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Department of Psychology
P.O. Box 248185
Coral Gables, FL 33124-2070
Telephone (305) 284-2814
Fax (305) 284-3402

Cognitive-Behavioral Stress Management Reduces Serum Cortisol By Enhancing Benefit Finding Among Women Being Treated for Early Stage Breast Cancer

DEAN G. CRUESS, PHD, MICHAEL H. ANTONI, PHD, BONNIE A. MCGREGOR, MS, KRISTIN M. KILBOURN, PHD, AMY E. BOYERS, MS, SUSAN M. ALFERI, MS, CHARLES S. CARVER, PHD, AND MAHENDRA KUMAR, PHD

Objective: This study examined the effects of a cognitive-behavioral stress management (CBSM) group intervention on serum cortisol levels in women being treated for stage I or II breast cancer. **Methods:** Participants were randomly assigned to undergo a 10-week intervention ($N = 24$) within 8 weeks after surgery or were placed on a waiting list ($N = 10$). Cortisol was assessed by means of a radioimmunoassay of blood samples collected at the same time of day just before the start of the intervention and immediately after its completion. The women also reported the degree to which breast cancer had made positive contributions to their lives. **Results:** Intervention participants showed increased benefit finding and reduced serum cortisol levels, whereas control subjects experienced neither change. Path analysis suggested that the effect of CBSM on cortisol was mediated by increases in benefit finding. **Conclusions:** These findings suggest that positive growth enhanced during a time-limited intervention can influence physiological parameters such as cortisol among women with early stage breast cancer. **Key words:** breast cancer, cortisol, benefit finding, cognitive-behavioral stress management.

CBSM = cognitive-behavioral stress management;
BFS = Benefit Finding Scale; POMS = Profile of Mood States.

INTRODUCTION

Alterations in hypothalamic-pituitary-adrenal axis functioning have been reported in women with breast cancer, including flattening of the circadian rhythm of cortisol secretion (1) and elevated plasma cortisol levels (2). Such differences may be due to disease- or treatment-related effects on endocrine regulation or perhaps due to the psychological challenges that breast cancer patients must deal with in their daily lives. Breast cancer patients confront a cascade of stressors, including the diagnosis itself, ongoing intrusive medical procedures and severe side effects of treatment, and a variety of personal, psychological, and physical losses (3, 4). Many studies have shown that adjuvant psychological interventions can reduce distress, anxiety, and depressed

mood and enhance quality of life among women with breast cancer (5, 6).

Far less research has examined change in indicators of hypothalamic-pituitary-adrenal axis activation. One study reported reductions in plasma cortisol levels in breast cancer patients completing a 13-week supportive group intervention (7). Postsurgical breast cancer patients in a 10-week psychological intervention displayed decreased plasma cortisol and increased circulating lymphocytes (8). Interestingly, neither of these studies showed cortisol reductions to be accompanied by a change in distress, suggesting that other psychosocial changes may have been at work.

Although a diagnosis of cancer is stressful and disruptive at many levels, the experience of having cancer may have sequelae that patients view as positive or beneficial. A number of patients report improved personal resources and skills, an enhanced sense of purpose, increased spirituality, closer relations with significant others, and changes in their life priorities (9). Although these changes apparently occur spontaneously in some cases, some have suggested that clinical intervention may foster this process (10). Breast cancer patients who participated in a CBSM intervention reported increased positive contributions from breast cancer (11). Might these positive growth experiences promote beneficial physiological changes? We are aware of no study that has considered this possibility. In the current study, we tested the impact of a CBSM intervention on serum cortisol levels and the relationship between changes in cortisol and reports of benefit finding.

From the Departments of Psychology (D.G.C., M.H.A., B.A.M., K.M.K., A.E.B., S.M.A., C.S.C., M.K.) and Psychiatry (M.H.A., M.K.), University of Miami, Miami, FL.

Address reprint requests to: Michael H. Antoni, PhD, Department of Psychology, University of Miami, Coral Gables, FL 33124-2070. Email: mantoni@umiami.ir.miami.edu

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METHODS

Subjects

Participants were recruited chiefly by physician referral. Subjects were women diagnosed with stage 1 or 2 breast cancer recruited within 8 weeks after surgery. Potential participants were excluded if they had a previous cancer diagnosis, a history of psychiatric illness, a major concurrent disease, or were not fluent in English. The main goal of the intervention was to assist women in their adjustment to early stage breast cancer by helping to reduce distress and increase positive contributions of living with breast cancer. Partway through the study recruitment period, participants provided additional data related to physiological functioning. These participants ($N = 34$) are the focus of this report. Serum cortisol was specifically added as an objective physiological indicator of both distress reduction and enhanced benefit finding from breast cancer. Participants who provided additional data for the current study did not differ from the larger sample ($N = 120$) at baseline on any of the pertinent demographic or outcome variables (p values $> .10$).

