

VESTIBULAR FUNCTION IN A GROUP OF ADULTS WITH HIV/AIDS ON HAART

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Abstract

Background: The high prevalence of HIV/AIDS and the established otological manifestations of the disease have important implications for research into vestibular function in this population.

Materials and Methods: The main aim of the current study was to investigate and monitor the vestibular status in a group of adult patients with AIDS receiving Highly Active Antiretroviral Therapy (HAART) and other therapies in a hospital outpatient clinic in Gauteng, South Africa. The study was exploratory and observational in nature, with repeated measures in the form of pre- and post-treatment survey; and a control group. The measures were taken before commencement of antiretroviral therapy (ARVs), three months after initiation of treatment and six months into therapy. A comparison of results of the control group and treatment group was done for all objectives. A total of 150 (104 in the treatment group and 46 in the control group) participants who were recruited through a nonprobability convenience sampling technique were included in the study. All participants were at stage three of HIV/AIDS according to their CD4+ T-cell counts at baseline. Data were analysed through descriptive statistics.

Results: Findings from the current study revealed occurrence of acute vertigo which spontaneously resolved in adults with AIDS on HAART over a monitoring period of six months; with this occurrence being higher in participants on HAART than in the control group. The symptoms occurred after diagnosis with HIV and mostly after HAART initiation; and participants who experienced vertigo did not report this to their attending doctor. Furthermore, there was a lack of a relationship between the increasing occurrences of hearing loss in the group to the presentation of vertigo over the six months of monitoring.

Conclusion: Findings from the present study which revealed occurrence of possible acute vertigo that spontaneously resolves in adults with AIDS on HAART, over a monitoring period of six months, add to the existing literature on vestibular function in this population. These findings raise important research as well as clinical assessment and management implications in this population.

Keyword: Adults, HIV/AIDS, HAART, Johannesburg, vertigo, vestibular symptoms, quality of life, South Africa.

Introduction

HIV/AIDS continues to be one of the biggest challenges faced by the South African Department of Health; with South Africa being dubbed the epicentre of the pandemic where the highest number of people on antiretroviral treatment resides. With as much as 36.7 million [34.0 million–39.8 million] people infected by the end of 2015 globally; statistics still indicate that Sub-Saharan Africa remains most severely affected (UNAIDS, 2016). Since the reports of the first few cases of HIV and AIDS in the late 1980s; proportion of South Africans infected with HIV reportedly increased from 10.6% (2008) to 12.2% (2012) (Shisana et al., 2014) to the current 19.2% (UNAIDS, 2016). Despite this known high prevalence of HIV/AIDS; treatment coverage data still indicates that there is no universal coverage yet.

Otological manifestations of the disease including those directly due to the virus (primary effects), those due to the opportunistic infections (secondary effects), and those caused by the various medical treatments prescribed in this population (iatrogenic effects) continue to be investigated and documented; with expected changes in iatrogenic effects due to the continued new advances in treatments (Bankaitis & Schountz, 1998, Kallail, Downs & Schertz, 2008; Harris & Heinze, 2013, Khoza-Shangase, 2014). With the availability and provision of highly active antiretroviral therapy (HAART) in South African public health facilities having been rolled out in the first quarter of 2004; significant progress has been seen in the achievement of sustaining the lives of the infected. The year 2013 saw the roll out of the fixed-dose combination (FDC) antiretroviral (ARV) medication (Davies, 2013). This raises a need for

pharmacovigilance where minimization or elimination of iatrogenic conditions is prioritized; with the goal of ensuring improved quality of life for those living with HIV/AIDS.

The medical treatment advancements as well as the setting of UNAIDS 90:90:90 by 2030 targets are laudable (UNAIDS, 2014) and raise implications for audiological understanding of and proper planning for HIV/AIDS and its otological manifestations. Although the UNAIDS 2030 targets seem to have a clear goal of sustaining life and preventing and/or eliminating the spread of the disease; it is important that the life-sustaining goals are paired with quality of life goals. As part of the rehabilitation team, it is important that audiologists constantly insert the importance of also focusing on the quality of the life of individuals with HIV/AIDS in as far as otological function is concerned. This added focus on quality of life, which falls within the realm of all healthcare providers, would include hearing and balance function as part of the sensory disabilities that may be experienced by people living with HIV/AIDS. It is for this reason that the current author argues that the 2030 target of having 90% infected diagnosed; 90% on treatment, and 90% virally suppressed should also include maintenance of at least 90% quality of life.

