Group Stress Management Helps Reduce HIV Viral Load

BY DAMIAN McNAMARA
Miami Bureau

MARCO ISLAND, FLA. — Semistructured group therapy improves mood state in HIV-positive men, which improves cortisol levels and immune function and thereby reduces viral load, Karl Goodkin, M.D., said at the annual meeting of the Academy of Psychosomatic Medicine.

Bereavement has long been known to be associated with immunosuppression and is also associated with increased mortality risk for surviving partners. The risk increases 40% for the first 6 months and 10-fold in the first year, the same time frame as observed decrements in the immune system, said Dr. Goodkin, professor of psychiatry and behavioral sciences, neurology, and psychology at the University of Miami.

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In a randomized controlled trial, Dr. Goodkin and his colleagues compared the intervention with usual care in HIV-positive and HIV-negative gay men who had experienced a loss in the previous 6 months. Although effects of grief were similar, the two-tier group intervention decreased overall psychological stress—which improved mood and immune measures, including CD4 counts and viral loads—and reduced physician health visits, compared with the usual-care control group.

Participants attended a 90-minute session once weekly for 10 weeks. The groups consisted of 6-10 attendees and two professional coleaders. Enrollment was ongoing throughout the study. The first tier of the intervention fostered grief resolution; the second tier fostered stressor management, including identification of stressor impact and maladaptive behaviors. In addition to specific grief-related topics for each session, including past experiences of personal loss, reactions to surviving and implications for one's spirituality and mortality, non–bereavement-related stressor management was planned as a major focus of this unique group intervention, he said.

The usual-care group received any medical and psychosocial care that they had begun prior to initial assessment. Furthermore, they received four telephone calls during the 10-week intervention period to assess their clinical status. The total time for these calls was limited to 90 minutes over the 10-week period. Study staff avoided any therapeutic interactions during these calls and maintained a log documenting call content.

In the study, 166 participants (97 HIV-positive and 69 HIV-negative) completed the intervention or community usual-care group conditions. Participants were primarily in their late 30s, employed, and college educated. More than one-third were members of an ethnic minority.

The Stressor-Support-Coping model appears to have utility "with or without bereavement. We found increase in positive life events in HIV-positive men after the intervention. Social support increased in the intervention group and declined in controls," Dr. Goodkin noted.

The investigators' theoretical model also predicts specific psychosocial treatment needs. If a person has a high life-stressor burden, stressor management would help. If a person has low social support, a social support group would be beneficial. Finally, if a participant demonstrated high passive maladaptive coping or low active coping, coping skills enhancement training would be helpful.

Evidence from the study suggests that increased serum cortisol from stress is associated with decreases in lymphocyte proliferation in response to the artificial stimulant phytohemagglutinin in HIV-positive men and women. This is a functional measure of immunity that tends to decrease before CD4 count, he said.

The intervention decreased overall psychological distress in HIV-negative men, compared with controls, according to scores on the Distress-Grief Composite Measure. However, the decreases in grief, specifically, were less prominent than those for distress or the composite of the two measures for both the HIV-positive and -negative men.

In terms of immune effects, HIV-positive people had a true increase in their lymphocyte proliferation response up to 2 years, and the intervention provided HIV-positive participants with a buffer against decreases in CD4 levels seen in controls. The decrement among HIV-positive participants was smaller, compared with HIV-negative groups, where there was a larger spread, Dr. Goodkin explained.

The researchers also looked for an effect at the physical health level. "There was a transition of the neuroendocrine changes to the immune level and, in turn, to the physical health level,"

All participants were asked to self-report physician health care visits in the 6 months prior to assessment; among HIV-positive participants, there was an increase in the control group that was not as great in the intervention group. Researchers found that the same pattern held true among HIV-negative individuals. There was increased health care utilization among control participants and a decrease among the intervention group. "We did not anticipate this. It indicated that this type of intervention is not only effective for improving the health of HIV-positive people but possibly for the entire population of people who lose a loved one," he said.

Researchers were not able to analyze whether all health care visits were HIV or symptom related, an important caveat of the study. Another potential limitation was the difference in atmosphere between HIV-positive and HIV-negative group sessions. "HIV-positive groups talked more about concerns around their own mortality, but nonetheless it is important to note the consistency in findings across multiple domains, especially the physical domains," Dr. Goodkin said.

