH "Peripheral Nervous System Disease" and "Antiretroviral Agents" or "Antiretroviral therapy." Review method: the PRISMA flowchart was used.

Result: A systematic search following PRISMA guidelines was carried out, and 12 specific articles/studies on the subject were selected. The results revealed that HIV therapy, aging, body mass index, height, and systemic conditions influence neuropathy conditions in HIV/AIDS patients. The multistudies focused on pain management approaches such as administration of pain medication, drug combination to prevent side effects, or ART with minimal side effects.

Conclusion: Sensory neuropathy is a frequent complication of HIV infection and ART. An understanding of the mechanism and pathophysiology of neuropathy in HIV is urgently required to develop alternative treatment modalities and to evaluate preventive strategies.

KEYWORDS
AIDS, antiretroviral therapy, HIV, neuropathy

1 | INTRODUCTION

More than 34 million people worldwide live with HIV/AIDS, according to the Joint United Program on Human Immunodeficiency Virus Infection/Acquired Immunodeficiency Syndrome (HIV/AIDS) (UNAIDS, 2019). One-third of those diagnosed with HIV/AIDS are reported to have systemic neuropathies that can be caused by the virus itself, opportunistic infections, or as a side effect of some drugs used. The most effective treatment for HIV infection is antiretroviral therapy. Nevertheless, the use of these medications, in

particular the use of nucleoside reverse transcriptase inhibitors, is associated with an increase in the incidence of severe peripheral neuropathy. This group includes medications zidovudine or azidothymidine, didanosine, zalcitabine (ddC), stavudine (d4T), lamivudine, and abacavir. ddC was one of the first HIV/AIDS-approved antiretrovirals and is now considered to be the most neurotoxic (Garcia-Perez, Solà, Sumalla, & Serra, 2015) The introduction of combination antiretroviral therapy (cART) dramatically reduced the morbidity and mortality associated with HIV among patients who have access to treatment.(Mwesiga, Kaddumukasa, Mugenyi, & Nakasujja, 2019).

Peripheral neuropathic pain associated with HIV is challenging to manage with pharmacological therapy. Many current therapies are not effective in treating this pain. The limited scientific knowledge of antiretroviral-mediated neuropathic pain may be one of the reasons for the shortage of effective care for this patient population. Systematic reviews of the natural consequence of antiretroviral therapy (ARV) in HIV/AIDS patients have been established. Thus, while the widespread use and side effects of ARV have been identified in HIV/AIDS patients, insufficient research has been done in the analysis and therapy of HIV/AIDS neuropathy patients. The purpose of this systemic review is therefore to examine scientific evidence on the complications of neuropathy of HIV/AIDS and determine the most effective pain management strategies.

2 | MATERIALS METHODS

2.1 | Protocol development

The PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analysis) checklist (Moher, Liberati, Tetzlaff, & Altman, 2009) was consulted and used as a guide for quality reporting of this systematic review.

2.2 | Focused question

Can ARV therapy in people with HIV/AIDS cause neuropathy and what is the most effective treatment for this condition?

2.3 | Search study for identification of studies

The PubMed (MEDLINE) database of the U.S National Library Medicine, Cochrane, and www.controlled-trials.com were used. Electronic search and a literature search were accomplished on articles from the inception of the respective database to June 28, 2019, by using combination of MeSH and free text words "Peripheral Nervous System Disease" and "Antiretroviral Agents" or "Antiretroviral therapy." The search was restricted to English language and published between 2009 and 2019.

2.4 | Selection criteria

Initially, studies were excluded based on assessment of relevance of title and abstract conducted by three authors independently. The remaining studies were evaluated in their entirety by the same authors, and those studies which met the following criteria were included: randomized controlled trial (RCT); HIV/AIDS patient with ARV treatment; and neuropathy.

2.5 | Data synthesis

Data were independently collected, and the following items were extracted: study design, characteristics of the population (sample, age, country of study), duration of the intervention, medications used, and clinical outcomes.

