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Effects of Paroxetine CR on Depressive and Anxiety Symptoms *in a Community Sample of Adult Hispanic Women with Major Depression or Generalized Anxiety Disorder*

ABSTRACT

Objective: Previous research reports higher rates of depression in Hispanic women than Caucasian or African American women. The effectiveness and tolerability of paroxetine CR (controlled release) was examined in women of Hispanic heritage with depression or anxiety.

Methods: Thirty-six Hispanic female patients 18 years or older meeting DSM-IV criteria for major depression or generalized anxiety disorder diagnosis with an initial Hamilton Depression Rating scale (17 item) ≥20 or Hamilton Anxiety Rating scale ≥18 measuring no less than 4 on the Clinical Global Impression Severity scale received paroxetine CR (12.5–50mg/day) for 29 weeks of open label treatment. Analysis was conducted using repeated measures methodology.

Results: Significant symptom reduction was observed on all scales. Mean dose was 31.7mg. The side effect of sexual dysfunction (17%) appeared most frequently but did not cause any patients to cease study participation.

Conclusions: Paroxetine CR was an effective and generally well tolerated treatment in this population.

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INTRODUCTION

In 1999, the National Institute of Mental Health reported that depression and anxiety disorders are the two most common mental illnesses in the United States with women experiencing depression every year at twice the rate of men.[1] The National Women's Health Information Center stated in 2002 that twice as many women as men suffer from anxiety disorders in the United States, regardless of race.[2] The US Public Health Service reported in 2001 that America's minorities face severe economic, cultural, linguistic and physical barriers in receiving treatment of mental illness, difficulties that prevent thousands from being properly treated.[3] Supporting this statement are facts often noted in studies focusing upon the Hispanic population, such as the following: Hispanic people experience higher rates of major depressive disorder than Caucasian or African American people; Hispanic people born in the US appear more likely to suffer from mental illness than those born in Mexico or living in Puerto Rico; Hispanic people are less likely to seek mental health treatment as well as less likely to receive treatment from mental health specialists; and the care Hispanic people do receive is often inadequate.[4]

The National Institute of Mental Health agreed in 2003 that the differences in accessing and the quality of care for Hispanic people was of concern, especially with the limited research focused upon the mental health of this population.[5] The National Congress for Hispanic Mental Health in Washington, DC, (2000), discussed issues currently plaguing and contributing to the insufficient mental healthcare provided to Hispanic people. Low levels of education, fewer economic resources, and having the lowest rates of insurance coverage combine to create formidable obstacles placing Hispanic people at greater risk for health problems in general and for also not receiving appropriate care for those problems. Experts state that while progress has been made pharmacologically for the general population, clinical trials of existing and new medications must be performed with Hispanic people to insure their effectiveness in this ethnic group.[4] Hispanic people are the largest minority group in the US with a population projected to grow significantly in the future. They are a diverse group, and these differences (socioeconomic, nationality, race, English language abilities, worldview and religion) must be carefully incorporated into the planning and implementation of mental health services.[6] It has been established that Hispanic people typically receive lower quality mental health treatment, if at all, and face many challenges when attempting to obtain care. Women, regardless of ethnicity, continue to experience mental health disorders in greater numbers than men. Considering more studies are needed both in the areas of women's mental health and particularly Hispanic mental health, studying the effects of paroxetine CR (controlled release) (Paxil® CR) on this specific group of individuals is indicated.

METHODS

Hispanic women ages 18 to 75 of self-defined Hispanic heritage (relating to or typical of people descended from Spanish or Latin American people or their culture) with major depressive disorder or generalized anxiety disorder as diagnosed by means on the Structured Clinical Interview for Axis 1 DSM-IV disorders were eligible for participation. Patients diagnosed MDD were required to have a ≥20 on the Hamilton Depression rating scale (17 item) at screen and baseline prior to randomization. Patients diagnosed GAD were required to have a ≥18 on the Hamilton Anxiety rating scale at screen and baseline prior to

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TABLE 1. Baseline and Final Observation Scores on the HAMD, HAMA and CGI.

