A Pilot Study of Peripheral Neuropathy in HIV Infected Patients in KwaZulu-Natal, South Africa

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Abstract

This pilot study aimed to examine neuropathy symptoms, self-care strategies, and use of traditional healing approaches reported by a convenience sample of 100 HIV positive patients who were seen in HIV clinics in KwaZulu-Natal, South Africa. The purpose was to measure the prevalence of neuropathy symptoms; self-care strategies; levels of physical, psychological, and social support; as well as pain ratings of HIV positive patients with neuropathy. The study also sought to determine self-reported use of traditional healing approaches. We collected self-report data from a convenience sample of HIV positive individuals on prevalence of neuropathy; pain ratings of neuropathy; self-care symptom management strategies; impact of neuropathy on physical, social, and psychological functioning; and use of traditional healing for neuropathy symptoms. Neuropathy was reported by 76% of the sample with average pain ratings of 7 to 10 on a 0 to 10 pain rating scale. Seventy-two percent of the sample reported neuropathy in the toes and 67% reported neuropathy in the feet/legs. The majority of the sample also reported co-morbid illnesses with most indicating co-infection with tuberculosis (TB). Over 70% reported an AIDS diagnosis and over half were living with HIV for seven years. Traditional healing was reported as a symptom management strategy by 30% of the sample. Recommendations include the need to further explore the prevalence of neuropathy and appropriate symptom management strategies including traditional healing approaches.

ABBREVIATIONS

HIV/AIDS: Human Immunodeficiency Virus; AIDS: Acquired Immune Deficiency Syndrome; TCAM: Traditional, Complementary, and Alternative Medicine (TCAM); SSC-HIVrev: Sign and Symptom Checklist (Revised); TB: Tuberculosis

Neuropathy-related symptoms are the most common neurological complication in HIV disease (Kaku et al. [1], Lehmann et al. [2]). Peripheral neuropathy is a painful sensory condition that primary affects the feet, toes, and lower extremities as well as the hands, fingers, and arms. Neuropathy is also known as distal sensory peripheral neuropathy (DSPN) or distal sensory polyneuropathy (DSP). This condition is common in several chronic conditions including diabetes (diabetic peripheral neuropathy), those with TB who are taking anti TB medications, and in those living with HIV. For those living with HIV, DSPN is commonly associated with several of the antiretroviral (ARV) medications including ddi and d4t. A recent review of DSPN in HIV Nicholas et al. [3] suggests that neuropathic pain is associated with both certain ARV regimens and also with nerve...
damage that occurs directly from the HIV virus and progression of disease. Other researchers in HIV-related neuropathy have suggested that mitochondrial toxicity and the direct effects of some medications in causing nerve damage are toxic, thus leading to severe neuropathic pain (Lehmann et al. [2]). Although the pathogenesis of HIV-related neuropathy is not fully understood, Lehmann and colleagues [2] suggest that neuropathy may occur due to damaged mitochondrial DNA that accumulates in distal nerve segments, and that a spatial pattern of mitochondrial dysfunction leads to degeneration of distal sensory nerve fibers. Wantland, Mullan, Holzemer, Portillo, & McGhee [4] noted that DSPN affects quality of life, but is also often undertreated and may be linked to fatigue symptoms. Griswold, Evans, Spielman, & Fishman [5] studied coping strategies of HIV patients with peripheral neuropathy. Their study suggests that “chronic pain patients who endorsed more behavioral strategies as a way of coping with pain also reported less pain, psychological distress, and higher self-efficacy (p. 718).

The literature on neuropathy in HIV disease indicates that neuropathy is a common and vexing complication, particularly in sub-Saharan Africa (Shaikh et al. [6], Tumusiime et al. [7], Wadley et al. [8]). In one recent study in Rwanda, Tumussime and colleagues found an over-reporting of neuropathy symptoms, however other literature suggests that neuropathy is a common and debilitating symptom (Tumussime et al. [7], Wadley et al. [8]). In a study on HIV neuropathy risk factors and symptom characterization in stavudine-exposed South Africans, Wadley et al. [8] found that approximately 25% of the sample had moderate to severe symptoms of neuropathy with all patients having symptoms in the feet. In this study the prevalence of neuropathy was reported by nearly 60% of the study participants and that “the extent and severity of pain observed in their cohort had a major impact on quality of life and may reduce adherence to antiretroviral drug adherence” (p. 705).

