

A Comparative Study between Three Different SSRIs in the Treatment of Bulimia Nervosa

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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). At present, the physiologic basis of this disorder is not yet completely understood. In this study we have conducted a randomized controlled trial to compare the efficacy of three different SSRIs, fluoxetine, fluvoxamine, sertraline, in patients with a diagnosis of BN. Sixty female outpatients aged 18 to 34 years with a diagnosis of BN-binge purging (as defined by the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders [DSM IV]*) were randomly assigned to 3 group of treatment: the fluoxetine 60 mg/die group; the fluvoxamine 200 mg/die group and the sertraline 100 mg/die group. The patients underwent weekly clinical assessments for 10 weeks. At the end of treatment, there was a statistically significant reduction in the numbers of bulimic and purging episodes more in the fluoxetine and fluvoxamine group than the sertraline group. In no case was the treatment interrupted for emergent side effects. These findings support the hypothesis that the SSRIs are well tolerated and effectively reduce the bulimic crisis and purging episodes in patients with BN.

Keywords: Bulimia nervosa, Eating disorders, SSRI

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Introduction

Bulimia literally signifies, in Greek, hunger of ox and with this term we intend an alimentary behaviour characterized by episodes of convulsive and uncontrolled ingestion of big quantity of food with high caloric contents. It is a trouble rarely cited in the medical publications antecedent to 1960. Bulimia has been considered, for many years, a variant of anorexia nervosa (AN) or a form of obesity. Even on the strictly terminological front, it was difficult that this disease has conquered the current definition of Bulimia Nervosa (BN), after having been labeled for years as 'disorexia', 'compulsive alimentation', 'anorexia nervosa', 'syndrome of altered alimentary behaviours' in fat or thin subjects [1]. In spite of the fact that bulimic behaviours have been present in psychiatric diseases (schizophrenia, affective troubles, hysteria), AN, obesity and varied neurological diseases, BN for along time, had been considered a symptom and not a syndrome apart [1,2].

Bulimic episodes, frequently, happen in solitude and they are taken to be a sense of incapacity to control the impulse, by a sense of guilt and/ or psychic depression [1,2].

The DSM IV, in addition, to stigmatize a diagnostic criterion of BN, identifies these manifestations, used to avoid weight increase, like compensatory purging behaviours [3].

The diagnostic criteria, established for BN in *International Classification of Diseases (ICD-10)*, are nearly the same as of the DSM IV, except for the relation between BN and AN; in fact, while in DSM IV the diagnosis of BN is excluded if the bulimic episodes show exclusively in case of AN; in the ICD-10 it is not possible to elaborate the diagnosis of AN if the clinical picture has been characterized by a regular presence of bingeing [3].

The patients learn that it is possible to remove the excess calories with self-induced vomiting or abuse of laxative or diuretics. These abnormal behaviours succeed in preserving the body weight within acceptable limits for the patients (the bulimic patients, in fact, are generally of normal body weight or slightly overweight) but they cause varied organic damages: mild ones like dental erosions, scar on the hands (sign of Russel), alteration of colic innervations; or more serious ones like abdominal pains concerning esophageal lesions, cardiac arrhythmia caused by hypokalemia, renal pathologies or even tetany caused by reduction of Ca^{2+} owing to alkalosis as a consequence of the loss of gastric juice [2].

In the clinical arena the neuroendocrinologic study of bulimic patients is a recent line of research. For this reason definitive data are missing and the results present in the literature are often contradictory.

Therefore, this group of researchers have tried to attribute to this sector a particular importance for the study and the comprehension of the areas of superposition that exist between BN and other eating disorders and between BN and mood trouble.

BN is more common than AN and it is found majorly in women. According to various authors, [1-3] women affected by BN consists of about 1-5% of the population and the age of onset is between 15 to 35 years. The alteration in behaviour usually appears in late adolescence. Besides, the bulimic patients have a high frequency of psychiatric co-morbidity like disorder of emotional sphere, anxiety disorder like obsession-compulsion, personality disorders and tendency to abuse alcohol and drugs [1-3].

Various authors have postulated that Eating Disorders (ED) like BN, are part of the so-called 'depressive spectrum' and they assume that in relation to age of onset, ED is in accordance with all other characteristic problems of that age. [1-3].

Besides, various pharmacological and neuroendocrinologic studies, show that in all these diseases there is an alteration of the modulation and of the transmission of some cerebral neurotransmitters like noradrenalin (NA), dopamine (DOPA) and in particular serotonin (5HT) [4].

Recent theories indicate the cause of BN as a dysfunction of the serotonergic system. In fact it has been reported that the prolactin (PRL) response level remained the same after administering both L-tryptophane (serotonin precursor) and m-chlorophenilpiperazine (agonist of postsynaptic serotonergic receptors) suggesting that the bulimic patients could have a reduced serotonergic activity [5,6].

In normal persons, the ingestion of carbohydrate induces an increase in the cerebral uptake of tryptophane, and bingeing could increase the synthesis of serotonin induced by diet, compensating, in this way, the reduced serotonergic tone. The serotonin concentration in the cerebrospinal fluid drops to a very low level in patients with a greater number of bingeing episodes [4-6]. The serotonergic hypothesis could also explain other psychopathological aspects that frequently are associated with ED, e.g., the non-control of impulses (self injury, low self esteem, kleptomania, abuse of alcohol and drugs), alterations of the *thymus activity* (secondary demoralization for the loss of control on the alimentation, major depressive episodes, affective temperaments), the obsessive-compulsive characteristics like the extreme care bound to the physical proportions, the ideational polarization on the food, the ritualization of the bulimic crisis [7-9].

