
REVIEW ARTICLES

Depression in women with metastatic breast cancer: A review of the literature

AUDE CAPLETTE-GINGRAS, B.A.,^{1,2} AND JOSÉE SAVARD, PH.D.^{1,2}

¹School of Psychology, Université Laval, Québec, Québec, Canada

²Laval University Cancer Research Center, Québec, Québec, Canada

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ABSTRACT

Objective: The aim of this article is to review the available literature on depression in women with metastatic breast cancer in terms of prevalence, potential risk factors, and consequences, as well as pharmacological and psychological interventions.

Method: An extensive review of the literature was conducted.

Results: The prevalence of depression appears to be especially elevated in patients with advanced cancer. Many demographic, medical, and psychosocial factors may increase the risk that women will develop depressive symptoms during the course of their illness. Despite the fact that depression appears to be associated with numerous negative consequences, this disorder remains underdiagnosed and undertreated. Both pharmacotherapy and psychotherapy have been found to treat effectively depressive symptoms in this population, but cognitive-behavioral therapy appears to be the most cost-effective approach.

Significance of results: Areas for future research are suggested.

KEYWORDS: Metastatic breast cancer, Depression, Correlates, Psychotherapy, Pharmacotherapy

INTRODUCTION

Depression is the psychiatric disorder that has received the most attention among cancer patients, particularly among breast cancer patients. In a recent literature review, Massie (2004) reported a prevalence rate of depression among women with breast cancer that varied between 1.5% and 46% across all stages of the disease. When the authors made a distinction between the prevalence of major and minor depression (e.g., clinically significant depressive symptoms, dysthymia, adjustment disorder with depressed mood or with mixed anxiety and depressed mood), it appeared that between 2% and 9.6% of women with breast cancer met the criteria for major depression, whereas between 24% and 57% suffered from minor depression (Sachs et al.,

1995; Aragona et al., 1996; Pasacrete, 1997; Kissane et al., 1998).

Compared to breast cancer patients at other stages of the disease (Massie, 2004), patients receiving palliative care appear to be more affected by depression. For example, Ciaramella and Poli (2001) evaluated the prevalence of major depression in 100 cancer patients with various types of cancer and stages. Patients with distant metastases (30%) showed a significantly higher prevalence of major depression. In fact, a review of the literature indicates that among this group the prevalence of major depression as assessed by a diagnostic interview varies between 5% and 26% with a mean of 15% (Hotopf et al., 2002).

Some studies have looked at the prevalence of depression specifically among women with metastatic breast cancer. However, most of these studies used the depression subscale from the Hospital Anxiety and Depression Scale (HADS-D; Zigmond & Snaith, 1983) rather than a diagnostic interview. By using a

Address correspondence and reprint requests to: Josée Savard, Laval University Cancer Research Center, 11 Côte du Palais, Québec, Québec, G1R 2J6, Canada. E-mail: josee.savard@psy.ulaval.ca

clinical score of 11 on the HADS-D, a prevalence of depression varying from 7% to 12.5% was observed across studies (Hopwood et al., 1991b; Pinder et al., 1993; Fulton, 1997, 1998; Love et al., 2004). To our knowledge, only one group of researchers (Kissane et al., 2004; Love et al., 2004) has evaluated the prevalence of depressive disorders in women with metastatic breast cancer using a structured interview based on the *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV;* American Psychiatric Association, 1994). Thirty-two percent of the 227 women interviewed met the diagnostic criteria for a depressive disorder: 7.0% with major depression, 25.5% with another depressive disorder (mostly an adjustment disorder with depressed mood or with mixed anxiety and depressed mood) and 1.3% with dysthymia. Another study by Okamura et al. (2005) used the criteria of the DSM-III-R and the DSM-IV to evaluate the prevalence of psychiatric disorders in 50 women with a first recurrence of breast cancer (98% were metastatic). Only 2% of the participants met the criteria for major depression, and 18% had an adjustment disorder with depressed mood or with mixed anxiety and depressed mood.