Ownby and Dunne [9] investigated the processes by which persons with HIV-related peripheral neuropathy manage their symptoms using a qualitative approach. They found that HIV-related neuropathy was associated with “difficulty in sleeping, lack of energy, difficulty in concentration, daytime drowsiness, and reduced employment as well as an overall decrease in quality of life” (p. 49). In addition, comorbid conditions such as depression were also common. Participants also indicated that neuropathic pain was associated with functional impairment, and affected their gait, balance, and fine motor coordination.

Peltzer et al. [10] studied the prevalence, predictors, and self-reported management of HIV symptoms in a sample of 735 consecutive patients. These patients were followed over six months with a final sample of 499 at 20 months on antiretroviral therapy. The results indicated that symptoms including diarrhea, headaches, rash, nausea, and neuropathy all decreased significantly during this longitudinal study. The mean number of symptoms decreased from 7.5 (SD = 9.6) to 0.2 (SD = 0.9) (F= 2193.69; p < .001).

Shaikh, Bentyl and Kamerman [6] examined the symptomatology of peripheral neuropathy in an African population (South Africa) and found that 94% of respondents reported neuropathic pain and 35% reported severe pain related to neuropathy. Seventy percent of the sample were women and 37% had a co-morbid diagnosis of TB. Similar to the present study, participants completed neuropathic pain screening tools in isiZulu and had significant similarity in the terms that they used to describe their pain.

In South Africa, Chetty et al. [11] suggested that there are a number of specific challenges to evaluating and treating neuropathic pain, included among these are lack of education and awareness among physicians, leading to suboptimal identification, assessment, and management. Use of non-steroidal anti-inflammatory agents (NSAIDS) and opioids, when available, is widespread and unfortunately, interventions such as back surgery may occur which is inappropriate in the treatment spectrum. Further Chetty et al. [11] suggest that pregabalin or amitriptyline are recommended as first-line agents with adjunct treatments including cognitive behavioral therapy and physical therapy. Their analyses resulted in the development of Clinical Practice Guidelines for Management of Neuropathic Pain: Expert Panel Recommendations for South Africa with specific approaches to differential diagnosis of neuropathic pain; bedside assessment of negative and positive sensory symptoms and signs in patients with neuropathic pain; recommendations for first- and second-line agents for neuropathic pain by international and regional guidelines; and recommended agents for specific peripheral neuropathy etiologies. A summary of recommended therapeutic agents for peripheral neuropathy in South Africa was also developed by Chetty and colleagues.

This pilot study focused on gaining further understanding of the symptom experience of living with HIV-related neuropathy. For those living in KwaZulu-Natal, South Africa, which is the epicenter of HIV and TB, the need to adhere to both ARVs and anti-TB medications often leads to an increase in the prevalence of neuropathy. As a pilot study, we approached 100 consecutive patients who had clinician validated neuropathic symptoms. Since neuropathy may occur related to HIV and TB, we included individuals who had HIV/no TB and those with HIV and TB.

**SOCIAL SUPPORT**

Social support is known to be important for coping with living with HIV/AIDS (Ncama et al. [12], Qiao, [13]. Ncama and colleagues investigated social support and medication adherence in HIV disease and found that social support was identified as important for those living with HIV but that social functioning was reported as low by the majority of participants in the study. This finding may be related to the stigmatizing nature of HIV disease particularly in resource-limited countries. Stigma is known to be associated with less access to social support and marginalization.

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>%</th>
<th>Mean</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days Experiencing Neuropathy</td>
<td>76</td>
<td>76%</td>
<td>4.76</td>
<td>1.99</td>
</tr>
<tr>
<td>Intensity of Neuropathy</td>
<td>75</td>
<td>75%</td>
<td>6.57</td>
<td>3.01</td>
</tr>
<tr>
<td>Distressfulness of Neuropathy</td>
<td>75</td>
<td>75%</td>
<td>7.38</td>
<td>2.96</td>
</tr>
<tr>
<td>Impact on Daily Life</td>
<td>75</td>
<td>75%</td>
<td>7.60</td>
<td>2.95</td>
</tr>
</tbody>
</table>

Table 1: Numbness/Neuropathic Pain Reported by Sample.
of individuals living with HIV. Qiao, Li, and Stanton [13] conducted a systematic review of the global literature on social support and HIV risk behaviors and found that HIV prevention intervention efforts need to focus on the positive effect of social support for various vulnerable and at-risk populations. They also suggest that “future efforts also need to incorporate necessary structure change and utilize technical innovation in order to maximize the protective role of social support in HIV risk prevention or reduction” (p. 441).

