Two patients with eating disorders treated by naltrexone

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Abstract

According to a recent literature review on the opioid mechanism in eating disorders, we found that there is increasing reason to re-examine the treatment potential of naltrexone. The endogenous opioid system belongs to the important modulators of food intake. The eating disorders share many traits with substance dependence models. We present two case histories of time-limited naltrexone therapy to show that, in clinical practice, individualized indication may contribute to short-term improvement and to prediction of a different long-term treatment outcome.

CASE REPORT

INTRODUCTION:

The opioid transmitter system is among the fundamental modulators of food intake as part of the reward system (Cota *et al.* 2005). Stimulation of opioid receptors (mainly OP3) increases the activity of the mesolimbic dopaminergic system and projection to the prefrontal cortex, striatum and nucleus accumbens (pleasure experience, elevation of dopamine). The higher release of β-endorphins inhibits GABA neurons, causing dopamine release and the "reward sensation". Stimulation of the opioid (OP3) receptor has a hyperphagic effect (Jonas & Gold 1987a). Patients with anorexia nervosa (AN) and bulimia nervosa (BN) have significantly lower levels of beta-endorphin in the cerebrospinal fluid, while the concentration of dynorphin does not differ significantly from healthy controls (Brewerton *et al.* 1992).

Eating disorders share symptoms very similar to unmanageable craving for drugs and alcohol (Jonas & Gold 1987a; Volkow & Wise 2005). The opioid compensation hypothesis could explain the craving and dependent behaviour of patients with eating disorders. Dependence on chocolate and chocolate "craving" have been frequently discussed (Rolls & McCabe 2007). But there are other eating disorder symptoms with characteristics shared with other dependencies: food craving and binging followed by purging behaviour and other forms of offsetting the caloric impact of an enormous amount of "forbidden food" such as the use of laxatives or excessive exercise. Patients with AN and BN also display high addictive personality scores on the dependence scale of the Eysenck Personality Questionnaire ("Addictive Personality") (Davis & Claridge 1998). The prevalence of substance abuse in eating disorders reaches 25–50%,

Glossary:

Naltrexone	– opioid receptor antagonist used in treatment of alcohol and opioid dependence;
Endogenous opioids	– in human body produced neurotransmitters, include endorphins, enkephalins, dynorphins, and endomorphins;
Bulimia Nervosa (BN)	– eating disorder characterized by episodes of binge eating and compensatory behaviour to prevent weight gain including persistent concern with body shape;
Anorexia Nervosa (AN)	– eating disorder characterized by low body weight, body image distortion, and obsessive fear of gaining weight.

and eating disorders are more frequent in patients with a history of substance abuse (Davis & Claridge 1998). An important part of their treatment consists of management of the withdrawal state with both its somatic and psychological symptoms.

Naloxone and naltrexone are opioid antagonists and have a hypophagic effect (Chabane *et al.* 2000, Chatoor *et al.* 1994).. An open case study of the long-term effect of naltrexone showed positive therapeutic response in 16 patients with BN (Jonas & Gold 1987b). After 6 weeks treatment at a higher dose of 200–300 mg p.d. (compared to 50–100 mg p.d.), patients displayed decreases in their binging and purging frequencies. According to the authors, the study shows that opioid blockade reduces the frequency of binging and purging as well as other symptoms caused by loss of control (e.g. automutilation). De Zwaan & Mitchell (1992) in their review showed that, in animal models, the endogenous opioid system plays an important role in food intake, while in humans naloxone, naltrexone and nalmefene cause only a 30% reduction in total food intake. In the short-term study, the treatments affected choice of food in individuals with normal weight as well as in obese and bulimic patients. The published data did not support routine use of opioid antagonists in Prader-Willis syndrome, obesity, BN or AN because of the unfavourable risk/benefit ratio (hepatotoxic side effects), and the authors recommended further research into newer opioid antagonists. Despite the negative findings of hepatotoxic effect in this medication by Jonas & Gold (1988) and Marrazzi *et al* (1997), no further trials have been since conducted.

Based on an increasing amount of literature presenting the importance of opioid dysfunction in eating disorders, we have decided to use short-term naltrexone therapy to help our patients with a positive family history of alcoholism, alcohol craving, pharmacoresistance and unsuccessful psychotherapeutic treatment. The patients themselves requested to try the new treatment and signed the informed consents.