In sum, few studies have until now looked at the prevalence of depression in women with metastatic breast cancer, and the results vary importantly from one study to the other. However, together these studies indicate that the prevalence of depression appears to be elevated among this population. Besides the diversity of measures, diagnostic criteria, and clinical thresholds which were used, the high variability in the results may be largely accounted for by participants' characteristics (e.g., age) as well as the time when the evaluation took place (e.g., soon following a diagnosis of metastasis, during palliative care, at the end of life). In fact, several factors associated with metastatic breast cancer may increase the likelihood of developing depressive symptoms.

RISK FACTORS AND CORRELATES

Medical

Severity of the Illness

As already mentioned, several studies suggest that cancer stage is a factor strongly associated with depression (Spiegel, 1993; Massie et al., 1994). The type of metastasis may also influence the presence of depressive symptoms given its strong association with prognosis. However, very few studies have investigated this hypothesis, and no evidence of an association was found (Pinder et al., 1993; Okamura et al., 2005).

It has also been suggested that the progression of the disease toward a terminal stage may be associated with an increase in psychological distress. For example, a study conducted by Butler et al. (2003) on 59 women with metastatic breast cancer showed that psychological distress, as measured by the Profile of Mood States (POMS; McNair et al., 1971), remained generally stable or decreased during the course of the disease, but increased significantly in the few months preceding death. In the cross-sectional study by Pinder et al. (1993), patients with advanced breast cancer who died in the month after they had completed the HADS-D displayed significantly more depressive symptoms compared to patients who survived longer. Finally, a study by Hopwood et al. (1991a), which also used the HADS-D on women with an advanced cancer, showed that the prevalence of depressive symptoms in patients who died during the course of their study was higher than in patients who survived longer, although this difference was not statistically significant.

Physical and Psychophysiological Symptoms

Only some studies have investigated the relationship between physical symptoms and depression in women with metastatic breast cancer, and the significant factors are noticeably the same as in the general cancer population (Ciaramella & Poli, 2001; Carpenter et al., 2004; Bender et al., 2005; Mystakidou et al., 2005a; Reuter et al., 2006). More precisely, pain (Hopwood et al., 1991a), fatigue (Kissane et al., 2004), insomnia (Koopman et al., 2002), an altered level of functioning (Hopwood et al., 1991a; Pinder et al., 1993), as well as shortness of breath and gastro-intestinal symptoms (Hopwood et al., 1991a; Fulton, 1997) have all been associated with increased depression in women with metastatic breast cancer. However, none of these cross-sectional studies permits us to establish a causal relationship between these factors and the development of depression. Stommel et al. (2004) assessed the longitudinal evolution of symptoms in 860 patients over the age of 65 suffering from a variety of cancers (i.e., breast, colon, lung, prostate). The analyses indicated that the severity of physical symptoms (e.g., nausea, pain, loss of appetite, fatigue, diarrhea) was a strong predictor of depressive symptoms in this population.

Cancer Treatments

The handful of studies that have looked at the impact of palliative treatments (i.e., hormone therapy, chemotherapy, Herceptin) on psychological distress suggest that chemotherapy may be associated with a higher prevalence of depression among women with advanced breast cancer (Miranda et al., 2002;

Okamura et al., 2005). Specifically, in the prospective study conducted by Miranda et al. (2002), the proportion of women with stage IIB and III breast cancer who were suffering from depression increased following their chemotherapy treatments, although this increase was not significant. The study by Okamura et al. (2005) examined the presence of mood and anxiety disorders, as evaluated by the Structured Clinical Interview for DSM-III-R (SCID) (Spitzer et al., 1990), among 50 women with breast cancer, mostly metastatic. The fact of receiving a certain type of chemotherapy (i.e., a combination of doxorubicin and cyclophosphamide) but no other type of treatment (docetaxel, paclitaxel, radiotherapy, hormone therapy) was significantly associated with the presence of a psychiatric disorder. A study by Byar et al. (2006) indicated that depressive symptoms as evaluated by the HADS-D reached their peak at the time of the fourth chemotherapy treatment and tended to return to baseline level 2 months after the end of the treatments.