Social Support and Quality of Life

Johnson, Stallworth and Nellands [14] found that HIV-positive persons living with HIV disease-related symptoms, but not medication side effects, had significant deleterious effects on quality of life. In their study, the prevalence of neuropathy was 71.6% with a mean score of the bothersomeness of neuropathic pain rated as 2.92 (SD = 0.91) on a 0 to 4 scale. The rating was 0 = not present, 1 = present but does not bother me, 2 = present and bothers me a little, 3 = present and bothers me, to 4 = present and bothers me terribly.

As part of a larger study investigating the prevalence of peripheral neuropathy symptoms, we examined social support, psychological functioning and physical functioning in those with HIV disease in KwaZulu-Natal, South Africa, which is the epicenter of HIV infection in southern Africa. Earlier studies have suggested that social support is an important aspect of quality of life in HIV disease and that social support may be impacted by HIV symptoms, co-morbid illness, and stigma related to HIV (Ncama et al. [12], Rao et al. [15]). In our earlier study on HIV and social support (Ncama et al. [12]) those living with HIV/AIDS and other comorbid illnesses had significantly lower scores on social support “perhaps indicating the difficulties of maintaining support relationships with poorer physical, emotional, and social functioning” (p. 1758). In addition, the challenges presented by HIV/AIDS as a stigmatizing disease in South Africa are linked with lower social support for those affected. Because neuropathic symptoms may limit functioning and quality of life, social support, psychological functioning, and physical functioning were included in the measures administered in this study.

Another recent study by Birbeck and colleagues [16] suggested that neuropsychiatric symptoms, socioeconomic and social circumstances as well as neuropathy-related symptoms were associated with poorer outcomes. Notably, they found increased mortality among those with neuropsychiatric symptoms, advanced HIV, peripheral neuropathy symptoms, food insecurity, and poverty. Rao and colleagues [17] found that social support mediated the relationship between HIV-related stigma and depression, as well as quality of life in HIV-infected individuals in China. In a study in China, Sun, Wu, Qu, Lu and Wang [18] found that those who acquired HIV via sexual behavior reported poorer physical health and social support.

Traditional, Complementary, and Alternative Medicine (TCAM) or Traditional Healing

Traditional, complementary, and alternative medicine (TCAM) or healing practices are commonly used in indigenous populations globally. The World Health Organization (WHO, 1993) suggests that 80% of people worldwide use traditional healing methods. These methods comprise a variety of remedies that include herbal remedies, spiritual practices, micronutrients (including vitamins), acupuncture/acupressure/moxibustion, massage, meditation, visualization, and therapeutic touch.

In KwaZulu-Natal, South Africa, traditional healing most often includes two main groups of healers: the iNyanga and the sangomas. “An iNyanga is essentially an herbalist who works mostly with indigenous plants (Giarelli et al. [19], p. 40).” Sangomas focus on the ancestral spiritual aspects of life. “A sangoma or diviner-medium, is believed to have the power to communicate and intercede with the spirits...and cultivates relationships with ancestral spirits and other spirits that are believed to have the ability for healing (Giarelli et al. [19], p. 40). Giarelli et al. [19] note that much of the history of the use of traditional healing methods is not recorded and solely passed down from one generation to the next in the rural areas. Further, they suggest that the use of roots, leaves, branches, bark, seeds and other herbs are common by traditional healers. Rural populations often rely heavily on these traditional healers to address a variety of HIV symptoms including pain and neuropathic pain in HIV. In a study of TCAM and ARV adherence in KwaZulu-Natal, South Africa, Peltzer, Friend-dyuPreez, Ramlagan, Fomundam, & Anderson [10] suggested that the use of TCAM decreased significantly after initiation of ARV treatment with a decrease from 36.6% prior to initiation of therapy to 7.9% at 6 months after initiation of therapy. Faith healing methods (spiritual practices and prayer) decreased from 35.0% to 22.1% while the use of micronutrients (vitamins etc) increased from 42.6% to 87.4%. It is interesting to note that there have been intensive efforts to engage the approaches to western medicine with the traditional healing community in KwaZulu-Natal (Puone et al. [20]). It is well established in rural areas of South Africa, that traditional healing is a commonly used method of self-care and that often there is limited access to western medicine.