CASE REPORT 1

38-year-old female, married, *(BMI before treatment: 19.3 kg/m^2; after the treatment: 20.2 kg/m^2),* high school graduate, mother of a 14-year-old girl, treated more then 10 years in an outpatient and inpatient facilities (hospitalized three times at Eating Disorders Unit). Both parents were alcohol dependent. Our patient with these dispositions showed also comorbid alcohol craving and alcohol abuse. The patient was treated with all available psychotherapeutic modalities by experienced cognitive-behavioral therapists as well as by well-trained psychologists and psychiatrists with psychodynamic orientation. She has been always cooperative and motivated to change and to achieve a normal eating pattern. It has taken several years to decrease her excessive exercise (a several-hour daily marathon distance run and swimming).

During the last years she felt that her sense of inferiority, need for bodily perfection and inability to relax

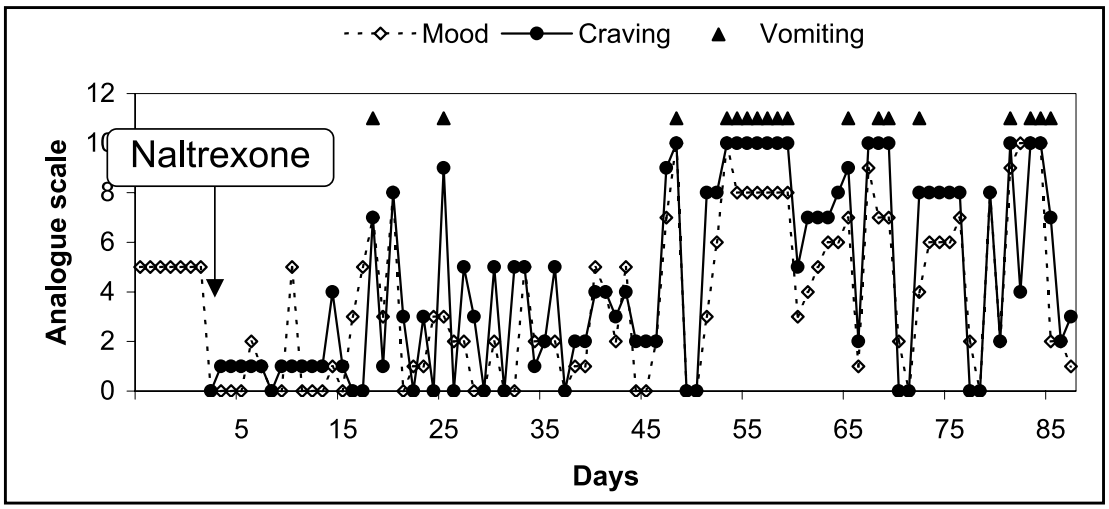

Figure 1. Self-evaluation of mood, food craving and vomiting in case history 1 during naltrexone treatment. The vertical axis represents the intensity of mood problems and food craving (0 means no problem, 10 – maximum) and the day of vomiting (indicated with triangle).

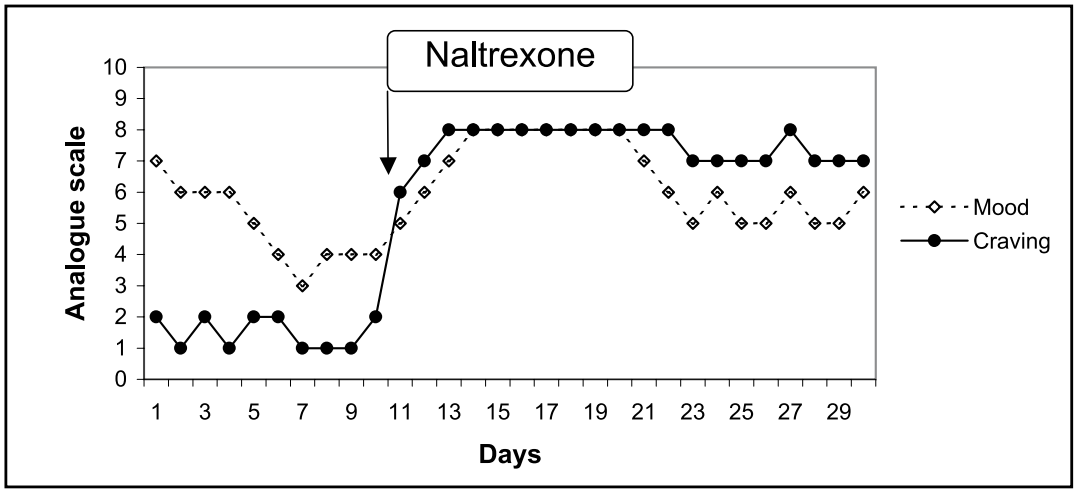

Figure 2. Self-evaluation of mood, food craving and vomiting in case history 2 during naltrexone treatment. The vertical axis represents the intensity of mood problems and food craving (0 means no problem, 10 – maximum).