On the other hand, Stommel et al. (2004) observed no effect of treatment (surgery, radiotherapy, chemotherapy) on psychological variables, and another study (Mystakidou et al., 2005a) found that the fact of *not* receiving anti-neoplastic treatments (chemotherapy or radiotherapy) was a predictor of depressive symptoms among patients with advanced cancers of all types (16.7% breast cancer). Additional longitudinal studies are therefore needed to better document the relationship between cancer treatments and depression.

Sociodemographic Factors

Gender

Among the general population, women are recognized as being approximately twice as susceptible as men to developing depression (Kessler et al., 1994). Hence, the prevalence of depression among breast cancer patients, almost all of whom are women, may be higher than in other types of cancer. In a review of the literature, Massie (2004) found that breast cancer was one of the four types of cancer that had the highest prevalence rates of depression (i.e., in order, oropharyngeal 22%–57%, pancreas 33%–50%, breast 1.5%–46%, lung 11%–44%). However, the prevalence of depression among women with a gynecological cancer was lower (12%–23%), even if this is exclusively a feminine type of cancer. Conversely, Parker et al. (2003) observed greater psychological distress (i.e., anxiety and depression) among women with exclusively feminine cancers like breast or gynecological cancer than among patients with urological and gastro-intestinal cancers, the former exclusively masculine and the latter

mixed. It was, however, impossible to assess the effect of gender on patients with gastro-intestinal cancer given the small size of this subgroup. When statistically controlling for the type of cancer, certain authors observed a higher depression rate among women (Pettingale et al., 1988; Stommel et al., 2004; Mystakidou et al., 2005a), whereas others did not arrive at this conclusion (Plumb & Holland, 1981; Kathol et al., 1990; Ciaramella & Poli, 2001; Hirai et al., 2002; Lloyd-Williams et al., 2004).

Age

Age also remains a controversial risk factor. In fact, most studies suggest that young adults with cancer are more at risk of depression than those who are older (Kathol et al., 1990; Potash & Breitbart, 2002; Parker et al., 2003; Lloyd-Williams et al., 2004; Wong-Kim & Bloom, 2005). For example, Kissane et al. (2004) found a significant association between lower age and depression among women with metastatic cancer, but not among women with a localized breast cancer. Contrary to this, other authors suggested that elderly cancer patients face greater losses (e.g., physical, financial, death of loved ones) and may therefore be more at risk of depression and suicidal ideation than younger patients (Massie et al., 1994). Consistent with this hypothesis, Mystakidou et al. (2005a) observed a significant correlation between higher age and depressive symptoms among a group of patients with advanced cancers of all types.

Socioeconomic Status and Education Level

Among women with advanced breast cancer, those with a lower socioeconomic status would appear to be more at risk of developing depressive symptoms (Pinder et al., 1993). Moreover, a higher level of education might prevent the onset of depression in cancer patients (Stommel et al., 2004), although this relation was not observed by some authors (Parker et al., 2003; Okamura et al., 2005).

Marital Status

Married persons or those living with a partner would appear to present fewer depressive symptoms than single, separated, and divorced people (Parker et al., 2003). Wong-Kim and Bloom (2005) did not, however, observe this protecting role. Another study by Shapiro et al. (2001) observed a significant relationship between the quality of the couple's relationship and the quality of life among women with stage II breast cancer. It may thus be hypothesized that the perception of received emotional support is a more important predictive factor than marital status.

