A Paradigm for Facilitating Pharmacotherapy at a Distance: Sertraline Treatment of the Night Eating Syndrome

Albert J. Stunkard, M.D.; Kelly C. Allison, Ph.D.; Jennifer D. Lundgren, Ph.D.; Nicole S. Martino, B.S.; Moonseong Heo, Ph.D.; Bijan Etemad, M.D.; and John P. O'Reardon, M.D.

Objective: To test a novel method of facilitating pharmacotherapy at a distance and assess the effectiveness of sertraline for the treatment of night eating syndrome (NES).

Method: The effectiveness of the selective serotonin reuptake inhibitor sertraline in the treatment of NES was assessed at a distance. NES is characterized by a delay in the circadian rhythm of food intake, with evening hyperphagia and/or nighttime awakenings and ingestions. Persons who contacted us through our Web site, e-mail, or telephone for help with their NES completed a Night Eating Questionnaire and received a semistructured interview (Night Eating Syndrome History and Inventory) to determine the presence of NES. Fifty such persons received treatment with sertraline from their own physicians, to whom we offered consultation. Participants completed questionnaires every 2 weeks for 8 weeks and received a final telephone interview to assess their progress. Outcomes were compared with those from an earlier face-to-face open-label trial of sertraline. The study was conducted from September 2003 to May 2005.

Results: Both the questionnaires and interviews showed improvements in 5 key aspects of NES: the general Night Eating Symptom Scale, evening hyperphagia, nighttime awakenings, nocturnal ingestions, and the Beck Depression Inventory (all $p < .001$), and the mean body weight of the 41 overweight and obese subjects, reported by survey, fell 3.0 kg ($p = .01$). These results are similar to those obtained in an earlier face-to-face trial of sertraline with NES.

Conclusion: The study confirmed the effectiveness of sertraline in the treatment of NES and introduced a paradigm for facilitating pharmacotherapy at a distance.

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Corresponding author and reprints: Albert J. Stunkard, M.D., 3535 Market St., Suite 3025, Philadelphia, PA 19106-3309 (e-mail: stunkard@mail.med.upenn.edu).

This report describes a new paradigm for the facilitation of pharmacotherapy at a distance. This opportunity was provided by the frequent requests to our program for treatment of night eating syndrome (NES). NES is a disorder characterized by a delay in the circadian rhythm of food intake, manifested by evening hyperphagia and/or insomnia with food ingestions on awakening, and often associated with morning anorexia.[1–3] Patients are commonly obese and often depressed. The selective serotonin reuptake inhibitor (SSRI) sertraline has shown efficacy in the treatment of NES in both open-label[4] and placebo-controlled trials.[5]

A recent note in *The Journal of the American Medical Association*[6] described the rapid increase in "telemedicine," or conduct of medical practice at a distance, which has been used for the treatment of disorders such as obesity,[7,8] migraine,[9] pediatric recurrent pain,[10] and anxiety disorder.[11] Most of these programs relied on psychotherapeutic remedies, and their patients were within driving distance. We describe a program in which patients with NES, who were geographically remote from us, were treated with medication by their own physicians, to whom we offered consultation.

METHOD

Procedure

During the past 3 years, over 2000 persons have visited our Web site (http://www.med.upenn.edu/weight/nighteating.shtml) and completed a Night Eating Ques-

tionnaire (NEQ), which assesses night eating symptoms in general.[12] Many of the respondents were seeking help with NES, although they did not live close enough to our program to participate in onsite treatment. After completing an online or paper version of the NEQ, potential participants were sent a complete description of the study and an informed consent form by e-mail or mail. Upon return of a signed informed consent form, a trained clinician conducted a phone interview using the Night Eating Syndrome History and Inventory (NESHI; unpublished interview available from the authors upon request) and the associated Night Eating Symptom Scale (NESS).[4] If a diagnosis of NES was confirmed by interview and questionnaire, we recommended that participants contact their personal physicians, who also provided informed consent. Physicians were given information about the study and were offered consultation on the use of the SSRI sertraline for NES, which had proved effective in 2 earlier trials.[4,5] They then provided the treatment to their patients.