MATERIALS AND METHODS

Patients were selected from two HIV clinics in Durban, KwaZulu-Natal, South Africa (n=100). The sample was identified during routine clinic visits and the participants’ HIV status was verified by clinicians and medical record review. The participants were identified as living with HIV and/or AIDS and having a diagnosis of HIV-related peripheral neuropathy.

Study design, sample, and recruitment

This descriptive study used a cross-sectional self-report survey design to examine neuropathy characteristics, social support, illness characteristics and self-care management strategies. The parent study focused on the prevalence of HIV disease in a convenience sample of HIV-infected individuals who received care at clinics in rural KwaZulu-Natal, the epicenter of the HIV/AIDS epidemic in South Africa. Participants were recruited (n=100) and data were collected while they awaited clinic visits in the HIV clinic. Trained nurses or student nurses approached potential participants and requested their consideration of participation. Questionnaires were available in English and isiZulu. Instrument translation was accomplished with a forward and back translation by two HIV nurse researchers who were
fluent in the isiZulu language. The instrument was translated with all items equivalent in English and isiZulu. Completion of the questionnaires implied consent by participants. All participants received a voucher upon completion of the survey. Clinicians validated that the study participants had a diagnosis of HIV. The clinic staff also confirmed that respondents had neuropathic symptoms and pain based on medical record data. Some participants also had been diagnosed with TB (TB). Those individuals in the sample who had HIV as well as TB are known to be at increased risk of neuropathy and its painful sequelae.

**Measures**

Patients who met study criteria completed questionnaires on a demographic survey, the Sign and Symptom Checklist (SSC-HIVrev) (Holzemer et al, [21]), quality of life instrument (HAT-QoL), and a symptom management strategy instrument for neuropathy symptoms. Respondents were also asked about traditional healing practices for neuropathic pain.

**Demographic survey:** Demographic data including age, gender, income, race, marital status, and educational level were collected on the self-administered questionnaire. The demographic survey was developed in earlier work conducted by the University of California San Francisco HIV/AIDS International Nursing Network and has been used in five prior international research studies related to self-care symptom management.

**Sign and Symptom Checklist:** The Sign and Symptom Checklist (SSC-HIVrev) (Holzemer et al, [21]) is a list that captures the frequency and intensity of 64 common HIV signs and symptoms. The SSC-HIVrev consists of three parts: Part I has 45 HIV-related physical and psychological symptoms, with reliability estimates ranging from 0.76-0.91. Part II consists of 19 HIV-related symptoms that do not cluster into factor scores but may be of interest from a clinical perspective. Part III consists of eight items related to specific gynecological symptoms for women. Cronbach’s alpha factor reliability scores ranged from 0.85 to 0.90 for each of the factors and 0.92 for the overall 64-item instrument.

For the purposes of this study, the Peripheral Neuropathy Scale of self-care symptoms and self-care behaviors items were included to measure neuropathy symptoms and self-care behaviors. The Self-Care Symptom Management instrument was developed to measure HIV symptoms and self-care behaviors and is a reliable and valid tool for measuring symptoms (Holzemer, [22]). The self-care section describes self-care strategies for neuropathic symptoms, which were validated in previous studies.

To gather data on traditional healing, one open ended question addressed the following: Do you currently or have you ever used traditional healing to treat the symptoms of numbness or pain in your feet or hands?

**Measure of Physical Functioning, Psychological Functioning and Social Functioning:** Physical functioning, psychological functioning, and social functioning were measured using a 0 to 10 self-rating in response to the questions: How well do you see your physical functioning? How well do you see your psychological functioning? How well do you see your social functioning? The literature supports one item ratings of physical, psychological and social functioning as reliable and valid single-item measures of symptom severity, psychosocial functioning, and quality of life (Zimmerman et al. [23]).