Identifying the presence, severity and nature of vestibular manifestations in patients with HIV/AIDS is of vital importance to healthcare providers as vestibular symptoms can be debilitating and may negatively affect the patient's quality of life (Holmes & Padgham, 2010). Vestibular manifestations in the form of vertigo as well as its secondary symptoms are considerably debilitating for a patient. These manifestations affect the patient's ability to function and participate in everyday life, and consequently their quality of life (Holmes & Padgham, 2010; Heinze et al., 2011). Therefore, identification as well as appropriate referrals and management of these symptoms is essential. Evidence, however, suggests that patients infected with HIV/AIDS are rarely screened for vestibular pathologies (Heinze et al., 2011). Reasons for this lack of screening might include the fact that the primary focus is on sustaining life in this population; although paucity of research evidence on vestibular function in this population might also be a significant contributing factor.

As early as 1989, Hart and colleagues reported on pathological central nervous system signs and symptoms in the form of severe vestibular symptoms such as vertigo with severe vomiting in patients with HIV/AIDS. In a study, by Marra et al. (1997), 30% of patients with HIV on HAART experienced vertigo, while Khoza-Shangase (2011) found that 9% of participants in their study reported experiencing vertigo. Recently, an Italian study by Teggi, Giordano, Pistorio and Bussi (2006) suggested that as patients progress to the more severe stages of HIV/AIDS, the prevalence of vestibular pathologies, especially central vestibular pathologies, increases. Most recently, a South African study revealed that HIV positive individuals had a 16.61 times higher risk of developing vestibular pathology in their lifetime of living with the disease than HIV negative individuals (Heinze, Vinck, Hofmeyer, & Swanepoel, 2014). Evidence from post-mortem studies indicates that the virus appears to deteriorate the anatomy and physiology of the vestibular system (Pappas, Roland, Lim, Lai, & Hillman, 1995), and that it also appears to directly affect the central as well as the peripheral vestibular system. This conclusion was based on particles, characteristic of the HI virus, found in the central and the peripheral vestibular system (Pappas et al., 1995). Thus, a direct relationship between HIV/AIDS and the vestibular system seems to be present.

Although enough evidence has been documented proving the presence of vestibular pathology in HIV/AIDS, the presentation of the vestibular symptoms along the stages of the disease does not seem to have an established pattern. Studies have revealed that patients can present with vestibular pathologies at the initial stages of the disease, as well as in the later stages (Khoza-Shangase, 2011, Teggi et al., 2008, Heinze et al., 2011; Heinze et al., 2014). This essentially implies that the stage at which the HIV/AIDS virus is at does not seem to play a role in the occurrence or severity of vestibular symptom presentation (Heinze et al., 2011; Mathews et al., 2012). Furthermore, Heinze and colleagues (2011), in a review paper; concluded that age of the patient also does not influence the presentation of both peripheral and central vestibular disorders in this population.

The opportunistic infections and the usage of ARVs or other medication may be indirect causes of vestibular pathologies in this population (Teggi et al., 2006). In South Africa, the most common opportunistic conditions include tuberculosis (TB), cytomegalovirus (CMV), Hepatitis C (HCV), sexually transmitted infections, pneumonia, metabolic diseases, type two diabetes, blood disorders such as anaemia; and neurological disorders such as HIV dementia. Of these opportunistic conditions, otosyphilis and TB have a documented positive relationship with pathological vestibular symptoms; with syphilis presenting with symptoms in the form of vertigo and dizziness due to the damaged vestibular system (Macher, 2008; Harris & Heinze, 2013). As far as TB is concerned, many of the patients with HIV/AIDS contract TB as a result of being immune-deficient; with TB being one of the biggest causes of death in the HIV/AIDS population in South Africa (van Dyk, 2012).