Approval for this study was obtained from the Institutional Review Board of the School of Medicine of the University of Pennsylvania, and the study was conducted from September 2003 to May 2005.

Measures

Two types of outcome measures were utilized in this study. The first type of outcome measure consisted of 3 surveys, each completed at week 0, before medication was started, and at weeks 2, 4, 6, and 8. The first survey was the NESS, a 14-item scale that assessed the level of morning hunger, the proportion of food intake after the evening meal, cravings and compulsions to eat in the evening and nighttime, initial insomnia, and mood symptoms during the past week.[4] The NESS also assesses the number of awakenings and nocturnal ingestions (waking after sleep onset to eat) in the previous week.

The second survey was the Beck Depression Inventory-II (BDI-II), a 21-item questionnaire that assesses cognitive, affective, and somatic aspects of depression.[13,14] The third survey was the Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q),[15] which contains 14 items assessing global satisfaction with psychosocial and physical functioning. These surveys had been used in our earlier clinical trials.[4,5]

The second type of outcome measure was the NESHI interview, administered by telephone before week 0 and after week 8. The NESHI reviews the typical 24-hour food intake and estimates the percentage of food intake after the evening meal, the number of awakenings and nocturnal ingestions, and topics other than these. Participants reported their weight on the surveys and during the interviews. The average time between completion of the initial NESHI interview and the week 0 survey was 10.4 (SD = 11.0) days, while the time between the week 8 surveys and the final interviews was 12.4 (SD = 13.5) days.

Participants

A total of 113 persons signed informed consent forms, and 50 actively entered the long-distance treatment study. Sixty-three participants signed consent forms, but were ruled out of the trial for the following reasons: 9 persons returned consent forms but did not complete the initial interview, 21 completed consent forms and the initial interview but did not complete any surveys after the week 0 assessment, 9 had nocturnal sleep-related eating disorder,[16] 11 were taking psychotropic medications (SSRIs, sleep aids), 5 had sleep apnea, 4 had restless legs syndrome, 2 had bipolar disorder, 1 worked the night shift, and 1 returned unusable data. In addition to these exclusion criteria, persons could not enroll if they were currently participating in a weight loss program.

Of the 50 subjects who entered the trial, 39 (78%) were women. Participants were a mean age of 47.7 (SD = 12.5) years; ethnicity was not assessed. At the initial interview, the mean participant body mass index (BMI; kg/m^2) was 30.5 (SD = 6.7) kg/m^2, including 9 participants who were of normal weight (BMI < 25 kg/m^2). The average age at onset of NES was 26.0 (SD = 10.8) years.

Statistical Analyses

Descriptive statistics were used to present demographic data, and paired sample t tests were used to analyze differences in both interview and survey data at study beginning and end points. Fifty participants were interviewed by telephone before week 0, and 44 were interviewed after week 8. Fifty survey packets were returned at week 0 and 27 at week 8. Of the 6 participants who were lost to follow-up at the final interview, only 1 had responded favorably as assessed by the last survey. Therefore, paired-sample t tests with the last observation carried forward (LOCF) were used as a conservative method to account for missing data points for analysis of the surveys. SPSS, version 12.0 (SPSS Inc., Chicago, Ill.), was used.

