

## Case Report

# Topiramate Therapy: Night Eating Cure with Five Year Sustained Weight Loss in an Obese Patient with Type 2 Diabetes

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**Abstract**

Obesity is a leading cause of morbidity and mortality and it is essential to identify potentially treatable contributors. Night eating causes weight gain and obesity, predicts poor weight loss outcomes and is associated with poorer diabetes control as well as diabetes complications. We report the successful treatment of a 70 year old female with diabetes, fighting obesity for many years, complicated by longstanding and severe night eating. Topiramate therapy, prescribed for essential tremor, has achieved sustained weight loss with suppression of night eating without major side-effects for five years so far, after forty years of night eating behaviours. Improvements were also seen in the subject's glycaemic control and daily life.

**ABBREVIATIONS**

**NES:** Night Eating Syndrome; **SRED:** Sleep Related Eating Disorder

**INTRODUCTION**

Night eating has been discussed off and on in literature for sixty years, becoming of increasing interest in recent decades with rising obesity. The concept of night eating involves the intake of food during the normal night time fasting period. It was first reported in 1955 by Stunkard et al. [1] as Night Eating Syndrome (NES). NES, categorised an 'eating disorder not otherwise specified' in the Diagnostic and Statistic Manual (DSM) IV was first described in a subset of treatment-resistant obese subjects referred to a speciality centre [1,2]. The original criteria included evening hyperphagia (caloric intake taken after the evening meal), insomnia and morning anorexia. Expanded yet more stringent criteria for NES from 1999 [3], included at least one episode of night-time awakening (with the subject fully alert), consumption of food during these episodes and symptoms for at least three months.

More recently, research diagnostic criteria have been proposed following The First International Night Eating Symposium [4]. If NES is suspected, the Night Eating Questionnaire (NEQ) may be used as a screening tool, but should be followed by a clinical interview to confirm the diagnosis, as it may be oversensitive.

NES causes weight gain and obesity [1]. NES symptoms are exacerbated by stress and associated with depressed mood, low self-esteem, shame and a feeling of loss of control. These associated feelings of shame probably lead to under-reporting of NES, disguising its true prevalence. Patients report compulsive over-ingestion, feeling unable to return to sleep without eating. The food consumed by NES sufferers at night has high fat and high carbohydrate content, reported as a ratio of 7:1 carbohydrate:protein. It has also been suggested that people with NES choose these types of foods to improve sleep and mood by raising serotonin [3].

Another night eating disorder, Sleep Related Eating Disorder (SRED), was described by Schenck et al in the early nineties [5,6]. SRED involves involuntary night time eating in the absence of hunger. Often eating in a sleep state, sufferers report partial

or complete amnesia. However due to the significant variation of consciousness during night eating this characteristic is not required for SRED diagnosis. Importantly no SRED patients have eating problems before sleep onset [7]. Sometimes they ingest items that may be hazardous, such as extremely hot liquids or large pieces of food that may cause choking, as well as some foods that may be inedible or toxic, such as pet food, raw meat, buttered cigarettes and cleaning solutions [8]. People with SRED may also undertake dangerous food preparation which may result in serious injury. SRED is classified as a parasomnia and is often associated with other sleep disorders such as sleepwalking, restless leg syndrome and obstructive sleep apnea [8].

The literature discusses the importance of differentiating between NES and SRED; however, there are reports of overlap between them, especially relating to consciousness and sleep disorders [4,7,9]. Both NES and SRED are common in women and onset has been reported in young adulthood [10].

Night eating is more common in people with obesity [11,12] and diabetes [13,14,15]. Estimations of prevalence of NES are still preliminary due to the diagnostic criteria changes and small initial studies reported from obesity, diabetes and psychiatric clinics. The prevalence reported among obese is between 6 and 42% [11,12]. The prevalence in diabetes populations has been reported as 9.7%, in both type 1 and type 2, [13] and 3.8% [15] to 12.4% [14] in people with type 2 diabetes. People with diabetes and night eating behaviours show worse management of diet, exercise, and glucose monitoring and are more likely to be depressed [13,14,15]. Finding treatments for night eating behaviours is critical for these individuals.

We report effective topiramate treatment in a case of lifelong, severe night eating in an obese woman with type 2 diabetes. Topiramate, initially an anti-epileptic, is used for many conditions (reviewed in 16) including essential tremor [17] with lessening of appetite as a side-effect. The specific mechanism is unknown, but actions include blockage of voltage-dependent sodium channels, enhancement of GABA activity, kainate/AMPA/glutamatergic receptor antagonism and inhibition of mitochondrial carbonic anhydrase. Carbonic anhydrase is involved in several metabolic processes which may disrupt de novo lipogenesis and contribute to the weight loss effects of the drug [18].