TOOL	BASELINE MEAN ± SD	FINAL OBSERVATION MEAN ± SD	*P*-VALUE
Hamilton Depression	23.04 ± 6.16	5.75 ± 7.05	<0.001
Hamilton Anxiety	20.11 ± 4.48	5.43 ± 6.90	<0.001
CGI-S	4.39 ± 0.63	1.86 ± 1.21	<0.001
CGI-I	4.00 ± 0.28	1.56 ± 0.89	<0.001

randomization. Patients were also required a ≥4 on the Clinical Global Impressions Severity scale at screen and baseline prior to receiving study drug.

Patients were excluded if unstable major medical illnesses were present or if pregnant, lactating, or not agreeable to using medically acceptable contraception. The patients were clean of illicit drugs, excessive alcohol use, or a substance abuse diagnosis. Prior intolerance to paroxetine or use of any psychotropics or psychoactive herbals within two weeks prior to screen (4 weeks for fluoxetine) was prohibited.

After giving informed consent, meeting inclusion/exclusion criteria, completing all screening assessments, and following the one-week screening period, patients were treated openly for an optimum of 29 weeks. Paroxetine CR was initiated at 12.5mg daily, increased to 25mg daily after one week, and increased to 50mg daily two weeks later if judged clinically necessary by the investigator. The 23-week treatment period was followed by a 6-week taper period for those patients wishing to discontinue paroxetine CR therapy, while those wanting to continue study medication were permitted to do so for the study's duration. Dose increases could not occur beyond Week 4 and patients remained on maximally tolerated doses. However, patients could decrease their dose at any time during the study. Dose ranges were based upon previously established Glaxo-Smith-Kline prescribing safety guidelines.

Subjects were rated weekly, biweekly, and monthly. Paired t-tests were used on the HAM-D, HAM-A, and CGI from baseline to last follow up assessment using a paired t-test. No psychological therapy was permitted during the trial. Treatment adherence was monitored by capsule counts. Follow-up care was arranged for all patients (mental health clinics, primary care physicians, private psychiatrists) regardless of trial completion; however, keeping these appointments was each patient's responsibility.

RESULTS

Of the 56 patients who consented, 13 failed screening (nine due to positive drug screens). Of the 43 remaining patients, seven ceased participation too early for data analysis. Of those seven patients not included for analysis, five were lost to follow up and two discontinued early due to an adverse event (one patient reported a stomachache and the other patient reported dizziness). Both patients stated their adverse symptom abated when paroxetine usage was stopped. Therefore, data were analyzed on 36 patients (64.3% of the original sample).

All participants were outpatients, their mean age was 42.89±31.03 (Mean ± Standard Deviation). The mean dose of paroxetine CR was 31.7mg. Patients participated for a mean duration of 19.7 weeks. Seventy-eight percent of the patients were Puerto Rican, eight percent were Columbian, and three percent reported heritage from Spain, Cuba, Panama, Chile, and the Dominican Republic. Eighty-one percent of the patients were bilingual.

Forty-seven percent of the patients had no prior psychotropic use, 53 percent reported sporadic use of only one or two psychotropics at least one year prior to study participation. Eighty-four percent of those patients with past psychotropic usage had tried an SSRI with the most common being sertraline (Zoloft®), fluoxetine (Prozac®), mirtazapine (Remeron®), and paroxetine, while 16 percent had experience with amitriptyline (Elavil®) or venlafaxine (Effexor®). Thirty-seven percent of the subjects stopped their psychotropics due to a side effect or non-response, 37 percent stopped because they couldn't afford it, and 26 percent stopped usage due to symptom improvement, hence feeling medication was not necessary.

Forty-seven percent of the participants were single with children, 39 percent were married with children, and 14 percent were

single with no children. The stressors most often reported were job issues (75%), significant financial problems (69%), relationship problems with a partner or ex-partner (64%), transportation problems (47%), children with attention deficit disorders (28%), abusive partners (25%), seriously handicapped children (11%), and 17 percent admitted to past childhood abuse.