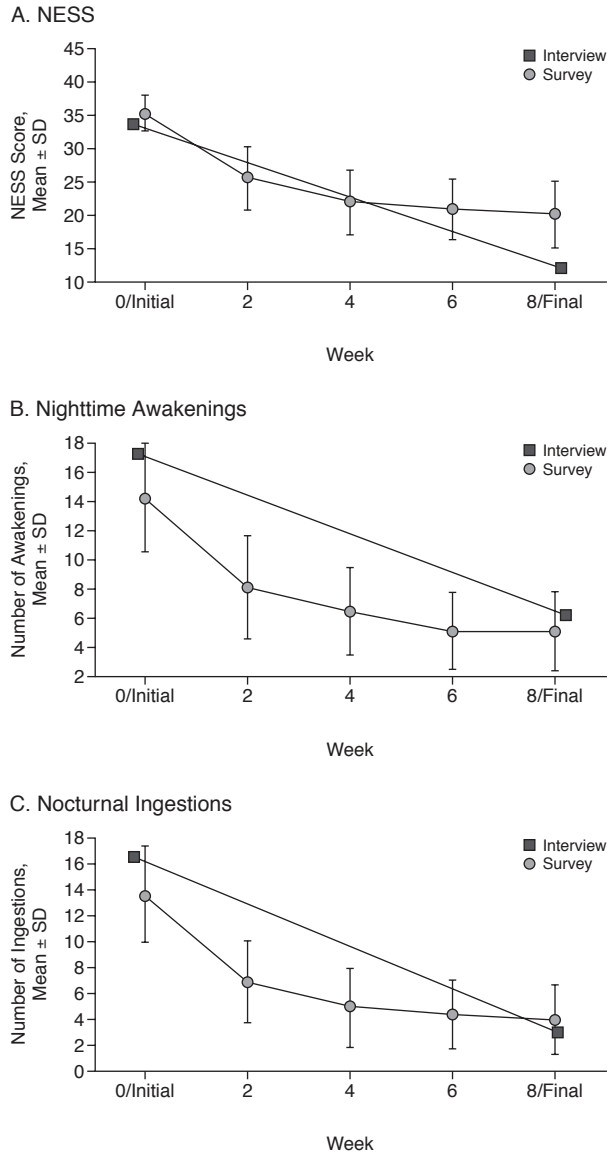
RESULTS

Long-Distance Study

The mean NESS survey score decreased from 35.4 (SD = 5.5) at week 0 to 20.5 (SD = 9.9) at week 8 ($t = 10.6$, $df = 48$, $p < .001$) (Figure 1). The NESS score obtained from the interview fell from 33.0 (SD = 5.0) to 13.3 (SD = 7.9) ($t = 14.9$, $df = 42$, $p < .001$). Survey values for nighttime awakenings decreased from 14.3 (SD = 7.5) per week to 5.1 (SD = 5.4) per week ($t = 8.2$, $df = 47$, $p < .001$). The mean interview value for nighttime awakenings fell from 17.4 (SD = 10.0) to 6.2 (SD = 7.8) ($t = 6.3$, $df = 37$, $p < .001$).

Nocturnal ingestions assessed by survey decreased from 13.6 (SD = 7.3) per week to 4.1 (SD = 5.4) ($t = 9.1$, $df = 47$, $p < .001$). The corresponding interview value fell

Figure 1. Decrease in Features of the Night Eating Syndrome During Sertraline Treatment[a]



[a]Figure 1 shows the changes in 3 major outcome variables during the first 8 weeks of treatment according to surveys conducted every 2 weeks and telephone interviews conducted at baseline and treatment end. The decreases in Night Eating Symptom Scale (NESS) scores, nighttime awakenings per week, and nocturnal ingestions per week from baseline to week 8 (or treatment end) were statistically significant ($p < .001$).

from 16.9 (SD = 9.7) to 3.5 (SD = 6.8) nocturnal ingestions per week ($t = 7.7$, $df = 37$, $p < .001$) (Figure 1).

The percentage of food intake consumed after the evening meal is often overestimated on surveys; accordingly, it was assessed by interview only. The percentage decreased from 53.2% (SD = 14.1%) at baseline to 17.9% (SD = 14.1%) ($t = 10.2$, $df = 28$, $p < .001$) at the final interview. Depressive symptoms on the BDI-II fell from 16.7 (SD = 11.3) to 7.1 (SD = 7.9) ($t = 7.0$, $df = 48$, $p < .001$). Quality of life as assessed by the Q-LES-Q increased from 46.5 (SD = 9.5) to 55.2 (SD = 9.4) ($t = 6.7$, $df = 48$, $p < .001$). The weights of the 41 overweight and obese participants assessed by survey decreased by 3.0 kg (mean = 90.74, SD = 22.8 kg to mean = 87.77, SD = 23.0 kg; $t = 2.7$, $df = 40$, $p = .01$). The decrease in weight as assessed by interview was 2.2 kg, from a mean of 89.1, SD = 22.4 kg, to 86.9, SD = 22.5 kg ($t = 4.5$, $df = 35$, $p < .001$).

