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Effects of behavioral stress reduction Transcendental Meditation intervention in persons with HIV

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Stress is implicated in the pathogenesis and progression of HIV. The Transcendental Meditation (TM) is a behavioral stress reduction program that incorporates mind–body approach, and has demonstrated effectiveness in improving outcomes via stress reduction. We evaluated the feasibility of implementing TM and its effects on outcomes in persons with HIV. In this community-based single blinded Phase-I, randomized controlled trial, outcomes (psychological and physiological stress, immune activation, generic and HIV-specific health-related quality of life, depression and quality of well-being) were assessed at baseline and at six months, and were compared using parametric and nonparametric tests. Twenty-two persons with HIV were equally randomized to TM intervention or healthy eating (HE) education control group. Retention was 100% in TM group and 91% in HE control group. The TM group exhibited significant improvement in vitality. Significant between group differences were observed for generic and HIV-specific health-related quality of life. Small sample size may possibly limit the ability to observe significant differences in some outcomes. TM stress reduction intervention in community dwelling adults with HIV is viable and can enhance health-related quality of life. Further research with large sample and longer follow-up is needed to validate our results.

Keywords: HIV infection; stress reduction; Transcendental Meditation; health-related quality of life; immune activation

Introduction

The number of HIV/AIDS survivors in the USA has increased from 16,875 to 48,796 between 1993 and 2009 (CDC, 2012). Improved survival implies that persons with HIV are vulnerable to HIV-specific and non-HIV-specific conditions such as immune activation and impaired well-being (Desai & Landay, 2010; Kovacs et al., 2010).

Living with HIV involves facing psychological and physical stressors. Relationship between stress, HIV, and health is complex (Bonneau, Padgett, & Sheridan, 2007; Cohen, Janicki-Deverts, & Miller, 2007; Funaz et al., 2009). Studies have explored the association between stress management and psychosocial outcomes in HIV (Carrico et al., 2006; Leserman, 2008; Robinson, Mathews, & Witek-Janusek, 2003). Cortisol is used as a measure of physiological stress (Cruess, Antoni, Kumar, & Schneiderman, 2000; Cruess et al., 2000; Goodkin et al., 1996; Ironson et al., 1996; Leserman et al., 2002). Some studies indicate improved immunological function for stress management groups (Antoni et al., 1991; Creswell, Myers, Cole, & Irwin, 2009; Robinson et al., 2003), while others report improvements for intervention and control groups, or no effect (Coates, McKusick, Kuno, & Stites, 1989; LaPerriere et al., 1990).

Psychoneuroimmunology (PNI) theory provides a framework for analyzing stress–disease relationships (Hand, Phillips, Dudgeon, & Skelton, 2005). Transcendental Meditation (TM) is a behavioral stress-reduction program that incorporates mind–body approach. Studies suggest that TM may improve outcomes across various illnesses (Castillo-Richmond et al., 2000; Jayadevappa et al., 2007; Rainforth et al., 2007; Schneider et al., 2001). Objective of our Phase-I study was to evaluate the feasibility of TM intervention in persons with HIV and analyze the potential effects of stress reduction on psychosocial, hormonal, and immunological outcomes.

Methods

This two arm single blinded randomized control trial (RCT) was approved by the Institutional Review Board.
Board. All participants provided written consent. Persons with HIV satisfying following criteria were eligible: age ≥ 18 years; stable on antiretroviral treatment; CD4+ T-cell count > 300 and plasma viral load of < 200 copies/ml in the past six months; no Hepatitis C, non-diabetic; not on steroids; mini-
mental test score of ≥ 25; and not participating in other studies. Intervention group underwent the TM program of six-month duration. Control group underwent a healthy eating (HE) education program of comparable length and structure. We used a community-based recruitment initiative. Between April 8 and May 10, 2011, 50 persons contacted the study team, 34 underwent eligibility assessment, and 22 were random-
mized after baseline measurements (Figure 1).

The TM intervention was conducted by a certified instructor and comprised of two phases. Intensive phase consisted of five consecutive sessions of two-hour duration each day. Follow-up phase involved bi-weekly sessions for three months, followed by monthly sessions for additional three months. Participants were asked to practice TM twice a day for 20 minutes each over the study period.