**Ethical approval**

Ethical approval was obtained at the University of KwaZulu-Natal, at the Partners Healthcare Institutional Review Board at the Massachusetts General Hospital, and at the clinic settings in rural KwaZulu-Natal. A letter was provided to potential participants in English or isiZulu to describe the purpose of the study and informed consent was obtained verbally as approved by the institutional review boards at the University of KwaZulu-Natal, the clinic setting, and the Spaulding Rehabilitation Hospital. IsiZulu speaking nurses were available to discuss the study and translate the instrument for those participants who chose this method of completion of the questionnaire.

**Data Analyses:** Data were analyzed using PASW version 18.0. Descriptive statistics including frequencies, means, and standard deviations were performed. Correlation analyses were conducted to examine relationships among the study demographic and illness variables and prevalence of neuropathy. Social support, physical functioning and psychological functioning variables were also analyzed and correlations with demographic, illness and other variables were conducted.

**RESULTS AND DISCUSSION**

**Patient characteristics**

Seventy-five percent of the sample were women (n = 75) and with a mean age of 35.6 years (SD = 9.1). Fifty-four percent were of Zulu background and 22% were Xhosa background with others indicating South African, black, or Sesotho background. Seventy-one percent reported that they had primary or some secondary educational background. Eighty one percent reported that their income level was totally inadequate. Only 7% of the sample reported the use of tobacco.

**Prevalence of Peripheral Neuropathy**

A majority of the participants (n = 76; 76%) indicated that they experienced painful neuropathy symptoms which were described as intense, distressful, and which had great impact on their daily lives. Of those who reported neuropathy symptoms, most (n = 54) had symptoms from 4 to 7 days per week. The intensity of pain related to neuropathy was high with most indicating a pain rating score of greater than 6 (on a 0 to 10 pain rating scale). Twenty six percent of respondents reported that the distress level caused by their neuropathy symptoms was rated 10 (on a 0 to 10 scale with 0 = no distress and 10 = high distress). Fifty-eight percent of the study population indicated that painful neuropathy impacted their daily life to a great degree rating the impact at 6 or higher on a 10 point scale. For women, 78.1% reported their neuropathy symptoms as severe on most days, whereas only 21.9% of males reported their neuropathy as severe.

Analyses of physical functioning, psychological functioning, and social functioning: The physical functioning scores (mean physical impact of disease) were reported as high (M = 6.17, SD = 3.12) in the sample suggesting that individuals were struggling with physical care and symptoms including neuropathy. Twenty
six percent rated their physical functioning as 10 (highest impact of difficulty on physical functioning).

Social support scores were low in this sample (M= 5.03, SD = 3.40). Twenty seven percent of the sample (n = 27) reported their social support rating as 1 on a 1 to 10 scale, indicating very low social support. A total of 46% of the participants rated their social support as 4 or lower. The impact of HIV/AIDS on psychological functioning was also rated as high by most participants. Forty one percent of the sample rated the impact of their disease on their psychological functioning as 10 on a 1 to 10 rating scale. The mean impact score was 7.75 (SD = 2.55). Twenty six percent of the sample indicated that the impact on their physical functioning was rated as 10 on the 1 to 10 rating scale. Mean score on physical functioning was 6.17 (SD = 3.12). For those who reported both TB and HIV, there was a significant difference in psychological functioning (F=4.17, df =97, p=.04). There were no significant differences in physical functioning (F=2.03, df =97, p= .16), and social functioning (F=.079, df=97, p=.78). There was no difference in the number of days/week affected, intensity level, distress level or impact on daily life in HIV patients with neuropathy for those who reported co-morbid TB and those who did not report TB.

Traditional Healing and Neuropathic Symptoms: Of those who reported the use of traditional healing (n=30), 93.3% reported that this self-care strategy worked well (rating of 6-10 a 0 to 10 scale). This finding is similar to other recent studies (Peltzer et al. [10], Manglos et al. [24]) that indicate that traditional complementary and alternative medicine practices are commonly used in South Africa. Manglos et al. [24] and Peltzer et al. [10] reported that traditional healing remains widespread in Africa particularly for management of HIV symptoms.