3 | RESULTS

3.1 | Identified trials and outcomes

A total of 576 relevant studies were found in these databases, and 4 additional records were identified through other resources. A total 534 references were excluded based on the randomized controlled trial and duplicate files, and 38 were selected for full-text analysis, of which 12 trials were selected for this review (Dinat, Marinda, Moch, Rice, & Kamerman, 2015; Ellis, Toperoff, & Vaida, 2009; Evans et al., 2011, 2012; Harrison et al., 2013; Jaquet et al., 2013; Lee et al., 2015; Leger et al., 2014; Phanuphak, Ananworanich, Teeratakulpisarn, Jadwattanakul, & Kerr, 2012; Shikuma et al., 2015; Simpson et al., 2014; Yeh, Evans, Gulick, & Clifford, 2010).

3.2 | Peripheral neuropathy in HIV patients treated with ARV

There were six trials comparing the effects of ARV treatment in HIV patients. Jaquet et al. (2013) assessed Health-Related Quality of Life (HRQOL) in HIV-positive participants started on highly active antiretroviral therapy (HAART) and followed up for several months. During the 12-month follow-up, they reported 31% having peripheral neuropathy. Leger et al. (2014) designed a study to compare antiretroviral drug regimens as initial treatment for HIV-1 infection. They included 254 patients, of which 90 patients (35.4%) had peripheral neuropathy. Yeh et al. (2010) evaluated the effect of vicriviroc (VCV), which was considered to be potentially more neuroprotective than other antiretrovirals, but this study on the contrary showed that most participants had neuropathy in both placebo and VCV treatments. Evans et al. (2011) estimated neuropathic sign/symptom rate with initiation of combination antiretroviral therapy (cART). They found 32.1% of participants had peripheral neuropathy at 3-year follow-up, out of 2,141 participants. In Thailand, 20.4%

participants on zidovudine (AZT) treatment and 4.2% participants on tenofovir (TDF) treatment had peripheral neuropathy by week 24 (Phanuphak et al., 2012). Lee et al. (2015) showed prevalence of peripheral neuropathy initially increased and remained stable in 31% of this population (996 participants).

3.3 | Additional factors may underline neuropathy in HIV patients treated with ARV

There were two trials of the other predisposing factors that may affect peripheral neuropathy in HIV patients with ARV treatment. Shikuma et al. (2015) described epidermal nerve fiber density (ENFD) as a validated predictor of HIV-SN risk, they found large individual variation in change in ENFD with the first-time ART initiation, and this result is caused by various body composition measurements and blood pressure in their samples.

Evans et al. (2012) evaluated neurologic outcomes in ACTG Longitudinal Linked Randomized Trials (ALLRT) participants with cART regimen therapy. They found that the likelihood of developing symptomatic sensory neuropathy is increased in those with asymptomatic dysfunction and non-insulin diabetic therapy appears to reduce the odds of converting to symptomatic sensory neuropathy.

3.4 | Management strategies of neuropathic pain associated with HIV neuropathy

Four trials that studied the efficacy of pain treatment in HIV neuropathy patients were included in this review. One of these studies trialed amitriptyline for analgesia in painful HIV-SN (Dinat et al., 2015). This study showed that there were no significant differences in mean pain scores for ARV user receiving amitriptyline or placebo over six-week treatment.

Existing analgesic and adjunct treatment appear inadequate to treat neuropathic pain in HIV. Ellis et al. (2009) trialed smoked medicinal cannabis in the treatment of this condition. Smoked cannabis at maximum tolerable dose significantly reduced neuropathic pain intensity in 30% of HIV patients. Simpson et al. (2014) assessed the efficacy and safety of pregabalin in the treatment of HIV-associated neuropathic pain. Evaluation of the numeric rating scale (NRS) revealed that there was no difference between pregabalin and placebo groups.