The HE education control program was designed to mirror the effects of personal interaction and attention that are part of TM program. This course was conducted by a nurse and addressed more in-depth nutritional information than generally is provided in HIV care. Similar to TM intervention, intensive phase of HE program consisted of five consecutive sessions of two-hour duration each day. Follow-up phase involved bi-weekly sessions for three months, followed by monthly sessions for three additional months, and were conducted by the same nurse. Participants were asked to engage in an activity, e.g., reading, twice a day for 20 minutes during the study.

Outcomes

Outcomes were assessed at baseline and at six month. We conceptualized feasibility as response to recruit-
ment, and acceptability as study compliance.

Endocrine response was measured by serum norepinephrine and cortisol levels. Blood draws were done between 9 and 10 am and 25 μl of sera was used to quantify norepinephrine levels (BA E-5200 Rocky Mountain Diagnostics, 2012). Cortisol

![Recruitment flow diagram](image-url)
levels were quantified using assay from Parameter
Cortisol Assay (R & D Systems, 2011). Immune
activation was measured by expression of CD38 and
HLA-DR on CD4 and CD8 T cells and was analyzed
using FlowJo (Treestar, 2011).

Table 2. Comparison of outcomes.

<table>
<thead>
<tr>
<th>Variable (mean ± standard deviation)</th>
<th>Transcendental Meditation (n = 11)</th>
<th>Healthy eating (HE) (n = 11)</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Six month</td>
<td>Baseline</td>
</tr>
<tr>
<td></td>
<td>2.36 ± 1.30</td>
<td>2.21 ± 1.65</td>
<td>2.59 ± 1.17</td>
</tr>
<tr>
<td>Hormonal outcomes</td>
<td>1.05 ± 0.31</td>
<td>0.91 ± 0.58</td>
<td>0.93 ± 0.20</td>
</tr>
<tr>
<td>Cortisol (ng/ml)</td>
<td>19.6 ± 3.4</td>
<td>18.4 ± 5.0</td>
<td>18.6 ± 4.9</td>
</tr>
<tr>
<td>Norepinephrine (ng/ml)</td>
<td>18.4 ± 9.2</td>
<td>13.5 ± 11.5</td>
<td>19.7 ± 7.7</td>
</tr>
<tr>
<td>Psychological outcomes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PSS</td>
<td>60.9 ± 15.4</td>
<td>55.5 ± 24.84</td>
<td>48.3 ± 26.69</td>
</tr>
<tr>
<td>CESD</td>
<td>75.0 ± 40.3</td>
<td>70.5 ± 41.56</td>
<td>50.0 ± 41.46</td>
</tr>
<tr>
<td>FAHI</td>
<td>72.7 ± 41.68</td>
<td>75.8 ± 42.40</td>
<td>62.9 ± 35.14</td>
</tr>
<tr>
<td>Physical function</td>
<td>46.0 ± 19.42</td>
<td>69.9 ± 19.13</td>
<td>48.6 ± 25.15</td>
</tr>
<tr>
<td>Role physical</td>
<td>60.9 ± 15.14</td>
<td>74.1 ± 19.98</td>
<td>63.3 ± 18.54</td>
</tr>
<tr>
<td>Role emotional</td>
<td>60.2 ± 23.59</td>
<td>73.9 ± 24.66</td>
<td>63.9 ± 27.56</td>
</tr>
<tr>
<td>Vitality</td>
<td>51.4 ± 21.34</td>
<td>66.8 ± 18.48</td>
<td>70.0 ± 20.92</td>
</tr>
<tr>
<td>Mental health</td>
<td>29.2 ± 72</td>
<td>36.2 ± 4.2*</td>
<td>28.1 ± 0.23</td>
</tr>
<tr>
<td>Social function</td>
<td>28.1 ± 8.9</td>
<td>34.3 ± 6.0</td>
<td>25.7 ± 6.71</td>
</tr>
<tr>
<td>Bodily pain</td>
<td>34.6 ± 11.2</td>
<td>38.1 ± 10.1</td>
<td>34.6 ± 10.26</td>
</tr>
<tr>
<td>General health</td>
<td>22.4 ± 7.4</td>
<td>23.0 ± 9.3</td>
<td>18.7 ± 8.51</td>
</tr>
<tr>
<td>Cognitive functioning</td>
<td>8.7 ± 2.9</td>
<td>9.3 ± 2.9</td>
<td>8.6 ± 2.35</td>
</tr>
<tr>
<td>Total score</td>
<td>123.0 ± 28.2</td>
<td>140.8 ± 26.5</td>
<td>115.6 ± 25.27</td>
</tr>
<tr>
<td>Quality of well-being</td>
<td>0.69 ± 0.19</td>
<td>0.72 ± 0.22</td>
<td>0.60 ± 0.22</td>
</tr>
</tbody>
</table>