DISCUSSION

We found that our sample of adults living with HIV in KwaZulu-Natal had a high frequency of self-reported neuropathic pain with pain intensity ratings as severe. The main findings indicated that participants reported low levels of social support, psychological functioning, and physical functioning. Regarding social support, since HIV disease remains a stigmatizing disease, particularly in South Africa, focusing on strengthening social support in those affected is important. In KwaZulu-Natal, and particularly in the rural areas that represent the epicenter of HIV in South Africa, social support may be limited due to low educational levels and lack of understanding of the transmission, course of HIV infection, treatments, and symptoms such as neuropathic pain that affect those with HIV/AIDS.

Peltzer’s study suggested that symptoms decreased over time for those on antiretroviral medication and there was a significant decrease in neuropathy of the feet/toes, legs, arms, and hands/fingers. As a cross-sectional study, our results cannot be generalized to time on antiretroviral medications, nor can symptom burden be attributed to immune status. Further research that controls for time on medications, comorbid conditions, and immune status is needed.

The use of traditional healing was reported by a third of the participants in the study. This prevalence of traditional, complementary, and alternative approaches (TCAM) is similar to the findings of Peltzer et al. [10] who reported that 35.6% of their sample of HIV patients in KwaZulu-Natal used TCAM. Peltzer and colleagues noted that use of traditional healing methods with the exception of micronutrients decreased after the initiation of ARV treatment, perhaps reflecting a reduction in symptoms such as painful neuropathic pain since there would likely be immune reconstitution which may result in alleviation of pain.

Of note, is that 75% of the sample were women. Most women indicated that they had severe neuropathy on most days of the week, while male respondents indicated that 28.8% had severe neuropathy. Some studies on peripheral neuropathy have suggested that males have a greater frequency of severe neuropathic symptoms, however this requires further investigation.

Since this study focused on the relationships of physical functioning, psychological functioning, and social functioning in patients living with HIV in KwaZulu-Natal, South Africa, it is interesting to note that all aspects that impact quality of life were reported as negatively impacted by HIV-related neuropathic symptoms. Physical functioning in this rural population was rated as low, which affected activities of daily living. Psychological functioning was also rated as low in this sample; it is known that stigma is common in rural KwaZulu-Natal, thus psychological functioning may be low due to the isolation of HIV disease. The highest mean score related to impact on daily life for the sample, thus indicating that neuropathic pain was a symptom limiting individuals’ quality of life.

Further study on the relationship of social support in HIV disease is needed to support those living with the disease and to decrease the stigma associated with HIV/AIDS. Education programs in KwaZulu-Natal are aimed at decreasing HIV transmission, but should also focus on supporting those infected/affected by HIV/AIDS. In addition, symptom management including limiting pain and neuropathy are critical in South Africa where few pharmacological and non-pharmacological treatments are available to treat neuropathic pain. Because TB is also a frequent co-morbid infection and TB medications may cause neuropathy, there may be an exponential effect on prevalence of neuropathy in those living with HIV in South Africa. Most importantly, social support is likely to be diminished for those living with neuropathic symptoms that may also limit mobility and access to social gatherings, work, and other activities.

LIMITATIONS

The limitations include the nature of the study as a pilot study with a convenience sample of 100 HIV-infected individuals. The results were also self-report in nature, although presence of peripheral neuropathy and HIV disease were validated by clinicians in the settings where data were collected. In addition, no objective assessment of neuropathy was obtained from participants. The lack of available treatments to manage neuropathic pain is a major challenge in South Africa.

CONCLUSION

Further study of the meaning of symptoms of neuropathy in African populations is also needed. Shaikh, Bentley, & Kamerman [6] investigated the symptomatology of peripheral neuropathy.
in Africa particularly because they note that "data on the prevalence and impact of pain of neuropathic origin in Africa are poor" (p. e63986). It is also important to note that developing accurate tools for the measurement of neuropathic pain that are accurate and capture cultural and language nuances is critical. For example, Shaikh, Bentley, & Kamerman [6] describe the complexity of translating existing tools when for example, South Africa has 11 official languages and that some adjectives may have subtle meanings and may lack sensitivity and specificity in other cultures. In their study, they found that knowledge and understanding of English terminology related to neuropathic pain was variable. They suggested that there was significant similarity in the term used to describe neuropathic pain, however further study of translation of English language instruments into African languages is critical.

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