Psychosocial Factors

Social Support

Different psychosocial variables may influence the risk of depression among patients with metastatic breast cancer. In particular, good social support may be effective in helping people with cancer adapt to their illness (Massie et al., 1994; Shapiro et al., 2001; Potash & Breitbart, 2002). For instance, the perception of adequate social support has been associated with better psychosocial indices (e.g., anxiety, depression, overall mental health) among a group of patients with cancers of various types and at various stages (Parker et al., 2003). However, results of a prospective study (Ranchor et al., 2002) contradict these findings. What these researchers observed was an association between a high level of premorbid social support (i.e., before the cancer diagnosis) and an increase in long-term psychological distress (i.e., 1 year after the diagnosis). This unexpected relationship was explained by the potential negative influence of excessive support or overprotection on the ability of a person to adapt over the long term to a major life event like a cancer diagnosis. It appears, therefore, that the relation between social support and depression is more complex than was initially thought.

Coping Strategies

Coping strategies employed by women with breast cancer may also influence the development of depressive symptoms. Studies on the subject generally suggest that a higher perceived level of control and active coping styles are associated with better adjustment to cancer (Dunkel-Schetter et al., 1992; Hirai et al., 2002). Likewise, people with higher perceived self-efficacy would appear to be less depressed (Hirai et al., 2002; Ranchor et al., 2002). Additionally, it has been observed that older women with stage IV breast cancer employed coping strategies characterized as less fighting spirit, more hopelessness/helplessness, and more fatalism and were comparatively more anxious and depressed than younger women with nonmetastatic cancer (Schnoll et al., 1998). Thus, it would appear that coping strategies have a mediating role between some sociodemographics and depression.

Psychiatric History

Most authors agree that patients with a personal history of depression are more at risk of developing depressive symptoms following a cancer diagnosis (Plumb & Holland, 1981; Potash & Breitbart, 2002; Meyer et al., 2003). In a longitudinal study conducted by Ranchor et al. (2002), 99 patients with mixed

cancer sites and stages were evaluated before confirmation of their diagnosis (T0), as well as at 2 (T1), 6 (T2) and 12 (T3) months after the diagnosis. The results showed that premorbid distress (T0) was a significant predictor of short- (T1) and long- (T3) term distress. In the case of women with metastatic breast cancer, some researchers have observed that a past history of depression was significantly associated with the presence of current major depression (Kissane et al., 2004; Okamura et al., 2005), whereas others were unable to show this relationship (Pinder et al., 1993).

In summary, numerous demographic, medical, and psychosocial factors may increase the risk that women with metastatic breast cancer will develop depressive symptoms. The results have frequently been contradictory, notably with regard to cancer treatments, demographic factors, and social support. More large-scale longitudinal studies are needed to establish the contribution of each of these factors and their interaction with each other in the development of depression in women with metastatic cancer.

CONSEQUENCES

Psychological

In metastatic breast cancer patients, as for other types of cancer, the studies have frequently associated depression with a decreased quality of life (Weitzner et al., 1997; Skarstein et al., 2000; O'Brien, 2003; Badger et al., 2004). Results of two studies that looked at the quality of life of people with cancer using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (Aaronson et al., 1993) suggest that depression is significantly associated with an alteration in physical, emotional, cognitive, and social dimensions of quality of life as well as with a decrease in overall perceived state of health and an increase in fatigue (Smith et al., 2003; Mystakidou et al., 2005a). Another study by Rustøen et al. (2005) evaluated predictors for the quality of life among a sample of 157 patients with bone metastases (48% of whom were women with breast cancer). Results showed that depression was the most important predictor for quality of life, compared to pain and physical and social functioning. Likewise, a study conducted among breast cancer patients, for the most part with metastases, showed that participants with a psychiatric disorder had a significant decrease in the quality of life, with regard to the functional state (i.e., emotional functioning, self-image, perspective on the future), and to certain physical symptoms (i.e., loss of appetite, diarrhea, fatigue, nausea/vomiting), compared to

women with no psychiatric diagnosis (Okamura et al., 2005). Finally, a recent longitudinal study showed that sleep disturbances over a period of 12 months were significantly predicted by depression at baseline (Palesh et al., 2007).