South Africa has one of the highest rates of drug-resistant tuberculosis (MDR-TB) worldwide (Statistics South Africa, 2014). Because of the mortality linked with TB, patients are often required to take ARVs and TB medication (aminoglycosides) simultaneously (Harris & Heinze, 2013). Enough evidence exists that shows vestibular toxicity due to TB medications (Rogers & Peterson, 2011; Harris & Heinze, 2013). Enough evidence also exists that establishes a relationship between HAART and vestibular function (Palacios et al., 2008; Harris & Heinze, 2013; Khoza-Shangase, 2014; Khoza-Shangase & Van Rie, 2016). Concomitant use of anti-TB and antiretroviral medications could present compounding effects and result in severe damage to the vestibular system. It is important to note that vestibular symptoms may present with hearing symptoms because the medications may be vestibulocochleotoxic, and so South African patients on HAART and aminoglycosides simultaneously are more likely to acquire a sensorineural hearing loss, tinnitus and vestibular damage than a patient who is solely on aminoglycosides or HAART (Harris & Heinze, 2013).

Review of the literature indicates that vestibular pathology, particularly when chronic (Holmes& Padgham, 2010) is distressing and debilitating for the patient. It affects their psychological state and their ability to independently function and participate in everyday life, consequently affecting their quality of life (Holmes& Padgham, 2010; Heinze, Swanepoel & Hofmeyer, 2011; Khoza-Shangase & Van Rie, 2016). If symptoms occur after commencement of treatment, adherence to the treatment plan may be negatively affected if the symptoms are not identified and appropriately treated; hence the importance of the current study.

Materials and Methods

Research design

The study was exploratory and observational in nature, with repeated measures in the form of pre- and post-treatment survey; and a control group. In this repeated measure design, each participant served as his or her own control, allowing for the difference in performance associated with the use of antiretroviral drugs and other therapies to be observed despite differences in individual baseline performance. The measures were taken before commencement of antiretroviral therapy (ARVs), three months after initiation of treatment and six months into therapy. A comparison of results of control group and treatment group was done for all objectives.

Sample

A total of 150 participants from the research site who volunteered to participate in the study were included in the study. However, because one of the aims of the study was to attempt to establish the possible impact that antiretroviral drugs may have on vestibular function, it was crucial to apply a rigid set of participant inclusion criteria after baseline measures had been taken (i.e. for all participants that were going to participate in session 2 and 3 of the study). Given the fact that paucity of published research on this aspect of HIV/AIDS in South Africa exists, the researcher believed that it was crucial to have a high degree of control over variables which could confound the results of the study (e.g. noise exposure, syphilis, and so forth); hence the inclusion and exclusion criteria listed in Tables 1 and 2 below. A nonprobability convenience sampling technique was utilized since the sample was restricted to a part of the population that was readily available.

The treatment group (those patients on HAART) comprised 104 participants and the control group (those patients not on HAART) comprised 46 participants. All participants were at stage 3 of HIV/AIDS according to their CD4+ T-cell counts at baseline.

Participant selection criteria

Table 1 depicts the inclusion criteria while Table 2 depicts exclusion criteria adopted in the current study.

Table 1: Summary of participant Inclusion Criteria following baseline measures

Criterion	Treatment group	Control group
HIV/AIDS positive serology	Yes	Yes
On ARVs	Yes	No
Age between 18 and 50 years	Yes	Yes
Alert and oriented	Yes	Yes
Normal pure tone audiometry (thresholds better or equal to 25dBHL)	Yes	Yes

Table 2: Summary of participant Exclusion Criteria following baseline measures

Criterion	Treatment group	Control group
Noise exposure	Yes	Yes
Recent (less than 3 years) or current history of treatment for TB and radiotherapy	Yes	Yes
Positive clinical or serological evidence of syphilis	Yes	Yes
Middle ear pathology	Yes	Yes
Presence of tinnitus	Yes	Yes
Recent (less than 3 years) history of previous ARV use	Yes	Yes

Testing protocol

Prior to commencement of the study, permission to conduct the research project was secured from the University's Human Research Ethics Committee. Moreover, the Nuremberg code of ethics in research was adhered to throughout the research process. Permission to conduct the study at the HIV/AIDS clinic was obtained from Hospital management and from the Heads of the Audiology and HIV/AIDS clinics. Once permission was obtained and ethical

clearance secured, the researcher spent time at the research site, conducting detailed case history interviews and reviewing patient files at all three sessions as part of data collection.

