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Relief of depression and pain improves daily functioning and quality of life in patients with major depressive disorder

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ABSTRACT

Objective: The objective of this study was to investigate the effects of depression relief and pain relief on the improvement in daily functioning and quality of life (QOL) for depressed patients receiving a 6-week treatment of fluoxetine.
Method: A total of 131 acutely ill inpatients with major depressive disorder (MDD) were enrolled to receive 20 mg of fluoxetine daily for 6 weeks. Depression severity, pain severity, daily functioning, and health-related QOL were assessed at baseline and again at week 6. Depression severity, pain severity, and daily functioning were assessed using the 17-item Hamilton Depression Rating Scale, the Short-Form 36 (SF-36) Body Pain Index, and the Work and Social Adjustment Scale. Health-related QOL was assessed by three primary domains of the SF-36, including social functioning, vitality, and general health perceptions. Pearson's correlation and structural equation modeling were used to examine relationships among the study variables. Five models were proposed. In model 1, depression relief alone improved daily functioning and QOL. In model 2, pain relief alone improved daily functioning and QOL. In model 3, depression relief, mediated by pain relief, improved daily functioning and QOL. In model 4, pain relief, mediated by depression relief, improved daily functioning and QOL. In model 5, both depression relief and pain relief improved daily functioning and QOL.
Results: One hundred and six patients completed all the measures at baseline and at week 6. Model 5 was the most fitted structural equation model ($\chi^2 = 8.62$, df = 8, p = 0.376, GFI = 0.975, AGFI = 0.935, TLI = 0.992, CFI = 0.996, RMSEA = 0.027).
Conclusion: Interventions which relieve depression and pain improve daily functioning and QOL among patients with MDD. The proposed model can provide quantitative estimates of improvement in treating patients with MDD.

1. Introduction

Depression and pain frequently occur together. In one study of 150 depressed inpatients (Corruble and Guelfi, 2000), 92% reported at least one pain symptom, and 76% complained of the presence of multiple pain symptoms. According to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) (APA, 1994), pain is not a diagnostic symptom in major depressive disorder (MDD). Furthermore, pain is less emphasized in standard measures of depression severity, such as the Hamilton Rating Scale for Depression (Hamilton, 1960). However, growing evidence suggests that pain and depression may operate within similar areas of the brain regulating both mood and the affective components of pain (Giesecke et al., 2005). Some of the overlap between depression and pain can be explained biologically, in that pain and depression appear to share common pathways and neurotransmitters. For example, serotonergic pathways are considered to play a role in both depression and pain (Suzuki et al., 2004). This suggests that depression and pain respond to similar treatments, and also that they exacerbate one another. Pain relief has therefore been associated with depression relief (Feinmann, 1985; Von Korff et al., 1988).

Three theories have been postulated to explain the relationship of pain and depression (Bair et al., 2003; Lepine and Briley, 2004). The

Abbreviations: AGFI, Adjusted Goodness-of-Fit Index; AMOS, Analysis of Moment Structures; BPI, Body Pain Index; CFI, Comparative Fit Index; CGI-S, Clinical Global Impression of Severity; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; GFI, Goodness-of-Fit Index; GH, General Health Perceptions; HAMD-17, 17-item Hamilton Depression Rating Scale; MDD, Major Depressive Disorder; QOL, Quality of Life; RMSE, Root Mean Square Error of Approximation; SEM, Structural Equation Modeling; SF, Social Functioning; SF-36, Short-Form 36; TLI, Tucker–Lewis Index; VT, Vitality; WSAS, Work and Social Adjustment Scale.

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first theory suggests that pain is caused by depression (Leino and Magni, 1993). The second theory proposes that depression is caused by pain (Fishbain et al., 1997; Hendler, 1984). The third theory suggests that the direction of causality between depression and pain may operate in both directions (Hotopf et al., 1998; Von Korff and Simon, 1996).

Quality of life (QOL) refers to the ways in which health, illness and treatment affect a personal's perception of functioning and well-being (Jacobson et al., 1997). The assessment of QOL should consider patients' subjective views of their life circumstances (Rapaport et al., 2005). In clinical trial, QoL measurement could capture subtle differences after treatment, not displayed in symptom scales (De Fruyt and Demyttenaere, 2009). Improvement in daily functioning and QOL are still recognized as the goal in treating depressed patients (APA, 2010). Depression and pain have negative effects on a patient's daily functioning (Gambassi, 2009; Greer et al., 2010; Mavandadi et al., 2007; Smith et al., 2001; Sullivan et al., 2001) and QOL (Greer et al., 2010; Gureje et al., 1998; Lin et al., 2003; Munoz et al., 2005; Pyne et al., 1997; Rapaport et al., 2005). Although severity of depressive symptoms is related to QOL, some treatments that improve depressive symptoms are not adequately reflected in enhancing QOL (Hirschfeld et al., 2002). For example, when patients received a new treatment with fewer side effects than the old one, they would have better QOL. Even this new treatment was no more effective (De Fruyt and Demyttenaere, 2009). Therefore, QOL has become an outcome measure, going beyond measures of symptom reduction. Either depression relief or pain relief has also been reported to improve daily functioning and QOL (Brennan et al., 2007; Lin et al., 2003; Wise et al., 2008). However, Bair et al. (2003) indicate that very few trials for treating depression have assessed whether pain improves in concert with depression symptoms, and whether greater relief from either pain or depression relates to greater improvement in the other condition.