Data on the instruments can be found in Table 1. Significant improvement was observed on all instruments as measured with paired t-tests from baseline to last follow-up. Hamilton anxiety scores improved by 75.1 percent and Hamilton depression scores improved by 73.0 percent over the study period. Similar results were seen on the CGI scales (57.6% for CGI-S and 61.0% for CGI-I).

The most common adverse event was sexual dysfunction (17%), though this issue did not cause any patients to stop their study participation. Weight gain was defined as a change in weight (mean absolute change in pounds, mean percentage change, and number of patients who had a 7% or greater increase in weight, which is considered the standard of extreme weight gain in clinical trials) from baseline to last study visit. By this standard, no patient met criteria for weight gain; however, three patients experienced a 6.8-percent increase in weight. Four patients experienced breakthrough anxiety symptoms, but two of these were not at an optimal dose level. Two patients experienced breakthrough depressive symptoms (one markedly depressed and one severely depressed); the severely depressed patient entered the hospital and received venlafaxine, quetiapine, and temazepam, while the markedly depressed patient received outpatient treatment with venlafaxine and lorazepam. Both attained remission of their acute symptoms. Two patients felt agitated: one discontinued and the other patient's agitated symptoms appeared transient and she continued participation.

No abnormal lab changes were observed in any of the patients from initial screen labs to last visit labs.

Female members of racial and ethnic minority groups, as a group, are in poorer health, use fewer health services, and continue to suffer disproportionately from premature death, disease, and disabilities.

DISCUSSION

Female members of racial and ethnic minority groups, as a group, are in poorer health, use fewer health services, and continue to suffer disproportionately from premature death, disease, and disabilities.[7] The high level of poverty and relatively low levels of educational attainment place Hispanic people as a group at greater risk for physical and mental health problems than non-Hispanic people and at a lower rate for obtaining appropriate care for their mental health problems.[4] As some recent studies conflict with past research regarding the depression and anxiety rates of Hispanic people compared to Caucasians and other groups, the current focus has shifted more toward Hispanic people not receiving adequate mental healthcare,[8] and if treatment is initiated, their significantly poor treatment adherence.[9] Not debated is the rate of depression in Hispanic/Latina women being twice that of their male counterparts,[10] thereby confirming the need for further examination of depression in Hispanic women. To our knowledge, this is one of the limited studies focusing upon Hispanic women. Data from this 7-month open-label study indicated that paroxetine CR was an effective treatment for symptoms of depression and anxiety in moderately to markedly ill Hispanic women who did not have a history of treatment resistance.

It appeared paroxetine CR was well tolerated in this population. Though the appearance of sexual dysfunction (17%) was the most common side effect and the emergence of non-statistically significant weight gain, these issues did not deter any of the women from their study participation. All of the women were informed of alternative treatments, especially those patients presenting with a side effect, but they repeatedly stated their improved mental health was the priority and refused a change in medication at that time with the primary concern being even a slight return toward their pre-study participation state. Upon discussion, the women verified understanding that a different antidepressant could provide them the same symptom

relief along with a lesser weight gain probability with the antidepressant trade names of Wellbutrin® (bupropion), Zoloft, Effexor, Prozac, Celexa® (citalopram), and Lexapro® (escitalopram oxalate) provided as effective treatment options.

For those women who continued study participation long enough to achieve alleviation of symptoms or remission, the majority of them made significant positive life changes, which included leaving abusive relationships, becoming more independent, obtaining further education, finding better jobs, and employing healthier coping mechanisms. It was through this relief of symptoms, which could have been attained by an antidepressant other than paroxetine, that enabled the women to experience an increase in motivation, positive feelings, activity levels, hope for the future, and the lessening of angry, agitated feelings, thereby improving their ability to make healthier decisions and choices for themselves.