Besides being associated with a noticeable reduction in the quality of life, depression may increase the risk of suicide in persons with cancer (Massie et al., 1994). In one study, women with mixed cancer sites and stages were two to three times more likely to commit suicide than women in the general population (Björkenstam et al., 2005). Moreover, the suicide rate was higher among those with a poor prognosis.

Several authors have studied the desire for premature death among persons in the terminal phase of cancer. All the studies reviewed suggest that depression is associated with a desire for premature death or increased suicidal ideations (Chochinov et al., 1995; Breitbart et al., 2000; Filiberti et al., 2001; Suarez-Almazor et al., 2002; Kelly et al., 2003; Mystakidou et al., 2005b; O'Mahony et al., 2005). A strong desire for premature death was reported in from 8.5% to 17% of patients in palliative care, and these rates may rise to between 40% and 47% in patients who are suffering from depression (Chochinov et al., 1995; Breitbart et al., 2000; Kelly et al., 2003; Mystakidou et al., 2005b).

Van der Lee et al. (2005) evaluated the relationship between depression and the rate of explicit requests for euthanasia in the Netherlands among 138 patients in the terminal phase of cancer. The results showed that the risk of requesting euthanasia among patients with depressive symptoms was 4.1 times higher than in nondepressed patients. Furthermore, there are some data suggesting that a decrease in depressive symptoms over time is associated with a decreased desire for premature death (O'Mahony et al., 2005). These data suggest that it is essential that a systematic evaluation of depressive symptoms be made among patients who request euthanasia and highlight the importance of treating depression in terminally ill patients.

Medical

Although there is still no consensus due to the contradictory results obtained, certain studies have observed a link between depression and progression of cancer (Spiegel & Giese-Davis, 2003). Although further research is needed to elucidate the mechanisms, this relationship may be explained by the impact of depression on the immune system, on the neuroendocrine system, and/or on health behaviors (e.g., adherence to treatments, tobacco use, alcohol use, sleep habits; Werth et al., 2002; Reiche et al., 2004;

Watson et al., 2005). A group of researchers (Watson et al., 1999) looked at the type of coping strategies used by 578 women recently diagnosed with breast cancer. Higher levels of hopelessness and helplessness were found to significantly increased risk of recurrence or death at 5 years, but not depression. In a large-scale study by Goodwin et al. (2004), breast cancer participants who had been diagnosed with depression in the 2 years prior to their cancer diagnosis were significantly more likely to see their tumor and the stage of their cancer progress more rapidly. In addition, women with a previous history of depression were 42% more likely to die of their breast cancer within 3 years of their diagnosis. Finally, Meyer et al. (2003) followed the evolution of depressive symptoms in 45 advanced cancer patients over a period of 6 months. They observed that an initial depression (i.e., at the first time of measurement) was not a predictor for survival, but an increase in depressive symptoms over time was significantly associated with an earlier decease.

In spite of the elevated prevalence of depression among cancer patients, particularly at the advanced stages, as well as its potentially harmful psychological and medical consequences, depression currently remains undertreated in this population (Block, 2000; Bowers & Boyle, 2003; Greenberg, 2004).

TREATMENT OF DEPRESSION IN METASTATIC BREAST CANCER

Pharmacological

Antidepressants are the most widely used treatment for depression, both among the general population and in cancer patients (Fisch, 2004; Williams & Dale, 2006). Pharmacotherapy may also be used in patients with advanced cancer or in the terminal stage in order to reduce their depressive symptoms and suicidal ideation (Massie et al., 1994; Potash & Breitbart, 2002). It has been suggested that selective serotonin reuptake inhibitors should be used as the drug of choice because of their lesser side effects when compared to tricyclics (Potash & Breitbart, 2002). Incidentally, certain antidepressants may also be effective for other symptoms frequently associated with breast cancer, such as fatigue, sleep difficulties, and hot flashes (Weitzner et al., 2002; Ladd et al., 2005).