4 | DISCUSSION

The most common neurologic complication of HIV infection is peripheral neuropathy but this has been widely under-detected and undertreated. The principal symptom of neuropathy may be allodynia or hyperalgesia. Studies have reported neuropathy prevalences ranging 30%–60% (Dubey, Raghuvanshi, Sharma, & Saxena, 2013; Ferrari et al., 2006). This increase has been linked to the use of ART regimens containing particular nucleoside reverse transcriptase inhibitors, notably stavudine. Despite the World Health Organization (WHO) recommending that the use of stavudine is phased out, stavudine-based treatment programs continue to be introduced and expanded in many countries because of lack of cost-effective alternatives. Therefore, stavudine-related toxicities are expected to increase (Beadles, Jahn, Weigel, & Clutterbuck, 2009; Wadley, Cherry, Price, & Kamerman, 2011).

There are two major mechanisms proposed for HIV-SN: neurotoxicity induced either by the HIV-1 envelope glycoprotein gp120 or by certain ART drugs. gp120 neurotoxicity is thought to result from its binding to CCR5 (C–C chemokine receptor type 5), CXCR4 (C–X–C chemokine receptor type 4), or both. The HIV indirectly infects neurons through infection of the supporting monocytes and Schwann cells, from the direct toxic effect of viral proteins such as gp120, Tat, and Nef protein on peripheral neurons, or a combination of both. Several viral products have been found to be neurotoxic (Kamerman et al., 2012; Mangus et al., 2014; Schütz & Robinson-Papp, 2013; Widyadharma et al., 2018) Mitochondrial dysfunction is a proposed mechanism for neurotoxicity of antiretrovirals. In vitro studies showed inhibition of mitochondrial DNA synthesis by the nucleoside analogues when phosphorylated to their active triphosphate form through the inhibition of DNA polymerase-gamma, leading to mitochondrial toxicity with resultant mitochondrial DNA depletion (Adam & Ellis, 2019; Roda & Hoke, 2019).

This systematic review found evidence that the first-line therapies (amitriptyline, pregabalin, methadone) recommended in management of neuropathic pain show no superiority to placebo in management of pain in HIV patients. There is evidence that capsaicin, smoked cannabis, and rhNGF can be effective in 30% of patients. But efficacy of capsaicin is only used topically, rhNGF is not available medically, and the use of smoked cannabis as daily therapy cannot be recommended because of the side effects (Phillips, Cherry, Cox, Marshall, & Rice, 2010). The reviewed literature suggests that HIV-SN is a frequent complication of HIV infection and ART. Understanding the mechanism and pathophysiology of neuropathy in HIV is urgently required to help develop alternative treatment modalities and to generate preventative strategies.

One of the limitations of this systematic review was that it was difficult to draw firm conclusions due to small number of RCTs included. It is also possible that some clinical trials were missed, although this is unlikely, as the databases searched are known to be comprehensive regarding clinical trials. Moreover, in the present systematic review, electronic literature search was supplemented by reviewing references from a variety of sources to retrieve any missing trials.

CONFLICT OF INTEREST

Authora declare that they are have no conflict of interest.

AUTHOR CONTRIBUTIONS

Conceived the study: SW (70%) and DR (30%); collected article data: SW (40%), DR (30%), DSE (30%); analyzed data : SW (40%), DR (30%), DSE (30%); developed and implemented SW (50%), DR (25%), DSE

(25%); wrote the paper SW (70%), DR (30%). All authors critically revised the manuscript and approved the final version.

REFERENCES

Adam, J., & Ellis, R. J. (2019). *HIV in the cART era and the mitochondrial: immune interface in the CNS*. Mitochondrial Dysfunction in Neurodegeneration and Peripheral Neuropathies (1st ed, Vol. *145*). Amsterdam, Netherlands: Elsevier Inc.