The goal of this study was to construct a set of viable models to investigate the relationships between depression relief, pain relief, daily functioning improvement, and QOL improvement of depressed patients after treatment.

2. Method

The study was approved by Kai-Syuan Psychiatric Hospital's institutional review board and conducted in accordance with Good Clinical Practice procedures and the current revision of the Declaration of Helsinki (Project number: KSPH-2007-16). Written, informed consent was obtained from the participants after a full explanation of the study's aims and procedures. This study has also been registered on Clinical.trials.gov (Identifier number: NCT01075529).

2.1. Subjects

Details of the patient sample have been presented elsewhere (Lin et al., 2011). In brief, subjects were recruited from Kai-Syuan Psychiatric Hospital, Kaohsiung, Taiwan. Participants were considered eligible if they were: new inpatients undergoing acute treatment, between 18 and 70 years old, physically healthy with all laboratory parameters within normal limits (including electrocardiography and chest X-ray), and had been diagnosed for a MDD using the Structured Clinical Interview for DSM-IV (First, 1997). The exclusion criteria applied were: a 17-item Hamilton Depression Rating Scale (HAMD-17) < 18 and a Clinical Global Impression of Severity (CGI-S) (Guy, 1976) < 4 at baseline, psychotic depression, bipolar I or II disorder, schizophrenia or any other psychotic disorder, a DSM-IV diagnosis of substance abuse or dependence (including alcohol) within the past 6 months, mental disorders due to organic factors, severe cognitive impairment, initiating or ending formal psychotherapy within six weeks prior to enrollment, treatment-resistant depression (defined as a lack of response to 2 or more adequate courses of antidepressant treatment), a history of poor response to fluoxetine (20 mg/day for ≥ 4 weeks), a history of electroconvulsive therapy, and pregnancy or lactation.

2.2. Procedures and assessments

After a washout period of at least 72 h, patients received open-label fluoxetine treatment at a fixed dose of 20 mg daily (Beasley et al., 2000) for 6 weeks. During the course of treatment, psychiatrists had the option of adding certain anxiolytic and/or sedative-hypnotic medications for brief periods, based on clinical necessity. No other psychotropic agents were used at bedtime for insomnia. Drug adherence was monitored and ensured by psychiatric nurses.

2.3. Independent variables

The independent variables were depression change and pain change after treatment. Depression severity was assessed at baseline, and again at weeks 1, 2, 3, 4, and 6 by trained and qualified psychiatrists using the HAMD-17. The intraclass correlation coefficient of reliability was 0.95 between the raters. To maintain high interrater reliability and prevent rater drift, raters met at least once a month for training and reliability re-testing. The research psychiatrists who conducted the clinical ratings did not know the detailed study design or the responder versus non-responder status of patients as defined during the study. Pain was measured by the Body Pain Index (BPI) of the Medical Outcomes Study Short-Form-36 (SF-36) (Bair et al., 2004; Karp et al., 2005; Ware and Sherbourne, 1992) at baseline and again at week 6. The BPI consisted of two items that measured: 1) pain severity (Item 7) ranging from 1 (none) to 6 (very severe), and 2) pain interference (Item 8) ranging from 1 (not at all) to 5 (extreme). The BPI was computed by summation then transformation of raw Likert-scale scores to a 0–100 scale. A higher score meant less pain. This approach has been used previously (Karp et al., 2005). The two independent variables were HAMD-17 score change and BPI score change. The other two were age (Campbell et al., 2003) and sex (Dowdy et al., 1996).

2.4. Dependent variables

The dependent variables selected for use in this study were daily functioning change and health-related QOL change after treatment. Daily functioning was assessed using the Work and Social Adjustment Scale (WSAS) (Mundt et al., 2002) at baseline and again at week 6. The WSAS is a self-rated scale. It consists of five Likert scales that measure an individual's perception of work and social functioning, with higher scores representing greater impairment of daily functioning. Each item is scored from 0 (not affected at all) to 8 (severely affected), with a maximum total score of 40 (Mundt et al., 2002). At baseline and again at week 6, health-related QOL was assessed by three primary domains of the SF-36 (Ware and Sherbourne, 1992), including social functioning (SF), vitality (VT), and general health perceptions (GH) (Bair et al., 2008). A lower score represents a poorer health-related QOL. The four dependent variables were WSAS score change, SF score change, VT score change, and GH score change.

2.5. Statistical analysis

The data were analyzed using the SPSS version 17.0 for Windows and the Analysis of Moment Structures (AMOS) version 17 (SPSS Inc., Chicago, IL, USA). Statistical significance was set at $p < 0.05$. Paired *t*-test was used to analyze the six variable changes after 6 weeks of treatment. Correlations between measured variables were analyzed by Pearson's correlation coefficients. Based on the possible relationships, we proposed five hypothetical SEM models for further testing. In model 1, depression relief alone affected improvement in daily functioning and QOL. In model 2, pain relief alone affected improvement in daily functioning and QOL. In model 3, depression relief, mediated by