"That suggests that if you improve mood state, you will improve cortisol, and you will improve immune function, which relates to improvements in viral load," he said. The virology effect of the behavioral intervention was statistically significant, and Dr. Goodkin suggested that "it may ever be clinically significant, but we need to look at the latter effect on viral load seen in a subgroup over the long term in larger study groups." ■

New HIV Regimen Beats Standard Combination Therapy at 24 Weeks

BY MITCHEL L. ZOLER
Philadelphia Bureau

WASHINGTON — A new triple-therapy regimen for initial treatment of HIV-infected patients outperformed the conventional combination regimen in a preliminary 24-week analysis of a phase III trial with 509 patients.

If the results hold up for the study's prespecified 48-week duration, the new regimen "could change the standard of care," Scott M. Hammer, M.D., said at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy. "But 24-week data are too soon to judge," added Dr. Hammer, chief of infectious diseases at Columbia-Presbyterian Medical Center in New York City.

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The new regimen consisted of the nucleotide reverse-transcriptase inhibitor tenofovir (Viread), the nucleoside reserve-transcriptase inhibitor emtricitabine (Emtriva), and the nonnucleoside reverse-transcriptase inhibitor efavirenz (Sustiva). All three drugs were administered once daily, with tenofovir and emtricitabine combined into a single pill. The standard regimen that the new trio was compared against consisted of the nucleoside reverse-transcriptase inhibitors zidovudine (AZT) (Retrovir) and lamivudine (3TC) (Epivir), used in the single-pill formulation Combivir and administered b.i.d, along with efavirenz, given once daily.

The study, designed as a noninferiority trial, was sponsored by Gilead Sciences; Gilead markets both tenofovir and emtricitabine, as well as Truvada, the single-pill combination of 300-mg tenofovir and 200-mg emtricitabine. The study's primary end point was the time to loss of virologic response, an end point now required by the FDA for newly approved antiretroviral drugs. All five drugs included in the study are already approved as individual agents for use in the United States, and Combivir and Truvada also have FDA approval.

The edge that the new regimen had over the standard combination of zidovudine, lamivudine, and efavirenz seemed linked to tolerability and adherence. Among the 255 patients treated with tenofovir, emtricitabine, and efavirenz, 11% stopped taking their regimen during the first 24 weeks, compared with 21% of the 254 patients assigned to the standard regimen. The excess of dropouts was primarily due to adverse events, which led to 3% of patients stopping treatment in the tenofovir and emtricitabine arm, and 9% halting treatment in the zidovudine and lamivudine arm.

The most common adverse events in the zidovudine and lamivudine arm were anemia (5%), nausea, (2%), fatigue (1%), and vomiting (1%).

"The convenience and tolerability of an antiretroviral regimen is increasingly important, as patients remain on therapy for longer periods of time," said Brian Gazzard, M.D., a physician at Chelsea and Westminster Hospital in London, who presented the results at the conference. "Although both triple-drug regimens are relatively convenient, we observed a difference in the two arms, with more patients discontinuing in the Combivir group due to adverse events."

At 24 weeks, 87% of the patients treated with tenofovir and emtricitabine achieved and maintained a viral load of fewer than 400 copies of viral RNA/mL, and 73% achieved and maintained a viral load of fewer than 50 copies/mL. Among the patients treated with zidovudine and lamivudine, 78% maintained a viral load of fewer than 400 copies/mL, and 65% maintained a viral load of fewer than 50 copies/mL. The differences between the two regimens were statistically significant for both measures, Dr. Gazzard said at the conference, sponsored by the American Society for Microbiology.

Because the analyses were done on an intention-to-treat basis, with dropouts considered treatment failures, most of the difference between the two regimens was due to the difference in dropout rates.

Patients in the tenofovir and emtricitabine group also had a better immunologic response, gaining an average of 129 CD4 cells/ L, compared with an average gain of 111 cells/ L in the control arm, a statistically significant difference.

The two regimens showed no difference in the rate of emergence of drug-resistant virus. ■