has eased off to a certain degree. She has never experienced a serious medical problem and has always been satisfied with her family life (her husband, a sportsman involved in his wife's treatment, has supported her throughout, and she has maintained a good and trusting relationship with her daughter). However, she remained severely obsessed with extreme thinness, purging and excessive exercising. Several SSRI treatments (fluoxetine, sertraline) did have a time-limited partial effect on her anxiety, depression or binge/purge frequency. The patient described it as most difficult task to cope with, despite an evident progress in her insight therapy. She kept purging once per day and felt helpless in coping with the binging urge in the afternoon.

She expressed the need for a new approach but accepted the initial oral naltrexone (50mg) therapy with a certain mistrust. Surprisingly, several days later she sent the therapist the following comment: "Dear doctor, I started taking the medication on Friday. I was so afraid that the medication would again be a waste of money and I would not manage it. I have to tell you that I have never been so relieved in my life since my disease started." Her positive spontaneous reaction inspired us to write this case report. The patient took detailed notes of her symptoms (Figure 1.). Side effects reported at the beginning of the treatment included dyssomnia and exhaustion: "I cannot sleep, I cannot fall asleep, then I keep waking up. I feel physically tired, I am a little worried because like this I can then get to the point where I really will have no energy." Other side effects were noticed (Fig.1).

CASE REPORT 2

42-year-old female, married, mother of 3 children, at the time of the study admitted to an Eating Disorders Day Care Center for the second time due to worsening somatic and psychological symptoms of AN, purgative type *(BMI before treatment: 18,8 kg/m^2; after treatment: 17,83 kg/m^2).* Both parents also had severe drinking problems. She had also experienced symptoms of alcohol abuse. At a younger age she was also treated for anorexia nervosa at Eating Disorders Unit. She says she put on weight at that time quickly in order to be discharged soon and return home. Since then she has learned to purge and her eating pattern has gradually deteriorated. For years, she purges any time she eats a regular meal (mainly with her children). In addition to her anorexia diagnosis she has been diagnosed with a borderline personality. She binges and purges 1–3 times a day and suffers from persistent low self-confidence, perfectionism, hypobulia and affective lability. Motivation for change remains on the proclamation level. She feels forced into therapy by her family due to worsening psychological (fatigue and affective lability) and medical (stomach aches) complications. Previously, during outpatient treatment, she was taking an SSRI (fluoxetine) without any significant effect on eating pathology or depressive feelings. She has gradually lost control over food, expressed long-term dissatisfaction in her relationship with her husband and exhaustion due to housework overload.

At the time of the study she was admitted into a comprehensive program at Eating Disorders Unit to improve her chaotic eating regime (with food restriction), weight gain anxiety and negative body image. The patient learned about the possibility of naltrexone therapy and insisted on taking oral naltrexone (50mg). However, her expectations were unrealistic and treatment had to be terminated after 10 days due to the patient's subjective condition worsening (see figure 2). No other side effects were present.

CONCLUSION

These two case reports show the effect of short-term treatment with low doses of naltrexone. We selected patients with similar family histories of severe alcohol

dependency, long-term resistance to psychological and psychopharmacological therapy but different motivational level and personality structure. We demonstrate in the first case – with preserved motivation to change – that naltrexone served as "augmentation" to the treatment. The short-term improvement temporarily helped the patient to experience relief of major symptoms. At 3 years follow-up it seems that the experience was substantial. The patient later started a new university education and gradually experienced relief from the extreme drive for thinness and distorted body image, achieving partial remission.

The unrealistic expectation of a "magic effect" contributed to failure in the second case of short-term naloxone treatment. The second patient failed to experience, even briefly, a positive subjective feeling and relief from craving, and her condition persisted unchanged after 3 years.

The authors suggest that naltrexone therapy, even short-term, in a selected population of eating disorder patients may augment a comprehensive therapy program's effects, and that it may predict the long-term prognosis.

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