Night eating syndrome: How to treat it?

THISCiane FERREira PINTo1, FRANCisco GIRLEudo COUTINHO DA SILVA2, VERALiCE MEIRELES SALES DE BRUIN3,

PEDRO FELiPE CARVALHEDO DE BRUIN4*

1MSc in Pharmaceutical Sciences. Universidade Federal do Ceará (UFC), Fortaleza, CE, Brazil
2MSc in Medical Sciences. UFC, Fortaleza, CE, Brazil
3PhD in Psychobiology. Associate Professor, Department of Clinical Medicine, UFC, Fortaleza, CE, Brazil
4PhD in Medicine (Pneumology). Associate Professor, Department of Clinical Medicine, UFC, Fortaleza, CE, Brazil

SUMMARY

Night eating syndrome (NES) is characterized by caloric intake ≥ 25% of total daily after dinner and/or by two or more weekly nocturnal awakenings accompanied by food ingestion. Causes of NES are not entirely clear and seem to involve a desynchronization between the circadian rhythms of food ingestion and sleep, resulting in a delayed pattern of food intake. Estimates of the prevalence of NES in the general population are around 1.5%, and although much higher frequencies have been described in obese individuals, a causal relationship between NES and obesity is not clearly established. Since the first NES reports, several treatment modalities have been proposed, although, in many cases, the evidence is still insufficient and there is no consensus on the ideal approach. In order to conduct a critical review of proposed treatments for NES since its original description, a systematic search of articles published in journals indexed in Medline/Pubmed database in the period 1955–2015 was performed. Seventeen articles addressing non-pharmacological and pharmacological therapies met the selection criteria. Based on the articles analyzed, we conclude that serotonergic agents and psychological interventions, particularly cognitive behavioral therapy, have been shown to be effective for the treatment of NES. A combination of non-pharmacological and pharmacological therapies must be considered in future studies on the treatment of these patients.

Keywords: circadian rhythm, obesity, eating disorders, sleep disorders.

INTRODUCTION

Night eating syndrome (NES) was originally described by Stunkard et al., in 1955, in obese patients treated at a specialized clinic for nocturnal hyperphagia, insomnia, and morning anorexia.1 Its main feature is a delay in the pattern of food intake, usually defined by ingestion of at least 25% of total daily calories after dinner and/or during nocturnal awakenings. In the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), NES is classified in the category of eating disorders not otherwise specified.2,3

The prevalence of NES in the general population is approximately 1.5%. In contrast, this syndrome is present in 6 to 14% of patients in clinical follow-up for weight loss and 8.9 to 42% of candidates for bariatric surgery.4,6 High frequencies, close to 12%, have also been reported in psychiatric patients.7 A prevalence of 3.8% was observed for NES in elderly patients with type 2 diabetes,8 8.6% in patients with sleep apnea,9 and 17% in patients with restless legs syndrome.10

The causes of NES are not fully understood but appear to involve a desynchronization between the rhythms of food intake and sleep. Despite the delay in the circadian pattern of food intake typically observed in these patients, changes in sleep-wake rhythm (the beginning and end of the sleep time) have not been demonstrated in actigraphic and polysomnographic studies.11,12 In normal individuals, energy homeostasis is controlled by a neurohumoral system that minimizes the impact of small fluctuations in energy balance, and leptin and insulin are critical elements in this control. The nighttime sleep period is characterized by prolonged fasting, where the en-
Energy balance is maintained through hormonal changes. In patients with NES, leptin levels tend to be reduced at night, which may contribute to nocturnal awakenings accompanied by food ingestion. A reduction in the levels of ghrelin, probably due to the nocturnal food intake itself, has also been described in these individuals. Low levels of melatonin have been implicated in the desynchronization process found in NES.