Material

For data on vestibular function, the case history interview probed the following questions:

- Do you experience any dizziness or feeling of spinning of the house around you?
- If yes, when did you start experiencing this? Was it before or after you were diagnosed with HIV? Was it before or after you started taking ARVs? (treatment group)
- Have the symptoms changed (worse or better) or have they stayed the same?
- Have you reported the symptoms to your doctor?

Analysis of data and Statistical Procedures

In order to ensure research reliability, controls were exercised pertaining to participant variables, as well as parameters pertaining to the interview and data analysis procedures employed. Over and above conducting record reviews; utilising an independent rater during data analysis; a pilot study was also conducted to ensure reliability and validity. Data were analysed qualitatively through descriptive statistics. Quantitative data analysis, through the use of frequency calculations were condensed into tabular format for ease of frequency comparisons; and these were then depicted into graphical presentations.

Results

Description of Participants

The study at baseline (Table 3) comprised 150 participants (104 in the treatment group and 46 in the control group); 53 (35%) males and 97 (65%) females between the ages of 20 and 46 years with a mean age of 33.9 years.

Table 3: Demographic data of participants for the whole sample at baseline (N = 150)

FACTOR	SUB-CATEGORY	NO.
Age (Years)	Range	20-46yrs
	Mean	33.9yrs
Gender	Male	53 (35%)
	Female	97 (65%)
Ethnic Group	Black	141 (94%)
	White	0
	Coloured	9 (6%)
	Indian	0

All of the participants had been diagnosed with HIV/AIDS and were all at the AIDS stage of the disease. The average CD4+ count at the various sessions is depicted in Figure 1 and shows improving average counts with commencement of treatment and deteriorating counts in treatment naïve participants over time. The medications used in the current sample included 3TC, D4T, Nevirapine, AZT, Stocrin, Bactrim, Amoxyl, Facticin, Acyclovir, etc.

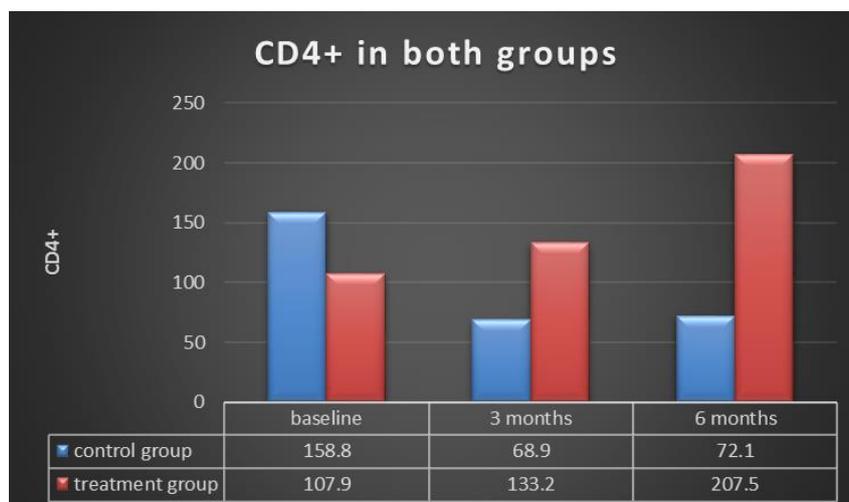


Figure 1: Average CD4+ counts for both groups over the 3 sessions

The occurrence of vertigo

On cross-sectional analysis of both groups at the beginning of data collection and at the end, overall findings revealed the occurrence of vertigo, as depicted in Figure 2. The results indicated vertigo in 4% of the HAART group and none in the control group at baseline, with this number increasing to 16% and 0.4% respectively over the 6 months monitoring period.