Very few studies have, nonetheless, looked at the efficacy of pharmacotherapy for the treatment of depression in a context of cancer. A recent literature review identified six randomized and placebo-controlled studies on the subject, most of which were double blind (Williams & Dale, 2006). In nonmetastatic patients, three studies evaluated the

efficacy of paroxetine for the treatment of depression in patients with various types of cancer (Morrow et al., 2003), with a melanoma (Musselman et al., 2001), or with breast cancer (Roscoe et al., 2005). The results indicated that a dose varying from 10 to 40 mg of paroxetine (average = 20 mg) was effective, both for the reduction of depressive symptoms and in reducing the number of patients who met the criteria of major depression in the short term (i.e., from 8 to 12 weeks of treatment). Only one of the three studies reported on the tolerability of the medication (Musselman et al., 2001), and findings indicated no significant difference in the types of side effects reported after 12 weeks of treatment between the group treated with paroxetine and the placebo control group. Three people out of 20 from the paroxetine group suffered retinal hemorrhages, but they also had other risk factors. One study examined the efficacy of fluoxetine among a group of patients with mixed cancer sites and stages suffering from a major depressive or an adjustment disorder ($n = 91$; Razavi et al., 1996). This study revealed no significant difference between the fluoxetine group and the placebo group after 5 weeks of treatment as far as the percentage of positive response was concerned, defined by a score of less than eight on the HADS-D. With regard to tolerability, no significant difference in side effects was observed between the fluoxetine and control groups after 5 weeks of treatment. Finally, a research team looked at the efficacy of mianserine, a tetracyclic antidepressant, for the treatment of depression in 55 women with nonmetastatic breast cancer (Van Heeringen & Zivkov, 1996). A greater reduction of Hamilton Rating Scale for Depression (HDRS; Hamilton, 1960) scores was observed in the group treated with mianserine compared to the placebo control group after 4 and 6 weeks of treatment. The number of patients responding favorably to the treatment, as defined by a reduction of at least 50% of the HDRS score, was also significantly higher in the mianserine group than in the placebo group at the same time points. With regard to tolerability, no significant difference was observed between the groups.

Even fewer studies have looked at the efficacy of antidepressants in patients with advanced cancer, and none has been conducted specifically in metastatic breast cancer patients. Fisch et al. (2003) assessed the efficacy of fluoxetine compared to a placebo to treat depressive symptoms and improve the quality of life in 163 patients with advanced cancer of various types. After 12 weeks of treatment, patients who had received fluoxetine showed a lower level of depression and a significantly higher level of quality of life than the placebo group. In this study the female gender was associated with better results,

both with regard to depressive symptoms and quality of life. Another group (Holland et al., 1998) assessed the efficacy and tolerability of fluoxetine and desipramine in the treatment of depressive symptoms in 40 women with advanced cancer (75% with breast cancer). Their results showed that these two medications were significantly more effective than a placebo in reducing depressive and anxiety symptoms and in improving the quality of life in this population after 6 weeks of treatment. Fluoxetine (20 mg/day) and desipramine (25–150 mg/day) would appear to be relatively well tolerated, though several side effects were felt, the most frequent being dryness of mouth, nausea, and pain. Six patients who were treated with fluoxetine along with four who were treated with desipramine abandoned the study because of the side effects (e.g., somnolence, tachycardia, depersonalization, pain). However, no comparison for tolerability was made between the groups treated with the antidepressants and the placebo group. Finally, amitriptyline and clomipramine, two tricyclic antidepressants, were found to be effective in treating major depression and reducing suicidal ideations and the desire for premature death in a limited number of patients ($n = 6$) in the terminal phase of cancer (Kugaya et al., 1999).