The relationship between NES and obesity is not fully understood. Studies in overweight and obese patients, usually recruited from specialized clinics, have shown a high frequency of NES compared to community controls, suggesting the existence of a relationship between NES and obesity. However, epidemiological studies have not confirmed whether this association exists and numerous cross-sectional studies show inconsistent results. These contradictory results can be attributed, at least in part, to methodological issues such as differences in the operational definition of NES, small variation in body mass index (BMI) in homogeneous populations or insufficient statistical power to identify differences between groups. In an attempt to overcome the limitations of previous studies, Colles et al. (2007) recruited 431 individuals with BMI ranging from less than 18 to over 65 kg/m² and identified an independent association between NES and BMI. Although a relationship between obesity and NES is considered probable, its exact nature remains uncertain. Adult obese patients with NES are, on average, older than obese individuals without NES, which suggests that NES leads to weight gain over time. A study including 2,317 individuals showed that women who eat between 11 pm and 5 am hours gain more weight, which suggests that NES leads to weight gain over time.

Recently, a study including 486 articles were retrieved (258 having as keywords “night eating syndrome”). After reading the summaries, 469 were
excluded because they did not address our subject of study. The 17 selected articles included case reports, case series, and clinical trials, involving non-pharmacological and pharmacological treatment modalities.

Non-pharmacological treatment
Administration of bright light in the morning has produced beneficial effects in patients with seasonal affective disorder, a condition in which changes in sleep and mood patterns, as well as in circadian neurobiological markers similar to those seen in NES, are observed.40,41 This led some groups to assess its applicability in the management of patients with NES. Friedman et al. (2002) reported that a patient with NES treated with 40 mg/day of paroxetine for depressive symptoms, who underwent 14 morning sessions of phototherapy with 10,000 lux white light for 30 minutes, showed improvement of depression and symptoms of night eating. After one month, there was a recurrence of eating-related symptoms, although the intensity of depressive symptoms remained low. The authors decided to start the morning phototherapy, obtaining complete suppression of eating-related symptoms after 12 sessions.42 Subsequently, the same group reported the case of a non-obese patient with NES and depression, who underwent morning phototherapy with 10,000 lux of white light for 30 minutes; after 14 sessions, improvement of depression and symptoms of NES was observed.43

The effect of progressive muscle relaxation therapy on stress, mood, hunger, and eating pattern was evaluated by Pawlow et al. (2003) in 20 individuals with NES randomly assigned to a treatment or control group. In the latter, patients remained at rest for the same time duration of the therapy session. There were two sessions lasting 20 minutes each, carried out one week apart. The levels of stress, relaxation, and salivary cortisol were determined before and after each session. In addition, in the first and eighth day, the authors evaluated the mood. It was observed that progressive muscle relaxation reduces the levels of stress, anxiety and salivary cortisol immediately after the session. This technique was associated with increased morning hunger and reduced night eating.44

Cognitive behavioral therapy (CBT) has been successfully used in the management of various conditions, including depression, insomnia, and some eating disorders. Allison (2012) proposed a brief but intensive model of CBT for NES that includes information on NES, guidance on sleep hygiene and healthy nutrition, self-monitoring of eating habits, exercise, and relaxation strategies.45 A non-controlled pilot study with 25 participants (19 female) on the use of CBT in cases of NES showed an improvement in symptoms and weight loss.46

Vander Wal et al. (2015) conducted a clinical trial involving patients with symptoms of NES randomized to receive only educational measures, educational measures, and relaxation with exercise, or educational measures and relaxation without exercise. The three groups showed a reduction in symptoms of NES, depression, anxiety, and perceived stress. The reduction in the percentage of food eaten after the last meal was higher in the group with educational measures and relaxation without exercise. These results suggest that educational measures associated with relaxation techniques have a promising role in the management of patients with this condition.47 Studies on non-pharmacological treatment of NES are summarized in Table 1.