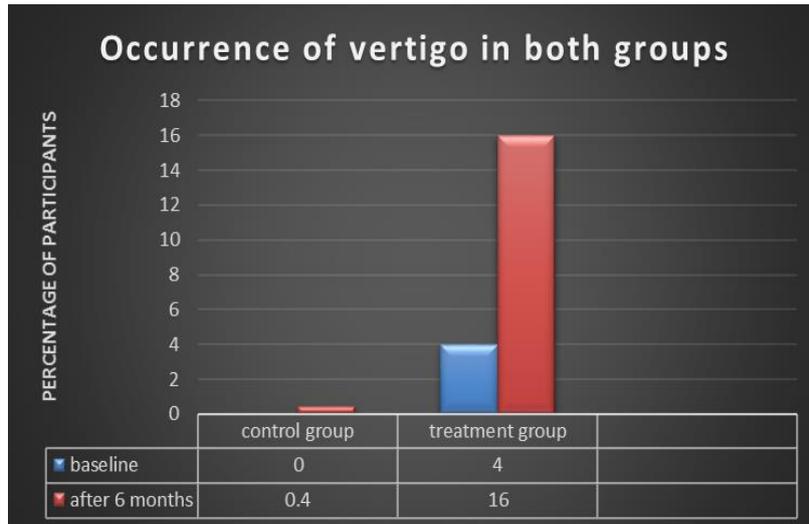


Figure 2: The occurrence of vertigo in both groups over the 6 month period (N=150)

The time of onset and development of vertigo

The time of onset and development of vertigo, as depicted in Figure 3 revealed no distinctive pattern; although there was an obvious increase in the number of participants reporting vertigo at the three months assessment session after commencement of HAART. This number decreased to 0% over time in both groups; which raised an index of suspicion about possible early vestibular side effects of HAART, which subsequently subsides on its own or the patients habituate to the vestibular dysfunction and do not complain about it anymore.

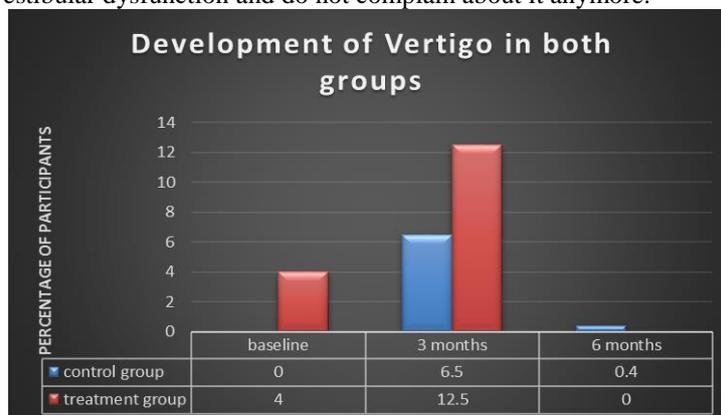


Figure 3: The onset and development of vertigo in both groups over the 6 month period

Comparing the results of the group on HAART with those of a control group who were not on HAART

A comparison of the findings in both groups, as depicted in Figure 3 and Table 5 indicates no vertigo after 6 months of follow up; regardless of the increased prevalence of hearing loss (additional analysis below) in both groups over time. The clear increase in vertigo occurrence at 3 months occurred in both groups with this completely subsiding over time. Furthermore, all participants with vertigo in both groups reported symptom presentation only after diagnosis with HIV/AIDS; with 13 of the 17 in the HAART group reporting vertigo only after initiation of HAART. All vertigo sufferers reported spontaneous resolution of vertigo; even for the two participants in the HAART group who had complained about the vertigo to their doctor without any subsequent treatment prescribed for the vertigo.

Table 4: Comparison of symptom presentation in both groups

Question	Control Group (n=3)	HAART Group (n=17)
Onset of vertigo	After diagnosis=3	After diagnosis=17 After HAART=13
Progression of vertigo	Vertigo better=3	Vertigo better=17
Vertigo reported to doctor?	No=3 Yes=0	No=15 Yes=2

Additional Analysis

Hearing function in the group

Hearing function assessment, as depicted in Figure 4, revealed hearing loss in 10% of the sample at baseline, with this increasing to 28% over the 6 months monitoring period.