The proposed model theorizes that at the basis of BN exists an increased receptorial sensitivity to the serotonin; the treatment with inhibitors of reuptake of serotonin could induce a down-regulation of receptors, normalizing the serotonergic tone [9,10].

This explains, in accordance with the international literature, in BN, the use of drugs, which are able to modulate transmission of these neurotransmitters, such as the tricyclic antidepressants particularly the selective serotonin reuptake inhibitors (SSRIs) [7-9].

The object of our work is to compare three different drugs, namely, fluoxetine, fluvoxamine and sertraline belonging to the SSRI category, in the treatment of BN.

Patients and Methods

In this study we have selected 60 female patients aged 18 to 34 years, suffering from (in accordance with the diagnostic criteria of DSM IV and the IDM scale) BN with purging behaviours (BN-BP bingeing-purging). They were randomly divided into 3 groups of 20 patients each. The patients in the first group received fluoxetine at a dose of 60 mg/day for 10 consecutive weeks. Patients in the second group received fluvoxamine at a dose of 200 mg/day for 10 consecutive weeks and the patients in third group received sertraline at a dose of 100 mg/day for 10 consecutive weeks.

All patients were monitored, in outpatient regime, twice a week for proper clinical and any possible collateral effects. All the patients kept an accurate alimentary diary where they registered the alimentary choice, the bulimic episodes, the weight and the possible compensatory behaviours.

Results and Conclusions

At the end of 10 weeks of treatment, in the first group of patients, who received fluoxetine, there was a mean decrease of 75% of bulimic episodes and a reduction of 68% of purging episodes (self-induced vomiting). The mean caloric intake was decreased by about 10% with a marked reduction in the glucidic due. In the second group of patients, who received fluvoxamine, there was a mean decrease of 59% of bulimic episodes and a reduction of about 62% of purging episodes. The mean caloric intake was reduced by about 8% showing however, a reduction in the total intake of carbohydrates. In the third group of patients, who were given sertraline, the mean decrease of bulimic episodes however, was not much significant, and about 18% of them showed no change in purging behaviour (Figs. 1 A,B). The mean caloric intake in these patients showed no variation.

The body weight was reduced to about 7% in the first group and to about 5% in the second group; while in the third group it remained practically steady.

The collateral effects as verified during the treatment were as follows: first group (fluoxetine): irritation and

anxiety in 90% of the patients; insomnia in 50% of the patients; headache and perspiration in 15% of the patients. Second group (fluvoxamine): 70% of the patients felt sedation and 25% of patients complained of dryness of throat. Third group (sertraline): only 30% of the patients suffered from insomnia and light asthenia during the treatment.

However, no patient left the trial because of serious collateral effects.

Given the above evidences, we may conclude that the use of some SSRIs, like fluoxetine and fluvoxamine, in accordance with the most recent international literature, [9] induces both a reduction in the bulimic episodes and a reduction in the compensatory behaviours that, as we have said previously, induces various organic diseases.

On the other hand, the drugs also reduce, even if indirectly, the mean caloric intake and the craving for carbohydrates. In our opinion, the use of SSRIs, like fluoxetine and/or fluvoxamine, (which act on the mechanism of serotonergic neurotransmission) may prove to be useful for the symptomatic treatment of BN.

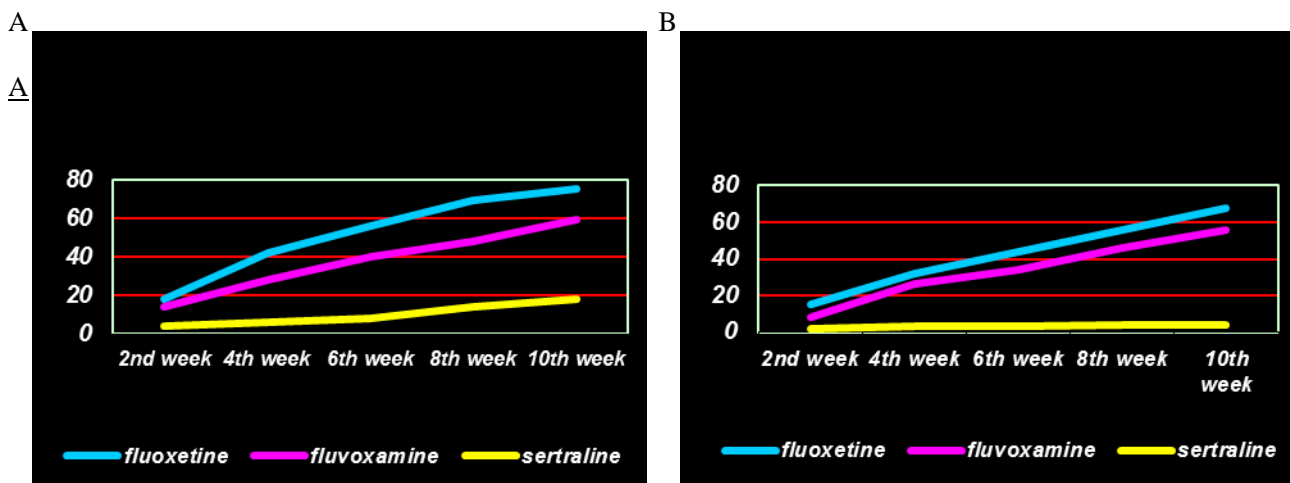


Figure 1. Percentage of reduction of the bulimic crisis (A) and of the purging behaviours (B) in patients with BN that assumed fluoxetine, fluvoxamine and sertraline. Results are expressed as mean ± S.E.M (n=20; t-Student for paired data).

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