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Short communication

The effectiveness of the combination fluoxetine-naltrexone in bulimia nervosa

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Summary – Four patients with DSM-IV bulimia nervosa were treated in a crossover trial with naltrexone alone, fluoxetine alone, and a fluoxetine-naltrexone combination. Three patients presented a complete remission when treated with the fluoxetine-naltrexone combination.

fluoxetine / naltrexone / bulimia nervosa / crossover trial

INTRODUCTION

The cerebral mechanisms that regulate food intake seem to be controlled by a serotonergic system. Serotonergic dysregulation may be involved in eating disorders, including bulimia nervosa.

Controlled clinical studies support the efficacy of selective serotonin reuptake inhibitors (SSRIs) in the treatment of bulimia nervosa. Fluoxetine in particular has been found to be useful in reducing food intake (Freeman et al, 1988; Enas et al, 1989; Montgomery, 1989; Morley, 1989; Orsulak and Waller, 1989; Solyom et al, 1990; Kaspers et al, 1992; Spigset, 1992). Nevertheless, its clinical effectiveness has only been demonstrated in under 50% of the patients studied (Solyom et al, 1990) and when a long-term follow-up was performed, the relapse rate was found to be high (Goldbloom and Kennedy, 1991; Hollander et al, 1992).

A dysregulation of the endogenous opiate system in eating disorders has also been postulated. The efficacy of naltrexone has been investigated (Jonas and Gold,1986, 1988); preliminary results demonstrate that a higher dose (200 and 300 mg/day) is more effective than that commonly used in the treatment of opiate drug addiction (Childs, 1987; Jonas and Gold, 1988; Mitchell and Groat, 1984). Such a high dose may be associated with hepatic toxicity.

The use of fluoxetine and naltrexone in combination may prove effective in the treatment of bulimia nervosa. As we have observed in the treatment of opiate drug addiction, the anti-craving action of fluoxetine may allow naltrexone to be used at a lower dosage (Maremmani et al, 1995).

PATIENTS AND METHODS

In this study four examples of the therapeutic effectiveness of the combination of fluoxetine and naltrexone as compared to the use of fluoxetine or naltrexone alone have been presented in a controlled crossover trial.

In the first 4 weeks of this 3 month protocol, the four patients fulfilling DSM-IV criteria for bulimia nervosa received naltrexone alone at the dose of 100 mg/day. Following a washout period of 7 days, fluoxetine was then administered at a dose of 60 mg/day for 4 weeks. During the next 4 weeks, patients received a combination of fluoxetine and naltrexone at the same doses specified above. At baseline, the patients were evaluated by means of clinical

global impression (CGI), Hopkins symptomatology checklist (SCL-90), and by a checklist consisting of 9 items: number of episodes of 'stuffing oneself' per week; sense of loss of control and worry about one's figure and weight (on an analogical 0-100 scale); vomiting, use of diuretics, use of laxatives (five levels of severity); dietetic restrictions, periods of fasting, physical activity (two levels of severity). The same rating scales were administered at the end of each phase of treatment by a researcher who was uninformed as to the treatment implemented.

Patient 1

Patient 1, 21 years old, from central Italy, demonstrated the onset of symptoms when she was 15 years old and initially developed restrictive anorexia. After about a year she began showing bulimic behavior which remained unchanged up to the beginning of this evaluation. The patient responded partially to both fluoxetine and naltrexone when used alone. The case attained clinical remission only by administration of the two drugs in combination.

Patient 2

Patient 2, 36 years old, from central Italy, demonstrated the onset of symptoms at age 26 following a depressive episode and the use of amphetamines and benzodiazepines. She responded better to naltrexone than to fluoxetine. A more complete remission with the combination of naltrexone-fluoxetine was observed.

Patient 3

Patient 3, 23 years old, from central Italy, demonstrated the onset of symptoms at age 12 years. She showed an extremely limited intake and restrictive selection of food. At age 16 she began to 'stuff herself' and ocasionally use laxatives. There was little effect using either of the drugs alone. A good response was obtained using the combination of naltrexone-fluoxetine.

Patient 4

Patient 4, 21 years old, came from northern Italy. During her adolescence she went on a restrictive diet; this was followed by bulimia, which worsened over time. Her condition became particularly serious during the last 4 years, with the hoarding of food and stealing money from the family to buy an excessive amount of food. She showed noteworthy improvement with naltrexone, little response with fluoxetine and total remission using the combination of both.

RESULTS

The episodes of 'stuffing oneself', the sense of loss of control during these episodes and the tendency to fast after the episodes of 'stuffing oneself' were significantly reduced only after the third phase of treatment. It should be noted that the improvement in anxiety regarding body shape and weight and in the qualitative dietetic restriction was limited. Physical activity to burn 'calories' remained unchanged (table I). No side effect was observed.

Table I. Efficacy of a naltrexone-fluoxetine combination in four patients with bulimia nervosa.

Symptoms	*Baseline*	*N*	*F*	*N-F*
No of weeks on eating binge				
Case 1	20	8	10	2
2	9	6	10	0
3	8	7	7	2
4	6	1	5	0
Lack of control				
Case 1	90	43	68	12
2	80	70	81	0
3	80	73	73	70
4	70	22	80	0
Anxiety regarding body shape and weight				
Case 1	80	60	70	34
2	80	82	85	42
3	82	74	74	80
4	85	22	70	15
Self-induced vomiting				
Case 1	5	4	5	1
3	4	4	4	1
4	3	2	3	0
Dietetic restriction				
Case 1	Yes	Yes	Yes	No
2	Yes	Yes	Yes	No
3	Yes	Yes	Yes	Yes
Fasting				
Case 1	Yes	No	No	No
2	Yes	No	Yes	No
3	Yes	Yes	Yes	No
Excessive exercise				
Case 3	Yes	Yes	Yes	Yes

N: after naltrexone therapy; F: after fluoxetine therapy; NEF: after naltrexone – fluoxetine combination therapy.

DISCUSSION AND CONCLUSION

The small sample size does not allow definite conclusions to be made, but the combination of fluoxetine and naltrexone seems to have a specific effect on the main components of bulimia nervosa, such as the number of episodes of 'stuffing oneself' and the accompanying sense of loss of control. We are of the opinion that it is possible to draw an analogy between the episodes of 'stuffing oneself', loss of control regarding eating behavior in bulimic patients are the use of heroin with crav-

ing in drug addicts (Maremmani et al, 1995). Fluoxetine and naltrexone used in combination in drug addicts seem to help prevent relapse into substance abuse. The effectiveness of a naltrexone-fluoxetine combination in the treatment of bulimia nervosa may not only constitute a therapeutic breakthrough, but also lend support to the theory that bulimia nervosa might be nothing more than a particular type of substance abuse.

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