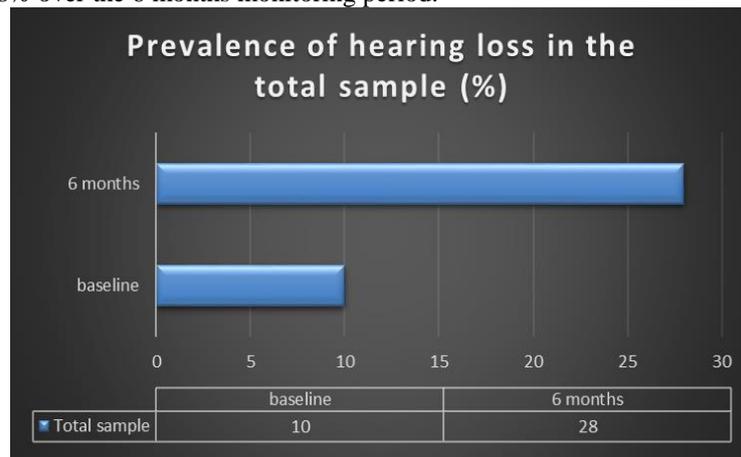


Figure 4: The percentage of prevalence of hearing loss at baseline and 6 months (N = 150)

Discussion

The current sample can be argued to be a fair representation of individuals infected by HIV/AIDS in South Africa; and Sub-Saharan Africa. Firstly, the age, gender and racial distribution reflects that of the country's demographic profile for individuals accessing public healthcare where more women are infected than males at these particular average ages. Secondly the low CD4+ count is typical of that of patients in the AIDS stage of the disease; which is the stage at which the South African public health care system offers HIV/AIDS treatment.

Current findings on the occurrence of vertigo in this population add to the documented evidence on presence of pathological vestibular symptoms in HIV/AIDS (Hart et al., 1989; Khoza-Shangase & Van Rie, 2016). In the current study; the higher prevalence in the HAART group when compared to the non-treatment control group seems to support possible influence of HAART on vestibular function (Macher, 2008), albeit temporary. Because current findings revealed vertigo which subsequently subsided without intervention in the HAART group; it is important that more detailed and long term follow up of patients is done to ensure that the symptoms are not recurrent in nature. Objective measures of this is also important to ensure that the origins of the dizziness as vestibular is categorically established.

A number of studies have suggested that there is a relationship between HIV/AIDS and the vestibular system (Teggi et al. 2006; Teggi et al., 2008; Macher, 2008; Selimoglu, 2007). In South Africa, the correlation between HIV/AIDS and the vestibular system is a fairly new area of research focus; nonetheless documented evidence does seem to suggest a positive relationship between the two (Khoza-Shangase, 2011; Heinze et al., 2011; Khoza-Shangase & Van Rie, 2016). Findings from the current study also support this evidence of there being an occurrence of vestibular abnormalities in the HIV/AIDS population; although this presentation appears to be acute with spontaneous recovery; maintaining what Holmes and Padgham (2010) assert when they claim that vestibular symptoms can also occur acutely and spontaneously recover. It is in fact this spontaneous recovery that these authors blame for the underreporting of symptoms to medical professionals by patients. These findings have implications for the clinical management of these patients because vertigo as well as its secondary symptoms are considerably debilitating for a patient. Vertigo is reported to have an influence in the patient's ability to function and participate in everyday life, with serious implications for the health and safety of the affected individual and those around him/her (Holmes & Padgham, 2010; Heinze et al., 2011). For this age group, the implications extend to their ability to remain productive members of the country's economy.