The majority of participants were white ($N = 23$) or Hispanic ($N = 6$). Most were employed full-time ($N = 30$). Twenty-one were married or in an equivalent relationship, and 13 were single, widowed, divorced, or separated. Mean age was 45.65 years ($SD = 7.61$ years), and educational level averaged 15.50 years ($SD = 2.22$ years). The women reported consuming an average of 1.85 ($SD = 3.05$) alcoholic beverages per week, with 18 women reporting no alcohol use. The majority of women ($N = 26$) were nonsmokers. Average coffee consumption was 6.03 ($SD = 7.20$) cups per week. The sample was evenly divided between women with stage I ($N = 17$) and stage II disease ($N = 17$). Nodal involvement ranged from 0 to 6 (mean = 0.63, $SD = 1.29$). None of these demographic, health behavior, or medical variables differed significantly between the CBSM and control groups (p values $> .10$). No health behavior or medical variables significantly changed over the 10-week span of the intervention (p values $> .10$).

Fourteen of the women had lumpectomies, 15 had mastectomies, and 5 had bilateral mastectomies. Before the study, 13 women had adjuvant therapy (chemotherapy, 11; radiation, 1; and tamoxifen, 1). The CBSM and control groups did not differ at baseline or at postintervention assessment on adjuvant therapy status or type of cancer treatment (p values $> .10$). There was also no reported change in adjuvant therapy status or cancer treatment across the 10-week intervention ($p > .10$).

Procedures

At baseline (time 1), participants signed an informed consent form, completed questionnaires assessing their psychological responses to having been treated for breast cancer, and provided a blood sample for an endocrine assay. The women were randomly assigned to undergo the CBSM intervention ($N = 24$) or placed on a waiting list (control, $N = 10$). After the intervention or 10-week wait-list period (time 2), participants completed a second assessment and provided another blood sample. To control for the diurnal rhythm of cortisol, all blood was collected at the same time of day (6:00 PM) at both time points.

The intervention was a group-based CBSM program consisting of 10 weekly meetings of approximately 2 hours each. It included both stress management (eg, cognitive restructuring, coping skills training, assertiveness, anger management, and social support utilization skills) and relaxation training components (eg, progressive muscle relaxation, meditation, abdominal breathing, and guided imagery). Group discussions included personal experiences, experiential exercises, role-playing, and review of homework exercises emphasizing

stress management concepts and relaxation practice. Groups were led by a postdoctoral fellow and an advanced clinical psychology graduate student (both female) and were audiotaped; tapes were reviewed by a licensed clinical psychologist to ensure compliance with the treatment protocol. After time 2 assessments were completed, control subjects were offered a 1-day stress management seminar incorporating techniques similar to those provided during the CBSM intervention.

Measures

Cortisol. Cortisol was measured in serum by means of radioimmunoassay using a commercially available kit (DSL-2100, Diagnostics Systems Laboratory). Intra- and interassay sensitivity of the kit are 8.4% and 9.1%, respectively. To control for time of menses, we also assayed for estradiol levels using an additional kit (DSL-4400, Diagnostic Systems Laboratory, Webster, TX). Intra- and interassay sensitivity of this estradiol kit are 5.3% and 8.1%, respectively.

Benefit finding. Perceived positive contributions were assessed using the BFS (11), which consists of 17 items scored on a five-point scale. Each item is a statement beginning "Having had breast cancer has . . ." and ending with some positive gain from the experience. The items assess a variety of positive domains, including acceptance (eg, "has led me to be more accepting of things"), interpersonal growth (eg, "has brought my family closer together"), and a stronger sense of purpose in life (eg, "has helped me become more focused on priorities, with a deeper sense of purpose in life"). The internal consistency of the BFS averaged across assessments is 0.95 (11).

Distress. We also monitored distress levels with an abbreviated version of the POMS (12), which assesses mood on several dimensions during the past week using self-descriptive adjectives rated on a five-point scale. This 22-item version of the POMS, developed by Carver et al. (13), has been widely used in studies of interventions with breast cancer patients. As in prior studies, we used a total composite distress score, which includes anxious, depressed, and angry mood states. The average α value of this POMS scale is 0.86 (11).