The mean daily dose of sertraline was 122.5 (SD = 50.1) mg based on survey data at week 8 and 125.6 (SD = 59.9) mg based on the final phone interview.

Comparison of the Long-Distance Study to an Open-Label Trial of Sertraline

How are we to evaluate these results? How do they compare with traditional face-to-face treatment? Fortunately, data on traditional face-to-face treatment are available from the open-label trial of sertraline reported above.[4] These data provide an impressionistic comparison with the results of the long-distance study. Statistical comparisons were not attempted because of the differences between the 2 samples and their treatment protocols.

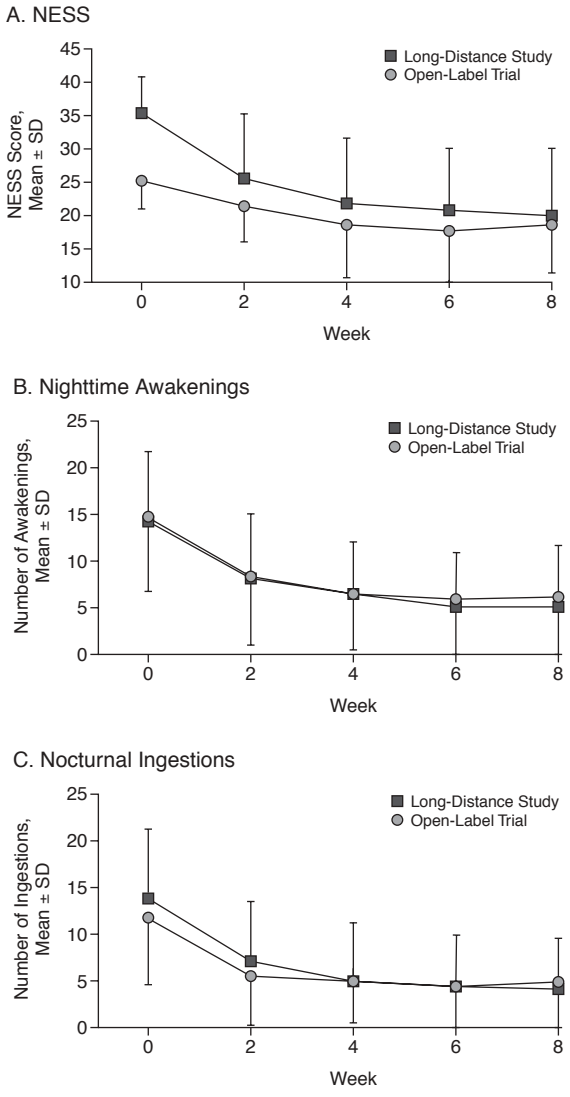
The face-to-face trial was conducted in our clinic with 17 night eaters whose characteristics have been described previously.[4] Subjects completed the same surveys as in the long-distance study: the NESS, BDI-II, and Q-LES-Q measures. In addition, they completed a rigorous diagnostic procedure that involved 7-day food and sleep records.[3] Data were collected every 2 weeks, as in the current study. Treatment in the face-to-face study was of 12 weeks' duration, permitting comparisons of its results with those of the long-distance study at 8 weeks.

Both studies showed significant decreases in NES features, as measured by the biweekly surveys. Figure 2 shows the long-distance survey results plotted against the face-to-face survey data. The long-distance results compared very favorably with those of the face-to-face study.

The NESS ratings of the long-distance patients were initially higher than those of the face-to-face patients, and they fell more rapidly so that the groups achieved similar results at week 8. Figure 2 also shows the remarkable similarity between the results of the 2 studies in both awakenings and nocturnal food ingestions. The 2 groups started at comparable (and elevated) levels and fell markedly to almost normal levels by 8 weeks.