During the screening period, many women failed due to positive drug lab results. It was stated by all of the patients admitting to marijuana use that they self-medicated themselves for anxiety, agitation, or insomnia symptoms. The marijuana gave them a sense of calm, slowed down racing thoughts, blunted agitated or angry feelings, and also helped them fall asleep at night. The women felt it was easier, cheaper, and sometimes more acceptable to use marijuana than to seek medical help. They were not regarded as "crazy" by family or friends for using marijuana.

The main limitation of this study was its open-label design; the inclusion of a 37.5mg dose of paroxetine might have benefitted certain patients and controlled adjunct benzodiazepine use.

Seeing the need for improved mental health education, easier access to mental health resources, more frequent visits at mental health clinics, and better quality treatment in this community suggests further studies should be carried out in the Hispanic population.

CONCLUSION

The typical profile of participants in this open-label outpatient study utilizing paroxetine CR were depressed and/or anxious Puerto Rican women aged 42 with children who had never used a psychotropic or had limited experience with one or two antidepressants at least a year prior to study entrance, with medication stoppage related to a non-response, side effect, or cost. These women were also attempting to cope with similar stressors, such as job, financial, relationship, transportation, and child problems. For those women achieving alleviation of depression or anxiety symptoms over the treatment period, they believed this relief affected their life in a positive manner.

Sexual dysfunction as the most common adverse issue and a weight gain of nearly seven percent for three women arose during the course of this study but were seemingly secondary to the patients in comparison to their improved mental health at that time. This occurrence raises questions in itself: Is it possible the women did not want to leave the study site? Did they develop a trust with health professionals that was usually difficult for them to do? Did they feel they were receiving better quality care at the site compared to what they'd experienced in the past? Were they substantially fearful of experiencing symptoms again or of trying a new medication?

It was noted that marijuana appeared to be a significant form of self treatment for agitation feelings and insomnia without carrying the stigma of a psychotropic. Also noted was that by allowing the women to bring their children to their appointments and providing free transportation services, study visit adherence was facilitated.

Continued research is needed to better understand and treat the psychosocial complexities of special populations and women's mental health issues in the US.

REFERENCES

1. National Institute of Mental Health. (1999). Mental Illness and the Family. Reported by National Mental Health Association. (2001). Available at: www.nmha.org/infoctr/factsheets/15.cfm. Access date: April 24, 2006.
2. National Women Health Information Center. (2002). Women's Health Week Focuses on Minority Females. Reported by Healthlink. Medical College of Wisconsin. Available at: healthlink.mcw.edu/article/1021047874.html. Access date: April 24, 2006.
3. U.S. Public Health Service (2001). Minorities Lack Proper Mental Health Care. Reported by CNN (2001). Available at: www.cnn.com/2001/Health/08/26/mental.health/ Access date: March 30, 2003.
4. Lopez S. The mental health needs of Hispanics in the United States. Washington, D.C: National Congress for Hispanic Mental Health, March 2000. Available at: www.mentalhealth.org/cmhs/SpecialPopulations/HispMHCongress2000/appendice1.asp. Access date: April 24, 2006.
5. National Institute of Mental Health (2002). Available at: www.nimh.nih.gov/events/latino.cfm. Access date: Marchh 30, 2003.
6. Gonzales M (2000). Provision of mental health services to hispanic clients. Available at: www.naswnyc.org/d16.html. Access date: April 24, 2006.
7. Office on Women's Health. The Health of Minority Women. U.S. Department of Health and Human Services. Availble at: www.4women.gov/owh/pub/minority/index.htm. Access date: July 2003.
8. Harman JS, Edlund MJ, Fortney JC. Disparities in the adequacy of depression treatment in the United States. *Psychiatr Serv* 2004;55(12):1379–85.
9. Olfson M, Marcus SC, Tedeschi M, Wan GJ. Continuity of antidepressant treatment for adults with depression in the United States. *Am J Psychiatry* 2006;163(1):101–8.
10. Minority Women's Health. U. S. Department of Health and Human Services Office on Women's Health. Health Problems in Hispanic American/Latino Women: Depression. Available at: www.4women.gov/minority/hispanicamerican/depress.cfm. Access date: May 2003.