Note: *Significant at p < 0.05.
Results

Retention was 100% for TM group and 91% for control group, indicating good feasibility and acceptability of the intervention. Socio-demographic characteristics were comparable between groups (Table 1). Results of within-and-between group analyses are presented in Table 2. At follow-up, perceived stress in TM group was lower than baseline and remained mostly unchanged in the controls. Mean baseline cortisol was comparable between groups. Cortisol was somewhat lower in TM group at follow-up, and higher in the controls. Norepinephrine declined slightly in TM group, and remained unchanged in the control group. While there was no significant difference in level of T cell activation between groups, differences in TM group were closer to zero compared to the controls (Figure 2). Additionally, a two-part test comparing changes in T cell activation between groups found lower change in HD Effectors CD8+HLA-DR+CD38+freq of CD8+T cells for TM group (p = 0.0633), indicating possibility for immune activation stabilization.

For TM group, SF-36 domains of role emotional, vitality (p = 0.0133), mental health, social function, and general health showed improvement. General health improved in TM group, and declined in the controls (p = 0.0299). Among domains of FAHI, improvement in physical well-being was larger for TM group compared to controls (p = 0.0127). Between-group changes were significant for FAHI total score (p = 0.0393). Mean CESD score decreased in TM group and remained unchanged in the controls. The QWB improved in TM group, and declined in the controls.

Discussion

In this Phase-I, community-based RCT we observed the feasibility and acceptability of TM stress-reduction program in persons with HIV. The TM group exhibited significant improvement in generic and HIV-specific HRQoL. We noticed a pattern of improvement in physiological and psychological parameters in TM group. Some differences were
statistically nonsignificant, possibly due to small sample size and short follow-up.

Research using PNI framework reports benefits of stress reduction in HIV patients (Antoni et al., 1991; Coates et al., 1989; Ironson et al., 1996; Lutgendorf et al., 1997; McCain & Zelle, 1996). Stress reduction was associated with reduction in depression (Antoni et al., 1991; Lutgendorf et al., 1997), anxiety (Ironson et al., 1996; Lutgendorf et al., 1997), improvement in CD4 count (Antoni et al., 1991), Natural Killer (NK) cell number (Antoni et al., 1991), safer sexual practice (Coates et al., 1989), and emotional well-being (McCain & Zelle, 1996).

Per PNI theory, we conceptualized the pathway where psychosocial/psychological factors are immediately affected by stress. This may be one of the reasons why changes in generic and HIV-specific HRQoL and perceived stress were observed in TM group. Some studies have reported significant effects of stress reduction on cortisol (D. G. Cruess et al., 2000; S. Cruess et al., 2000; Ironson et al., 1996). However, our results are similar to studies that reported no significant change in cortisol (Leserman et al., 2002; McCain et al., 2003; Robinson et al., 2003). Reasons for differential findings may be sample size, length of follow-up, type of sample (serum, salivary, or urine), time of measurement, and length of HIV-infection.

This is the first study to explore application of TM in community-dwelling adults with HIV and adds to the existing evidence regarding association between stress and outcomes. Unique features of our study are RCT design and assessment across all domains of PNI framework. We note following study limitations. Small sample size may possibly limit the ability to observe significant differences in some outcomes. Also, data about mental health treatment or other stress reducing activities of participants were not collected. Finally, those who participated may be more committed to behavior change, leading to self-selection bias.

Increasing numbers of HIV survivors are facing psychological and physical stressors with debilitating effects on health outcomes. Thus, addressing stress reduction in persons with HIV is critical. Our research shows that behavioral stress reduction TM intervention was acceptable in persons with HIV and improved generic and HIV-specific HRQoL. Future research should validate our findings, and help establish TM in particular, and stress reduction in general, as a complementary technique in the battle against HIV.

Acknowledgements

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