Pharmacological treatment
It is believed that neuroendocrine alterations associated with changes in the rhythm of food intake are important in the pathogenesis of NES. It has been suggested that in these patients there would be a relative deficiency of postsynaptic serotonin in the mesencephalic nuclei, caused by hyperactivity of the carrier system, which would lead to a defect in the regulation by the central nervous system of sleeping and feeding rhythms. Thus, the use of selective serotonin reuptake inhibitors (SSRIs), which reduces the binding of serotonin transporters and increases postsynaptic serotonin, could restore circadian function and satiety.15,39 Favorable results of the use of SSRIs to treat obesity48,49 and other eating disorders such as anorexia nervosa and binge eating disorder have been reported.50-52 Miyaoka et al. (2003) prescribed paroxetine (n=3) or fluvoxamine (n=1), SSRIs, to four patients with NES characteristics and reported effective control of nocturnal eating episodes after 2 to 3 weeks of treatment.53 In an open clinical trial with 17 participants with NES characteristics, O’Reardon et al. (2004) evaluated the effect of other SSRI, sertraline, for 12 weeks on the number of awakenings, nocturnal food intake, and ingestion of food after dinner, and observed an improvement of all the aspects evaluated in all patients. Five patients had significant weight loss, close to 5 kg on average.58 O’Reardon et al. (2006) conducted a randomized double-blind placebo-controlled study to assess the efficacy of sertraline for 8 weeks in 28 patients with NES. The authors reported a significant reduction in the number of awakenings with nighttime eating. In addition, an average weight reduction of about 3 kg was observed in the sertraline group but not in the placebo group.53
TABLE 1  Summary of studies involving non-pharmacological treatment of patients with night eating syndrome.

<table>
<thead>
<tr>
<th>Author</th>
<th>Study type</th>
<th>Treatment</th>
<th>Sample characteristics</th>
<th>Duration</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Friedman, 2002</td>
<td>Case report</td>
<td>Phototherapy 10,000 lux for 30 minutes</td>
<td>1 female aged 51 years with NES, obese</td>
<td>14 days</td>
<td>Improvement of depressive symptoms and nocturnal eating</td>
</tr>
<tr>
<td>Pawlow, 2003</td>
<td>Controlled clinical trial</td>
<td>PMR</td>
<td>20 participants with NES (intervention, n=10; control, n=10)</td>
<td>1 week</td>
<td>Reduction of nocturnal appetite and increased morning hunger</td>
</tr>
<tr>
<td>Friedman, 2004</td>
<td>Case report</td>
<td>Phototherapy 10,000 lux for 30 minutes</td>
<td>1 male aged 46 years with NES, not obese</td>
<td>14 days</td>
<td>Improvement of depressive symptoms and NES</td>
</tr>
<tr>
<td>Allison, 2010</td>
<td>Non-controlled clinical trial</td>
<td>CBT</td>
<td>25 participants with NES (19 women)</td>
<td>12 weeks</td>
<td>Improvement of depressive symptoms and NES, weight loss</td>
</tr>
<tr>
<td>Vander Wal, 2015</td>
<td>Controlled clinical trial</td>
<td>CBT, exercise, and education</td>
<td>44 patients with NES (education, n=14; CBT without exercise, n=15; CBT with exercise, n=14)</td>
<td>3 weeks</td>
<td>Improvement of NES using any of the three interventions</td>
</tr>
</tbody>
</table>

NES: night eating syndrome; PMR: progressive muscle relaxation; CBT: cognitive behavioral therapy.

Stunkard et al. (2006) conducted an open clinical trial, at distance, to evaluate the effectiveness of sertraline in the treatment of NES. Patients who spontaneously sought the help of researchers via website, email or phone were asked to fill the Night Eating Questionnaire and underwent a structured interview to determine the presence of NES. Fifty participants were treated with sertraline, which was prescribed by their own doctors. To evaluate the response, the questionnaire was completed every 2 weeks and the interview repeated at the end of 8 weeks. The researchers reported improvement in nocturnal hyperphagia, nocturnal awakenings with food intake, and depressive symptoms. Vander Wal et al. (2012) conducted a randomized placebo-controlled trial of 40 patients with NES to evaluate the effect of escitalopram, an other SSRI, for 12 weeks, and found no difference between groups in the reduction of the symptoms of NES assessed based on the Night Eating Questionnaire, weight loss, mood, and adverse events. In contrast, Allison et al. (2013), in a clinical trial involving 31 patients with NES to evaluate the use of escitalopram, found a significant reduction in nocturnal hyperphagia and nocturnal awakenings accompanied by food intake, measured based on the Night Eating Symptom Scale, after 12 weeks.

