

## The Efficacy of Duloxetine in the Treatment of Bulimia Nervosa: Case Reports.

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### Abstract

**Bulimia Nervosa (BN) is one of the most common eating disorders in industrialized societies, characterized by uncontrolled binge eating and self-induced purging or other compensatory behaviours aiming to prevent body weight gain. It has been suggested that reduced serotonergic tone triggers some of the cognitive and mood disturbances associated with BN. In fact, in the active phase of BN the concentration of serotonin in cerebral fluid is reduced. For these reasons, the pharmacologic treatment of BN consists mainly of selective serotonin reuptake inhibitors (SSRIs). The physiological basis of this disorder is not yet completely understood. Recently, it has been reported that BN may be controlled also by using drugs involving the noradrenaline (NA) system thus suggesting a possible treatment of BN with tricyclic antidepressants or serotonin and noradrenaline reuptake inhibitors (SNRIs). Given the above evidences, it is reasonable to assume the use of duloxetine, a SNRI, in the treatment of BN. This paper presents a series of five clinical cases of patients suffering from BN Purging Type, with comorbid mood depression, treated with duloxetine at a dose of 60 mg / day. Five patients, all women aged between 24 and 35 years, were followed on an outpatient basis for a period of 16 weeks. At the beginning and at the end of the observation period, patients were weighed, BMI was calculated and assessed by the Hamilton Scale for Depression. Assessment of major cardiac and blood chemistry data were done as well. During the observation period, all patients maintained an accurate diary about their binge and self-induced vomiting. At the end of the observation period duloxetine treatment led to a 56% reduction of binge crisis, 63% of compensatory behavior and a reduction of 3.1% of body weight. HAM-D values decreased on an average from 21.6 to 10.2. Duloxetine was significantly effective in reducing binge crisis and the purging behavior possibly by inducing a positive effect on this comorbid depressive symptoms, without significant adverse events. However, these data need to be confirmed by RCT trial on a larger scale.**

**Keywords:** Bulimia Nervosa, Duloxetine, SNRI

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### Introduction

The term bulimia nervosa (BN) refers to an eating behavior characterized by episodes of compulsive, greedy, uncontrolled ingestion of large quantities of high-caloric foods in a short time. Compensatory behaviors to control body weight often follow these episodic crises and include self-induced vomiting or the abuse of laxatives or diuretics [1].

The DSM-IV TR, describes the binge eating crisis in terms of the amount of food eaten by the patient with loss of control on the impulse to eat. In addition, it identifies two subtypes of BN, in relation to the control mode: purging type, which is characterized by self-induced vomiting and abuse of laxatives or diuretics and non-purging type which is characterized by other behavioral measures such as fasting or exercise but not self-induced

vomiting [2]. The purging type is the more frequent and severe subtype of BN [3].

Although the BN patients are predominantly in the range of normal weight or slightly overweight, the thought of food intake and the fear of gaining weight are often dominant [4].

As with anorexia nervosa, BN patients also have a predominant idea focused on the fear of gaining weight, weight control and body shapes. Also frequently associated are comorbid psychiatric disorders such as, mood spectrum disorders, mainly depression manifestations of anxiety with panic attacks, obsessive compulsive symptoms, alcohol abuse or drug abuse and self-injurious behaviors, which sometimes can lead to suicide [5].

Clinical complications are associated with frequent episodes of binge eating and the consequential compensatory purging behaviors. These behaviors can lead to clinical problems of various kinds: damage to the esophagus, inflammation of the mucous membrane leading to its rupture because of large amounts of food introduced; from dental erosion to the electrolyte imbalance induced by frequent episodes of self-induced vomiting or misuse of laxatives or diuretics that may cause cardiac arrhythmias or renal failure [6].

BN has a prevalence in the general population, between 1 and 1.5%, with the later onset than anorexia nervosa, mainly in the third decade of life, with a tendency to self-perpetuation [7], with mortality estimated at 4% [8]. At the moment, there are no consistent data on predictors of outcome but various evidences of the literature indicate that childhood obesity, low self-esteem and personality disorders are associated with worse prognosis [9]. Several studies, not only clinical and psycho-neuro-endocrinological but also genetic and neuroimaging have shown dysfunction of serotonin etiopathogenesis of BN and have supported the use of drugs that act mainly on serotonin. [10].