## CASE PRESENTATION

A 65 year old professional woman referred for diabetes assessment gave a history of psychiatrist-treated chronic depression and "attention deficit hyperactivity disorder" treated with sertraline and dexamphetamine. The subject's records show that sertraline "reduced cravings" and on its cessation she reported "eating more".

Obesity had been a major problem for many years. She reported lifelong disordered eating: childhood "anorexia nervosa" with binge eating, followed by bulimic behaviour into her fourth decade. She had attempted multiple weight loss strategies, with variable success and inevitable weight regain. During a major depressive episode, sertraline was ceased and she began sodium valproate, with further weight gain. She also had type 2 diabetes from age 52, initially treated with metformin.

She had frequent dietitian review, discussing her eating

behaviours. Initially, she described carbohydrate craving with snacking after her evening meal. This rapidly progressed to episodes of compulsive night-time eating, usually with full awareness and recollection. She reported very rare episodes of amnesia for night-time eating.

After admitting to night eating, she reported commencing night eating at 21 years of age, just after having a baby, where she would have to get up regularly through the night to tend to the baby. She also reported a family history of sleep walking, affecting her and other family members in childhood.

In an attempt to control eating, she began locking herself in her bedroom at night, slipping the key under the door for her family to let her out next morning. However, she reported climbing out of her bedroom window into the kitchen, eating and returning to bed, slipping the key back for the morning.

Her weight reached a maximum of 108 kg; height 155cm and BMI 45.0. Her HbA1c rose to 10.0% necessitating insulin therapy. She was prescribed nocte temazepam by her psychiatrist, without effect on eating.

When she complained of bilateral hand tremor, she was reviewed by a neurologist and essential tremor was diagnosed. Topiramate was commenced: 25 mg daily for a week, increasing by 25 mg weekly to 50 mg twice daily. She experienced initial dizziness and somnolence, which improved with time. With topiramate she reported significant reduction in appetite, less thoughts about food and normalisation of her eating pattern to three meals per day with complete loss of night eating. She lost 20 kg in weight, now sustained for five years, with subsequent improvement in her glycaemic control. Her HbA1c at commencement of topiramate was 7.5% and together with decreased insulin requirements, fell to 6.7%. Both the essential tremor and the night eating symptoms however, are dosage sensitive with graded recurrence of both disorders if topiramate dose is reduced. Due to side-effects it was reduced to 100mg twice a day, which maintains effective suppression of night eating and weight loss.

The subject's daily life has significantly improved. Besides the expected physical benefits of 20kg weight loss, she no longer requires extreme measures, such as "jailing" herself overnight, to stop compulsive night eating. Without the night eating the subject has also been relieved of the guilt- and shame-associated behaviours of excessive night time eating.

## DISCUSSION

We discussed earlier the overlap between night eating disorders, NES and SRED, creating confusion around diagnosis. Some researchers describe these two disorders being extremes of a single condition where NES and SRED are at opposite ends of a night eating spectrum [8,9]. Auger [7] argues these conditions can be reliably diagnosed with a complete history of sleep, medical and psychological history, although he highlights recent blurring between the two disorders with the removal of state of consciousness from SRED criteria. Allison et al 2010 [4] reported that many patients with night eating behaviours manifest features of both NES and SRED but one disorder is dominant.

Our patient was not diagnosed by questionnaire. However,

the patient displayed many clinical features of NES. Initially, she described carbohydrate craving with snacking after her evening meal, characteristic of NES and not SRED. She also described episodes of compulsive night-time eating, usually with full awareness and recollection. Despite very rare episodes of amnesia for night-time eating (not characteristic of NES), the NES diagnosis was otherwise completely appropriate. At night she consumed high carbohydrate foods, such as sandwiches, which are commonly consumed by those diagnosed with NES. In a group of patients with NES Ceru-Bjork et al. [11] found sandwiches were the most commonly consumed food at night and were perceived to have contributed to the development of obesity in a substantial proportion of these patients. Importantly our patient never reported eating hazardous, inedible, toxic or inappropriate items as described in individuals with SRED.

Stressful life events have been associated with the onset of night eating [1] as seen in our patient where onset coincided with post partum. Also the frequent night waking and metabolic changes associated with pregnancy and post-partum may have added to the establishment of night eating.

The association of psychopathology features and NES has been well documented [19] and are seen in our patient with an extensive history of depression and eating disorders. Evidence of the shame, commonly associated with night eating, felt by our patient can be seen in the delay in divulging the night eating symptoms, only feeling comfortable to discuss it after building up trust with her health professionals.