The use of topiramate, an agonist of gamma aminobutyric acid, in patients with NES has been reported by some authors. Winkelman (2003) observed a reduction in nocturnal awakenings with food intake, improved sleep and weight loss in two patients who failed prior treatments with psychotherapy and pharmacotherapy. Tucker et al. (2004) reported the case of a 40-year-old obese woman treated with topiramate for 8 months, who achieved reduction in episodes of nocturnal awakenings accompanied by food intake. Cooper-Kazaz (2012) reported the case of a non-obese female patient under treatment for depression with venlafaxine, who developed NES and weight gain. She received topiramate for 6 weeks, with improvement of night eating symptoms, sleep quality, self-esteem and well-being, and weight loss.

A decrease in nocturnal melatonin levels in patients with NES has been reported. Based on this finding, agomelatine, an agonist of the MT1 and MT2 receptors, has been considered as an option for treatment of NES. Milano et al. (2013) gave agomelatine (25 mg/day during the first 3 weeks and 50 mg/day in the subsequent weeks) for 12 weeks to five patients with symptoms of NES and depression, and observed improvement in clinical symptoms, mood, and number of nocturnal awakenings, as well as weight reduction. Given the strong association between NES and changes in the sleep-wake and eating cycles, in addition to the frequent finding of depressive symptoms and low melatonin levels, new studies are required in order to properly assess the efficacy of agomelatine to treat this syndrome. Studies on the pharmacological treatment of NES are summarized in Table 2.

CONCLUSION
This critical review of the literature on the treatment of NES in the last 60 years shows that the number of studies is still insufficient, especially regarding controlled clinical trials with adequate sample size and methodology. The results above suggest that serotonergic agents and psychological interventions such as the CBT can be effective in the treatment of NES. Among the SSRIs, sertraline was the drug most studied for this condition. Preliminary reports of beneficial effects of topiramate and agomelatine justify further studies involving these substances and...
similar medications. Similarly, an initial report of benefits obtained with phototherapy suggests that chronobiological treatments can be useful and should be further examined. Finally, in view of the complexity of the manifestations of NES and its frequent association with obesity, mood disorders, and other comorbidities, the combination of non-pharmacological and pharmacological therapies coupled with a multidisciplinary approach needs to be considered in future studies on the treatment of these patients.

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Resumo

Síndrome do comer noturno: como tratar?

A síndrome do comer noturno (SCN) caracteriza-se por ingestão calórica ≥ 25% do total diário após o jantar e/ou por dois ou mais despertares noturnos semanais acompanhados de alimentação. As causas da SCN não estão totalmente esclarecidas e parecem envolver uma des sincronização entre os ritmos circadianos de alimentação e sono, resultando em um atraso do padrão alimentar. Estimativas da prevalência de SCN na população geral estão em torno de 1,5% e, embora frequências bem mais elevadas...
tenham sido descritas em obesos, uma relação de causa-

lidade entre SCN e obesidade não está claramente estabe-

lecida. Desde os primeiros relatos da SCN, várias modalida-

des de tratamento têm sido propostas, embora, em muitos casos, a evidência ainda seja insuficiente e não

existia um consenso sobre a abordagem ideal. Com o ob-

jetivo de realizar uma revisão crítica dos tratamentos pro-

postos para a SCN, desde sua descrição original, foi reali-

zada uma busca sistemática de artigos publicados nos periódi-

cos indexados na base de dados MedLine / Pubmed entre

1955 e 2015. Dezessete artigos, abordando terapias

não farmacológicas ou farmacológicas, preencheram os

critérios de seleção. Com base nos artigos analisados,

conclui-se que os agentes serotoninérgicos e intervençõ

es psicológicas, particularmente, a terapia cognitivo-com-

portamental, têm mostrado eficácia no tratamento da

SCN. Uma combinação de terapias não farmacológicas

e farmacológicas precisa ser considerada em estudos futuros

sobre o tratamento desses pacientes.

Palavras-chave: ritmo circadiano, obesidade, transtornos

alimentares, transtornos do sono.

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