In sum, antidepressants seem to be effective for the treatment of depression in cancer patients. However, additional studies are needed to investigate their efficacy among specific populations, like women with metastatic breast cancer. In fact, patients with advanced cancer may present a different response because of the physical symptoms that could arise from the illness and treatments and because of their poorest prognosis. Furthermore, the long-term efficacy and tolerability of antidepressants are currently not well known in the context of advanced cancer. Antidepressants appear to be associated with a number of negative side effects (e.g., dryness of mouth, nausea, constipation, anorexia, insomnia) that would be added to the symptoms of advanced cancer and its treatments. Finally, although statistically significant findings have been reported, little information is available on their clinical significance. Given their side effects and that a number of patients are reluctant to take antidepressants for various reasons (Sharpe et al., 2004; Brown et al., 2005), nonpharmacological interventions should be considered as a possible alternative in the treatment of depression in women with metastatic breast cancer.

Psychological

In the general population, certain forms of psychotherapy, notably cognitive-behavioral and interpersonal therapy, are recognized as empirically

supported treatments for depression (Chambless & Ollendick, 2001). Several studies have assessed the efficacy of psychotherapy in reducing depressive symptoms in patients with early-stage cancer. Most of these studies suggest that psychotherapy, particularly cognitive-behavioral therapy, is effective in reducing depressive symptoms in cancer patients (Marchioro et al., 1996; Antoni et al., 2001; Winzelberg et al., 2003; Given et al., 2004). Less numerous studies have looked at the efficacy of psychological interventions specifically in women with metastatic breast cancer. The psychotherapies that were most frequently investigated were support therapy, supportive-expressive group therapy, and cognitive-behavioral therapy, administered individually or in groups.

Supportive-Expressive Therapy

Spiegel et al. (1981) conducted a randomized and controlled study among women with metastatic breast cancer in order to evaluate the efficacy of supportive-expressive therapy ($n = 34$) compared to an untreated control group ($n = 24$). Compared to the control group, the total score of psychological distress on the POMS, as well as scores on subscales for tension-anxiety, vigor, fatigue, and confusion, improved significantly after 1 year of treatment. However, no significant difference in depressive symptoms could be observed between the groups.

The results of another study conducted in the same population by Edmonds et al. (1999) indicated that long-term supportive-expressive therapy (8 months), which included some cognitive-behavioral strategies, was associated with a reduction in feelings of helplessness and an increase in the quality of life. Again, no significant difference in depressive symptoms was observed between the treated and control groups as assessed by the POMS at the 4-, 8-, and 14-month follow-ups.

Two other randomized and controlled studies evaluated the efficacy of long-term supportive-expressive therapy on depressive symptoms in women with metastatic breast cancer (Classen et al., 2001; Goodwin et al., 2001). After controlling for between-group differences at baseline, no difference was detected at posttreatment between the groups on the different scales of the POMS in these two studies. However, Goodwin et al. (2001) observed that, among women who presented an elevated level of psychological distress at baseline, those who received the intervention showed a significantly greater reduction in depressive symptoms than those in the control group, whereas no difference was observed in women who showed little psychological distress at baseline. Alternatively, the results of the study conducted by

Classen et al. (2001) suggest that the absence of difference between the treatment and control groups may be due to the presence of women in the terminal stage of cancer. In fact, when the women who were in their final year of life were withdrawn from their analyses, the group receiving supportive-expressive therapy showed a significantly greater decrease in their psychological distress compared to the control group. Together, these results suggest that long-term supportive-expressive therapy may only be effective in reducing psychological distress for women with certain characteristics, such as a high baseline level of distress (possibly because of a floor effect) and a life expectancy of more than 1 year.

Cognitive-Behavioral Therapy

A first randomized study aimed to assess the effect of a combination of cognitive and behavioral strategies on the pain and mood of 24 women with metastatic breast cancer (Arathuzik, 1994). The therapy helped improve these women's capacity to control pain, but no difference was observed between the intervention and control groups as regards mood.