RESULTS

We examined relationships between the outcome measures (cortisol, BFS, and POMS) and a number of demographic, health behavior, and medical variables (eg, age, ethnicity, education, employment status, marital status, menopausal status, aerobic exercise, alcohol use, tobacco use, caffeine consumption, amount of sleep, cancer stage, surgical procedure, chemotherapy status, radiation therapy status, tamoxifen use, and positive nodes) to determine potential control variables. Age was significantly related to change in cortisol ($r = -.36$, $p < .04$), as was menopausal status ($r = .35$, $p < .05$), alcohol use ($r = -.35$, $p < .05$), chemotherapy ($r = 0.34$, $p < .05$), and estradiol change ($r = 0.44$, $p < .02$). These variables were used as covariates in cortisol analyses. None of the other demographic, medical, or treatment variables were significantly related to changes in cortisol or the psychosocial measures (p values $> .10$).

Intervention Effects

The intervention and control groups did not differ at baseline on any of the outcome variables ($p > .10$). An analysis of covariance was used to test for a posttreatment difference between the CBSM and control groups, controlling for pretreatment values. There was a significant difference in postintervention BFS scores between the CBSM (mean = 61.54, SD = 13.66) and control groups (mean = 48.31, SD = 13.47), controlling for baseline scores (CBSM: mean = 54.18, SD = 13.78; control: mean = 51.50, SD = 15.13; $F(1,31) = 9.08, p < .01$).

There was also a significant difference in postintervention cortisol levels between the CBSM (mean = 4.66, SD = 2.08) and control groups (mean = 6.15, SD = 2.49), controlling for baseline cortisol levels (CBSM: mean = 6.14, SD = 3.12; control: mean = 6.68, SD = 3.44), age, change in estradiol levels, alcohol use, chemotherapy status, and menopausal status ($F(1,27) = 4.59, p < .05$).

There was no significant difference in postintervention POMS scores between the CBSM (mean = 5.38, SD = 2.89) and control groups (mean = 5.23, SD = 4.09), controlling for baseline scores (CBSM: mean = 4.90, SD = 2.38; control: mean = 5.17, SD = 3.21; $F(1,31) = 0.17, p = .68$). No significant relationship was observed between changes in cortisol and POMS scores across the intervention period ($r = -.07, p > .10$).

Relationship Between Serum Cortisol and Benefit Finding

We examined the relationship between change in BFS scores and cortisol levels by first computing a residualized change score regressing postintervention cortisol levels on initial cortisol levels. This residualized change score was then regressed on change in BFS scores, controlling for age, change in estradiol levels, alcohol use, chemotherapy status, and menopausal status. Greater increases in the BFS score were associated with greater cortisol reductions ($\beta = -0.50, p < .01$). Examination of a scatterplot of the data determined that the association was not driven by outliers in the distribution.

Finally, we tested a model (Figure 1) in which PCS scores were hypothesized to mediate the effect of CBSM on cortisol reduction. There were significant associations between group assignment and PCS change ($\beta = -0.36, \text{adjusted } R^2 = .53, p < .01$), group assignment and residualized cortisol change ($\beta = 0.33, \text{adjusted } R^2 = .27, p < .05$), and residualized cortisol and BFS change ($\beta = -0.50, \text{adjusted } R^2 = .39, p <$

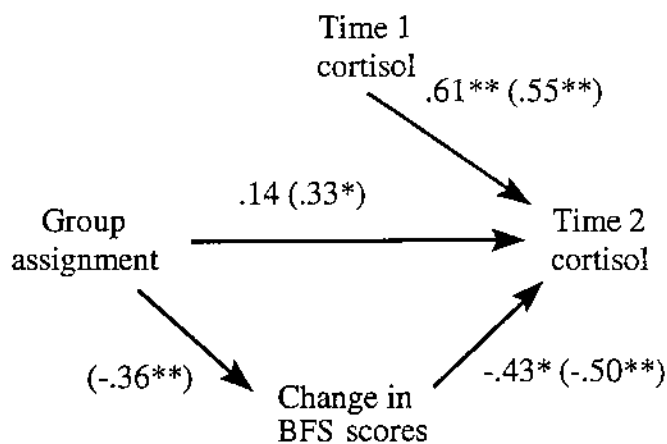


Fig. 1. Path model testing the mediating effect of change in Benefit Finding Scale (BFS) scores on the relationship between group assignment (CBSM vs. control) and serum cortisol change. Simple associations are shown within parentheses, and standardized regression coefficients from the full model are shown outside parentheses. $*p < .05$; $**p < .01$.