It can be argued that vertigo sufferers in the current study did not report the symptoms to their attending physicians because the symptoms were not severe and/or debilitating. However, in light of all the other medical conditions patients with HIV/AIDS experience, it is also possible that vertigo was low on the patients' priority lists when compared to what they might deem "life-threatening" conditions; hence them not reporting their symptoms for assessment and management. The fact that the symptoms occurred acutely and spontaneously recovered for all patients could have also played a role in the lack of reporting. Nonetheless; the current researcher is of the view that should all patients with HIV/AIDS report vertigo; current capacity versus demand with regards to availability of audiological and vestibular assessment and management resources would be mismatched. The current lack of adequate and sufficient vestibular assessment and rehabilitation specialists with sufficient training and appropriate objective equipment is an important consideration going forward for efficacious management of vestibular function in this population. Current findings therefore have important implications for planning around resource allocation.

The fact that in the current sample hearing loss was found and its occurrence increased over time is consistent with documented prevalence of hearing loss in AIDS due to the virus itself, opportunistic infections, and/or ototoxic medications used for treatment (Khoza-Shangase, 2010). The hearing loss occurred in both the control as well as

treatment groups, with high frequency sensorineural hearing loss being the nature and configuration of the loss in the majority of participants in the HAART group consistent with features of drug-induced hearing loss. The medications that were utilized in the current sample have been documented to have ototoxic effects (Khoza-Shangase, 2014). The fact that the prevalence increased over time also supports this phenomenon.

Current findings on hearing loss in this sample are consistent with documented evidence of auditory manifestations of HIV/AIDS and its treatments (Marra et al., 1997; Teggi et al., 2008; Khoza-Shangase, 2011; Khoza-Shangase, 2014); with some reports claiming many more reports of auditory manifestations than of vestibular manifestations in patients with HIV/AIDS (Heinze et al., 2011; Khoza-Shangase, 2011). Implications for assessment and management planning including ototoxicity monitoring, diagnostic audiology testing with appropriate referrals to otorhinolaryngology as well as audiological and vestibular habilitation are raised by current findings.

Conclusion

Findings from the current study revealed occurrence of possible acute vertigo which spontaneously resolves in adults with AIDS on HAART, over a monitoring period of six months, add to the existing literature on vestibular function in this population. Firstly, the fact that the symptoms reportedly occurred after diagnosis with HIV and mostly after HAART initiation; and the fact that higher occurrence was found in the HAART group than in the control group three months into the treatment, raises an index of suspicion about the involvement of ARVs in this presentation. Secondly, the finding that the reported vertigo was acute and spontaneously resolved without intervention raises a need for more careful and detailed investigation of this symptom in order to categorically establish its development and to determine if it is recurrent in nature. Thirdly, the reality that those who did experience vertigo did not report it to their attending physicians has serious implications for either the severity and/or debilitating nature of the symptoms to the sufferers or their awareness levels about what they should or should not report to the attending doctor. Lastly, the lack of a relationship between the increasing occurrence of hearing loss to the presentation of vertigo over the 6 months of monitoring raises implications for future research into this relationship in as far as cochlear as well as vestibular iatrogenic effects of HAART are concerned. This particular finding also raises an implication for future research utilizing objective measures of dizziness to ensure that the origin is in fact vestibular in nature.

Current findings need to be considered within the methodological limitations identified in the project. The fact that the study relied on only detailed case history interviews about vertigo and did not include objective vestibular assessment measures reduces the weight of the evidence. This is particularly important as dizziness could be due to causes other than vestibular pathology. Nonetheless; the established occurrence highlights the need for further research. Furthermore, current findings could be easier to generalize had a bigger sample size been included; and had participants not come from one research site in Gauteng. The fact that a relatively small number of participants presenting with vertigo were analysed from the total samples has implications for reaching conclusions about vertigo in this population. Despite these acknowledged limitations; current findings raise important implications for future research, clinical assessment and management of patients with HIV/AIDS, education and awareness campaigns around auditory and vestibular manifestations of HIV/AIDS amongst the patients and their various healthcare providers; as well as resource planning around vestibular assessment and management. All these implications are important to address in order to ensure holistic assessment and management of this population with the ultimate goal of improving both quantity and quality of life.

Ethical standards: The author asserts that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional guidelines on human experimentation (The University of the Witwatersrand Medical Ethics Committee) and with the Helsinki Declaration of 1975, as revised in 2008.

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