In another randomized and controlled study conducted in women with metastatic breast cancer, cognitive-behavioral therapy was associated with a significant improvement at posttreatment in depression, overall mood, and self-esteem as measured by the POMS subscales ($n = 43$), compared to the untreated control group ($n = 49$; Edelman et al., 1999a, 1999b). However, no difference was observed between the groups at the 3- and 6-month follow-ups. Among other possible explanations, the authors explained this weak sustaining of therapeutic gains over time by the fact that treatment was administered in a group and could not be individually tailored to each patient.

The efficacy of individual psychotherapy was first assessed in a pilot study conducted using a single-case experimental study (Lévesque et al., 2004). This study showed that individual cognitive therapy using Beck's model (Beck et al., 1979) was effective both in the short and medium term for treating depressive symptoms in women with metastatic breast cancer. Six participants with clinical levels of depression, that is, with a score of 17 or greater on the Beck Depression Inventory (BDI; Beck et al., 1961) or of 7 or greater on the HADS-D, were enrolled in the study. Intervention time-series analyses conducted on daily mood data revealed a statistically significant improvement of depression symptoms and, more importantly, anhedonia and associated features (i.e., anxiety, fatigue) for each participant. The visual inspection of HADS-D scores suggested that the introduction of cognitive therapy was associated

with a rapid reduction in depressive symptoms for three of the four completers, and depression scores began to decline at the end of the intervention for the fourth one. In addition, the improvements were judged to be clinically significant and were maintained at the 3- and 6-month follow-up evaluations.

These results were replicated in a randomized controlled trial conducted by the same research team (Savard et al., 2006). Forty-five women with metastatic breast cancer and with depressive symptoms (score of 7 or more on the HADS-D or 15 or more on the BDI) took part in this study. The results showed that women who received 8 weeks of cognitive therapy scored significantly lower on the HDRS, compared to the waiting-list control group at posttreatment. When both groups were pooled together after they all received therapy, a significant reduction in depressive symptoms from pre- to posttreatment as well as a significant decrease in associated symptoms like anxiety, fatigue, and insomnia were found. The better sustaining of therapeutic gains obtained in these two studies during follow-up can be explained by the fact that the treatment was administered individually or by the administration of three booster sessions following posttreatment.

In conclusion, it appears that psychotherapy can be effective at reducing depressive symptoms in women with metastatic breast cancer. Although no comparative study has been conducted, Beck's cognitive therapy appears to be the most cost-effective approach for treating women with metastatic breast cancer, given its short-term nature and the magnitude of effects observed. Further studies are needed to identify the best therapeutic approaches for depression in this population and to study the characteristics of women who best respond to psychological interventions.

CONCLUSION

Numerous women with metastatic breast cancer appear to suffer from depression, but further large-scale studies using diagnostic interviews are needed to determine its prevalence with more precision (Hotopf et al., 2002). Many factors can increase the risk that women will develop depressive symptoms, but additional longitudinal studies are needed to establish a causal link between some of these factors and depression in women with metastatic breast cancer and also to look at the evolution of depressive symptoms until the end of life (Fulton, 1997; Butler et al., 2003). Nonetheless, available data suggest that particular attention should be paid to women displaying certain characteristics (e.g., visceral metastases, severe physical symptoms, weak social support, antecedents of depression; Greenberg, 2004).

Despite the fact that depression appears to be associated with numerous negative consequences, it remains underdiagnosed and undertreated. There is, therefore, a need to offer treatment to women with metastatic breast cancer who suffer from depression. Currently, it appears that pharmacotherapy is associated with a decrease in depressive symptoms in this population. New studies are needed, however, to evaluate the long-term tolerability and efficacy of pharmacotherapy in cancer patients. Given its efficacy and short-term nature, cognitive-behavioral may be the most cost-effective treatment option for treating depression in women with metastatic breast cancer. However, further studies are needed to determine the specific characteristics of pharmacological or psychological treatments as well as of the cancer patients themselves in order to optimize the beneficial effects. In addition, there does not appear to be any data currently available on the efficacy of combining pharmacological and psychological therapies, although both treatments are commonly combined in clinical practice.

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