Beadles, W. I., Jahn, A., Weigel, R., & Clutterbuck, D. (2009). Peripheral neuropathy in HIV-positive patients at an antiretroviral clinic in Lilongwe, Malawi. *Tropical Doctor*, *39*(2), 78–80. https://doi.org/10.1258/td.2008.080213

Dinat, N., Marinda, E., Moch, S., Rice, A. S. C., & Kamerman, P. R. (2015). Randomized, double-blind, crossover trial of amitriptyline for analgesia in painful HIV- associated sensory neuropathy. *PLoS ONE*, *10*(5), 1–15. https://doi.org/10.1371/journal.pone.0126297

Dubey, T., Raghuvanshi, S., Sharma, H., & Saxena, R. (2013). HIV neuropathy in pre-HAART patients and it's correlation with risk factors in Central India. *Neurology India*, *61*(5), 478–480. https://doi.org/10.4103/0028-3886.121912

Ellis, R. J., Toperoff, W., Vaida, F.van den Brande G., Gonzales, J., Gouaux, B., … Atkinson, J. H. (2009). Smoked medicinal cannabis for neuropathic pain in HIV: A Randomized, Crossover Clinical Trial. *Neuropsychopharmacology*, *34*(3), 672–680. https://doi.org/10.1038/npp.2008.120.Smoked

Evans, S. R., Ellis, R. J., Chen, H., Yeh, T. M., Lee, A. J., Schifitto, G., … Clifford, D. B. (2011). Peripheral neuropathy in HIV: Prevalence and risk factors. *AIDS*, *25*(7), 919–928. https://doi.org/10.1097/QAD.0b013e328345889d.Peripheral

Evans, S. R., Lee, A. J., Ellis, R. J., Chen, H., Wu, K., Bosch, R. J., & Clifford, D. B. (2012). HIV peripheral neuropathy progression: protection with glucose-lowering drugs? *J Neurovirol*, *18*(5), 4280433. https://doi.org/10.1007/s13365-012-0119-9.HIV

Ferrari, S., Vento, S., Monaco, S., Cavallaro, T., Cainelli, F., Rizzuto, N., & Temesgen, Z. (2006). Human immunodeficiency virus-associated peripheral neuropathies. *Mayo Clinic Proceedings*, *81*(2), 213–219. https://doi.org/10.4065/81.2.213

Garcia-Perez, E., Solà, R., Sumalla, M., & Serra, J. (2015). Behavioral and electrophysiological abnormalities in two rat models of antiretroviral drug-induced neuropathy. *Pain*, *156*(9), 1729–1736. https://doi.org/10.1097/j.pain.0000000000000205

Harrison, T., Miyahara, S., Lee, A., Evans, S., Bastow, B., Gilron, I., … Clifford, D. B. (2013). Experience and challenges presented by a multicenter crossover study of combination analgesic therapy for the treatment of painful HIV-associated polyneuropathies. *Pain Medicine*, *14*(7), 1039–1047. https://doi.org/10.1111/pme.12084.Experience

Jaquet, A., Garanet, F., Balestre, E., Ekouevi, D. K., Azani, J. C., Bognounou, R., … Drabo, J. (2013). Antiretroviral treatment and quality of life in Africans living with HIV: 12-month follow-up in Burkina Faso. *Journal of the International AIDS Society*, *16*, 1–10. https://doi.org/10.7448/IAS.16.1.18867

Kamerman, P. R., Moss, P. J., Weber, J., Wallace, V. C. J., Rice, S. C., & Huang, W. (2012). Pathogenesis of HIV-associated sensory neuropathy: Evidence from in vivo and in vitro experimental models. *Journal of the Peripheral Nervous System*, *31*, 19–31.

Lee, A. J., Bosch, R. J., Evans, S. R., Wu, K., Harrison, T., Grant, P., & Clifford, D. B. (2015). Patterns of peripheral neuropathy in ART-naïve patients initiating modern ART regimen. *Journal of NeuroVirology*, *21*(2), 210–218. https://doi.org/10.1007/s13365-015-0327-1.Patterns

Leger, P. D., Johnson, D. H., Robbins, G. K., Shafer, R. W., Clifford, D. B., Li, J., … Haas, D. W. (2014). Genome-wide association study of peripheral neuropathy with D-drug-containing regimens in AIDS Clinical Trials Group protocol 384. *Journal of NeuroVirology*, *20*(3), 304–308. https://doi.org/10.1007/s13365-014-0235-9.