The reduction in the percentage of caloric intake after supper in the long-distance study (mean = 53.2%, SD = 14.1% to mean = 17.9%, SD = 14.1%) compared very favorably with that in the face-to-face study (mean = 51.8%, SD = 16.3% to mean = 29.4%, SD = 21.1%). Weight among the 41 overweight and obese participants in the long-distance trial decreased by a mean of 3.0 kg

Figure 2. Comparison of Long-Distance and Face-to-Face Studies of Sertraline in the Treatment of Night Eating Syndrome[a]



[a]Figure 2 shows the changes in the Night Eating Symptom Scale (NESS), nighttime awakenings per week, and nocturnal ingestions per week for the 2 independent studies: the long-distance study and the open-label trial, using the last observation carried forward. The results of the long-distance study compared favorably with those of the face-to-face study.

(SD = 7.1), whereas the weight of the 17 overweight and obese participants in the open-label trial remained stable from week 0 to week 8 (mean change = –0.15 kg, SD = 2.9).

The BDI-II was initially similar in the long-distance and face-to-face studies: mean = 16.7 (SD = 11.3) and mean = 18.4 (SD = 8.8), respectively. Values in the long-distance study fell to 7.1 (SD = 7.9), while those in the face-to-face study fell to 11.7 (SD = 8.2). The change in Q-LES-Q scores was also similar in the long-distance study (week 0 = 46.5, SD = 9.5 to week 8 = 55.2, SD = 9.4) and face-to-face studies (week 0 = 48.1, SD = 7.0 to week 8 = 53.8, SD = 11.3).

Survey data showed that the dosage of sertraline at week 8 was 122.5 (SD = 50.1) mg/day in the long-distance study and 101.5 (SD = 60.9) mg/day at week 8 in the face-to-face study.

DISCUSSION

This long-distance study demonstrated significant reductions in all measures including the NESS, evening hyperphagia, nocturnal awakenings, and nocturnal ingestions of food and improvement in mood and quality of life. Weight was also significantly decreased among the overweight and obese participants. Survey data showed less improvement than did the phone interview data, reflecting both the conservative influence of LOCF analyses and the omission of 6 participants who could not be reached for a final interview.

The importance of these results is indicated by the fact that the long-distance treatment with sertraline appeared to be as effective in the control of NES as had been our earlier face-to-face treatment.[4] As noted above, telemedicine has been successfully used in the treatment of a number of disorders, most of which relied on psychotherapeutic treatments. We believe that this is the first study to facilitate pharmacotherapy delivered at geographically diverse locations, through collaboration with local physicians.

This novel paradigm resulted in the pharmacotherapy of a number of persons who might not otherwise have received treatment. The results, however, were not achieved without difficulty: (1) determining the suitability of candidates for treatment required numerous complete (and incomplete) telephone calls; (2) during treatment, frequent telephone calls were required to obtain surveys; and (3) patient phone and e-mail contact frequently presented a dilemma (e.g., patients asked about use of the medication, including dosage and timing). It was necessary for study personnel to tread a fine line between providing general information and not dispensing specific advice on treatment, which might constitute the practice of medicine without a license. Even when patients were told that study personnel could not advise them on the specifics of treatment, it often required considerable skill to redirect patients back to their family doctors, who made all of the treatment decisions. Future efforts should anticipate these problems and provide special training of research assistants to deal with them.

Limitations of the study include the absence of a control intervention and the reliance on self-report of outcome measures. We considered the use of a control intervention, but concluded that it would not be feasible to recruit sufficient subjects at a distance for a placebo

intervention or to provide placebo to individual care providers.

Treatment studies of eating disorders traditionally use self-report to evaluate outcome variables, and this study is not unique in this regard. However, more contact between study personnel and the treating physician would have been helpful, particularly in validating reports of weight loss as well as the physicians' assessment of the value of our consultation.

In conclusion, this long-distance study confirmed the effectiveness of sertraline in an open-label treatment larger than that of our previous study. The study also introduced a paradigm for facilitating pharmacotherapy at a distance and educated community physicians on the treatment of NES. This paradigm may prove useful in facilitating and evaluating the effectiveness of long-distance pharmacotherapy of many other disorders.

Drug name: sertraline (Zoloft and others).

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