.01). Thus, conditions for testing a mediational model were satisfied (14). When BFS change scores were entered into the equation as a potential mediator before entering in group assignment in the overall model, the relationship between group assignment and cortisol levels decreased substantially, becoming nonsignificant ($\beta = 0.14, \text{adjusted } R^2 = 0.38, p > .30$). The amount of variance in residualized cortisol change accounted for in the path analysis significantly increased from 27% to 38% when change in BFS scores was entered into the overall model ($\Delta R^2 = .11, \Delta F(1,25) = 5.92, p < .03$). However, the relationship between BFS change and residualized cortisol change remained significant ($\beta = -0.43, \text{adjusted } R^2 = .38, p < .03$). This provides support for the notion that increases in the BFS may function as a mediator of CBSM-associated cortisol reductions.

DISCUSSION

This study documented significant physiological changes during a psychosocial intervention among women diagnosed with early stage breast cancer. We found that participants attending a 10-week group CBSM intervention had lower cortisol levels than control participants. Interestingly, the cortisol changes were not related to differences in distress. These two findings, an effect of therapy on cortisol and an absence of a relation with distress reduction, replicate data reported from other studies (7, 8). This is the first study, however, to show that intervention-induced positive growth changes are related to cortisol reductions. The positive responses examined here were par-

participants' perceptions of positive contributions in their lives (enhanced sense of purpose and meaning, better family relationships, and altered life priorities) arising from the cancer diagnosis. Path analysis demonstrated that CBSM-related cortisol reductions could be explained, in part, by the intervention's impact on such positive contributions.

The main goals of the intervention were to help reduce distress and to enhance benefit finding. Measures of such positive changes may permit assessment of variations in well-being even in circumstances in which distress is relatively low. This suggests that the lack of a relationship between distress and cortisol in prior breast cancer research, as well as the present study, was a consequence of low levels (and low variability) of distress. Another possible explanation for the low levels of distress and lack of change across the intervention may be that the POMS measures acute distress over the past week; multiple assessments over longer periods of time may be a better gauge of chronic distress. This also suggests that elevated cortisol activity may reflect a lack of positive affect or positive engagement. Evidence consistent with this reasoning has been obtained in recent work that measured positive affect and cortisol among healthy persons. Two studies induced increases in positive affect and reductions in cortisol by having participants' view a humorous video (15, 16). Another study assessed stressors and cortisol over a 2-day monitoring period and found that positive affect was related to lower cortisol (17). These findings, in conjunction with those reported here, suggest a link between positive experiences and cortisol.

The current study has some limitations that should be addressed in future work. First, the sample consisted of relatively healthy, highly educated women, which limits the generalizability of the findings. Second, this study did not compare the CBSM intervention with other treatments, which makes it difficult to determine which treatment component (eg, relaxation or stress management) was responsible for the enhancement in positive contributions and for reductions in cortisol. Third, we focused on changes in a relatively small sample across a 10-week period, which limited our ability to examine the clinical relevance of the effects of intervention, such as increased antitumor immunity, delayed time to recurrence, or enhanced survival. Fourth, the BFS includes only "positive" items, whereas an assessment of "negative" experiences might help clarify the relationship between cortisol and the total experience of being diagnosed with breast cancer. Future work should follow a larger sample over a longer term to examine relations between intervention-induced positive growth and

physiological response patterns over time as well as the clinical significance of these associations.

The results of this study have important implications for future research. Glucocorticoids have immunosuppressive effects (18), and CBSM interventions influence both cortisol (7, 8, 19) and immune functioning (20, 21). There is also recent evidence linking positive affect to enhanced immune functioning (22, 23). The overall pattern of evidence suggests the possibility that psychosocial interventions might influence immune functioning in cancer patients by fostering growth and modulating cortisol levels. Future research is needed to decipher these types of mechanisms.

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ERRATUM

In the Presidential Address entitled, *Stalked by the Past: The Influence of Ethnicity on Health* (2000;62:161-70), which appeared in the March/April 2000 issue, under the heading "Salt and Slavery" on page 164, the term ABP should read Δ BP.

The sentences should read: The Δ BP (high salt minus low salt) was calculated for each of our four patient subgroups. This Δ BP is one way of defining salt sensitivity.

We regret this error.