Pharmacological treatment of BN is focused primarily on the use of antidepressants, particularly the SSRIs, which have, in addition to a good efficacy in reducing the symptoms of BN, a better tolerability than tricyclic antidepressant (TC) [11,12]. At the moment, the only drug approved by regulatory international agencies, for the treatment of BN, is fluoxetine [13]. In recent years, however, the international literature has presented significant data to prove that other neurotransmitters are involved in the pathogenesis of BN. Alterations of noradrenaline (NA) activity have been described in patients with BN and other related disorders of eating behavior (14). In addition, various evidences have shown that drugs interacting with the NA may be

effective in the treatment of BN. However, some years ago, encouraging data have been reported with the use of tricyclic antidepressant drugs in noradrenergic prevailing action, such as imipramine and desimipramine, in the treatment of BN [15]. Furthermore, some authors, (though on a small series and case reports), interestingly, have reported that drugs such as reboxetine, which reduces the reuptake of NA (NRI), have been effective in reducing the binge crisis and purging behaviour [16,17]. Given the above evidences, Fava and Hazen [18] presented an impressive case report of the efficacy of duloxetine in the treatment of a patient with BN. Duloxetine is an antidepressant with a specific mechanism of dual action that inhibits the reuptake of serotonin and norepinephrine (SNRIs). Recent publications have also highlighted the effectiveness of duloxetine compared to placebo in reducing binge crisis and the weight as well in the treatment of patients with Binge Eating Disorder (BED) [19 – 22]. Therefore, the aim of this work is to present a series of five patients with BN - purging type with mood depression treated with duloxetine.

## Materials and Methods

Five patients were followed as outpatients. They were all women aged between 24 and 35 years, suffering from BN - purging type, according to the criteria of the DSM-IV TR, and comorbidity with a distinct depressive symptomatology, in treatment with duloxetine at dose of 60 mg/day, for a period of 16 weeks. The patients kept an accurate diary, for the entire period of observation, in which each one indicated their binge crisis and episodes of self-induced vomiting. At the beginning and end of the study each patient was assessed for their weight and height with BMI, and Hamilton Rate Scale for Depression 17 item [23], ECG and blood chemistry were also noted. The checks were carried out every two weeks for clinical evaluation and possible adverse events related to treatment.

## Results and Conclusions

At the end of the observation period of 16 weeks, the patients showed a reduction in the number of binge crisis and compensatory behavior (calculated on a weekly basis in the form of average of all patients). The binge behavior decreased from 18.6 to 8.2 (56% reduction), while the purging behavior decreased from 15.2 to 5.6 (63% reduction). The average weight of the patients was reduced by 3.1%, from an average of 67.2 to 65.1 kg, with a mean BMI reduction of 0.7 percentage i.e. from 25 to 24.3. Duloxetine was effective, as expected, also in reducing depressive symptoms, as reported by a reduction of the HAM-D, from an average of five patients of 21.6 to 10.2 points (Tables 1 and 2).

## Duloxetine in Bulimia Nervosa Treatment

None of the BN patients showed significant adverse events related to duloxetine treatment, only two patients reported in the first three weeks, a slight feeling of nausea and dry mouth sensation but without stopping the

treatment. Even the blood chemistry parameters monitored during treatment did not show any abnormality. The cardiological reports (blood pressure and ECG) were also regular.

**Table 1. Evaluation parameters of the five BN patients studied**

Before treatment	Patient 1 A C	Patient 2 R M E	Patient 3 B P	Patient 4 A G	Patient 5 A D M
<b>Age</b>	<b>24</b>	<b>28</b>	<b>32</b>	<b>35</b>	<b>33</b>
Height (cm )	158	166	170	162	165
Weight (kg)	64	68	74	68	62
BMI	25.6	23.7	25.6	26.0	23.0
HAM-D	22	19	21	24	22
N° Binge/week	14	19	20	22	18
N° Purging/week	12	16	18	16	14
<b>AFTER TREATMENT</b>					
Weight (kg)	62.5	66.5	73.3	66.0	62-5
BMI	23.8	24.1	25.1	25.1	23.1
HAM-D	6	12	12	7	14
N° Binge/week	5	8	9	10	9
N° Purging/week	3	5	8	6	6

**Table 2. Total Outcome for the five patients before and after treatment.**

Parameters	Baseline	16° week treatment
Middleweight (kg)	67.2	65.1
BMI	25	24.3
Average number of crisis binge x week	18.6	8
Average number of behavior Self-induced vomiting x week	15.2	5.6
Average score HAM-D	21.6	10.2

The data reported in this observational study, showed a 56% reduction of the binge crisis and a 63% reduction of the purging behavior, among patients followed during treatment. This study helps us to confirm the literature data [18-22] indicating that duloxetine is a drug useful in the treatment of BN. The reduction in seizure frequency of binge also led to a reduction in calorie intake, which led to a modest weight loss of 3.1% on average. Duloxetine, as expected, led to an improvement in depressive symptoms, comorbidities present in the BN, as showed by the marked reduction of the HAM-D.

It is therefore considered, even with all the limitations related to an observational study with only a limited number of clinical cases and without an adequate placebo control, that duloxetine, a drug that increases the effect of serotonin and norepinephrine at the level of the brain areas involved in regulation of food intake may have its precise utility in the treatment of BN. However, these preliminary data will be confirmed by controlled trials on a wider number of samples and for an extended period of time.

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