While our patient reported a family history of sleep disorders (sleep walking), which is commonly associated with SRED, de Zwaan et al. [9] reported a group of patients who were diagnosed with both NES criteria (1955 and 1999) and also commonly reported having sleep disorders. Sleep walking was reported in 12% of patients diagnosed with NES. Sleep apnoea was reported in over 9% of de Zwaan's patients; our patient was tested and found not to have sleep apnoea.

There are differences in the criteria used in night eating studies. For example for NES: different starting times of evening hyperphagia (5pm, 8pm, etc.), different amounts of food after the evening meal (25% and 50% of daily food intake), different requirements for morning anorexia (not hungry, skipped breakfast, etc.) [4]. Such differences make comparisons between studies difficult and convincing diagnosis problematic.

Interestingly, 25% of individuals studied by de Zwaan et al. [9] did not consider night eating to be a problem. However, those that did consider it a problem had a history of eating disorders (Anorexia Nervosa, Bulimia Nervosa or Binge Eating Disorder), were younger at onset, had higher BMI and had significantly less control over evening and night eating [9]. Our patient considered night eating to be a problem, demonstrated by the extreme measure of jailing herself in her bedroom to stop the behaviour. She greatly resembled the individuals that considered night eating to be a problem described by de Zwaan et al. [9] including a significant history of eating disorders, onset in her early twenties, a lifetime of weight problems and reports of complete loss of control over night eating.

Importantly NES is associated with less weight loss in obese

patients [19]. Our patient had tried multiple weight loss strategies with inevitable weight regain. With the assistance of topiramate treatment she has lost 20 kg, which has been sustained for five years.

Studies on effective treatments for night eating are few: suggested treatment approaches for NES include pharmacological interventions, cognitive behavioural therapy, behavioural therapy, progressive muscle relaxation, and phototherapy [20]. Non-pharmacological interventions alone are not beneficial in the treatment of night eating [7]. Pharmacological intervention strategies have been described for both NES and SRED [7,20]. The selective serotonin reuptake inhibitor sertraline has been suggested to achieve reduction or full remission of NES symptoms and weight loss in some patients while being well tolerated [21]. However, such studies involved small numbers predominantly in open-label fashion. Sertraline reduced cravings in our subject but without remission in night eating at psychotherapeutic dosage.

There have been many reports of the benefits of topiramate therapy for eating disorders, for example in binge eating/bulimia behaviours, NES and in particular SRED [8]. There has been only one small open-label study [10] and one case study [22] on the treatment of NES with topiramate. Both were short term (8.5 months and 3 months) with reported benefits. Our case study documents long term treatment over five years with dosage adjustment. We are unaware of such long-term remission of night eating symptoms and sustained weight loss with topiramate (or any other treatments).

A large study by O'Reardon et al. [23] based on food diaries and motion actigraphs in a large group of overweight NES subjects showed that the sleep duration, onset and offset in NES subjects did not differ compared to an overweight control group, despite the frequent awakenings experienced by NES subjects. Importantly, the 24 hr energy intake was not significantly different between the groups but the timing and distribution of food intake was significantly different. In NES subjects the intake was lower during the first 8 hours (6am-2pm), similar in the middle 8 hours of the day, and higher in the last 8 hours (10pm-6am). The study suggests a circadian phase delay in the timing of food ingestion relative to a normally timed sleep wake cycle [23].

In mammals, circadian rhythms control the timing of eating and sleeping, coordinated by a central pacemaker in the brain, resulting in humans not consuming food nocturnally. In NES, there is evidence that these rhythms coordinating the timing of eating and sleeping may have been disrupted. It has been hypothesised that such dissociation of the rhythm of eating and sleeping can be due to initial alternative timing of food ingestion somehow uncoupling the food intake rhythm from that of the central pacemaker [23]. This uncoupling may have occurred in our patient during early parenting behaviour, where she would have to get up several times a night to tend to the baby and eating for comfort or improve sleep. The prolonged successful remission in our patient suggests that such treatment may be beneficial in human disorders of circadian rhythms [3].

## CONCLUSION

### We report

1. An intelligent obese woman with severe night eating

received major, long term therapeutic benefit in night eating from topiramate treatment with successful, sustained weight loss despite prior years of counselling, diets and other psychotherapeutic agents. We are unaware of previous long-term remission of night eating symptoms.

2. Despite previous reports of benefit from topiramate in binge eating/bulimia and night eating disorders, concern about side effects may have prevented wider use. While only a single case, our subject experienced many benefits from topiramate: complete remission from night eating, reduction in appetite and thoughts about food, improved diabetes management, improved daily life, all without major side effects. As low-dose topiramate is now in use for obesity in a combination drug wider testing of topiramate may be appropriate for night eating to alleviate its major physical and mental burden. While the condition is more common in obese and/or subjects with diabetes, in the future other circadian dysrhythmias contributing to obesity may be amenable to topiramate treatment.

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