Mangus, L. M., Dorsey, J. L., Laast, V. A., Ringkamp, M., Ebenezer, G. J., Hauer, P., & Mankowski, J. L. (2014). Unraveling the pathogenesis of HIV peripheral neuropathy: Insights from a simian immunodeficiency virus macaque model. *ILAR Journal*, *54*(3), 296–303. https://doi.org/10.1093/ilar/ilt047

Moher, D., Liberati, A., Tetzlaff, J., & Altman, D. G. (2009). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *PLoS Medicine*, *6*(7), 1–6. https://doi.org/10.1371/journal.pmed.1000097

Mwesiga, E. K., Kaddumukasa, M., Mugenyi, L., & Nakasujja, N. (2019). Classification and description of chronic pain among HIV positive patients in Uganda. *African Health Sciences*, *19*(2), 1978–1987. https://doi.org/10.1017/CBO9781107415324.004

Phanuphak, N., Ananworanich, J., Teeratakulpisarn, N., Jadwattanakul, T., & Kerr, J. S. (2012). A 72-week randomized study of the safety and efficacy of a d4T to AZT switch at 24 weeks compared to AZT or TDF when given with 3TC and NVP. *Antiviral Therapy*, *17*(8), 1521–1531. https://doi.org/10.3851/IMP2497.A

Phillips, T. J. C., Cherry, C. L., Cox, S., Marshall, S. J., & Rice, A. S. C. (2010). Pharmacological treatment of painful HIV-associated sensory neuropathy: A systematic review and meta- analysis of randomised controlled. *Trials*, *5*(12), e14433. https://doi.org/10.1371/journal.pone.0014433

Roda, R. H., & Hoke, A. (2019). *Mitochondrial dysfunction in HIV-induced peripheral neuropathy*. Mitochondrial Dysfunction in Neurodegeneration and Peripheral Neuropathies (1st ed, Vol. *145*). Amsterdam, Netherlands: Elsevier Inc.

Schütz, S. G., & Robinson-Papp, J. (2013). Hiv-related neuropathy: Current perspectives. *HIV/AIDS - Research and Palliative Care*, *5*, 243–251. https://doi.org/10.2147/HIV.S36674

Shikuma, C. M., Bennett, K., Ananworanich, J., Gerschenson, M., Teeratakulpisarn, N., & Jadwattanakul, T. (2015). Distal leg epidermal nerve fiber density as a surrogate marker of HIV-associated sensory neuropathy risk: risk factors and change following initial antiretroviral therapy. *Journal of NeuroVirology*, *21*, 525–534. https://doi.org/10.1007/s13365-015-0352-0

Simpson, D. M., Rice, A. S. C., Emir, B., Landen, J., Semel, D., Chew, M. L., & Sporn, J. (2014). A randomized, double-blind, placebo-controlled trial and open-label extension study to evaluate the efficacy and safety of pregabalin in the treatment of neuropathic pain associated with HIV neuropathy. *Pain*, *155*, 1943–1954. https://doi.org/10.1016/j.pain.2014.05.027

UNAIDS (2019). Retrieved from https://www.unaids.org/en

Wadley, A. L., Cherry, C. L., Price, P., & Kamerman, P. R. (2011). HIV neuropathy risk factors and symptom characterization in stavudine-exposed South Africans. *Journal of Pain and Symptom Management*, *41*(4), 700–706. https://doi.org/10.1016/j.jpainsymman.2010.07.006

Widyadharma, E., Barus, J., Science, H., Katolik, U., Atma, I., Dewi, P. R., & Yaputra, F. (2018). Glial Cells Involvement in Pathogenesis of Human Immunodeficiency Virus-Associated Sensory Neuropathy (HIV-SN): Literature Review. *International Journal of Medical Reviews and Case Reports*, *2*, 49. https://doi.org/10.5455/IJMRCR.glial-cell-hiv-sn

Yeh, T., Evans, S. R., Gulick, R. M., & Clifford, D. B. (2010). Vicriviroc and peripheral neuropathy: Results from AIDS Clinical Trials Group 5211. *HIV Clinical Trials*, *11*(1), 51–58. https://doi.org/10.1310/hct1101-51. Vicriviroc

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