NALTREXONE IN PRIMARY HYPERPHAGIC OBESITY WITH HYPOCHONDRIACAL DISORDER - A CLINICAL STUDY

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ABSTRACT

Six well investigated patients of primary hyperphagic obesity with hypochondriacal disorder were sequentially treated with psychoeducational methods alone and psychoeducational methods with naltrexone hydrochloride 50 mg daily orally for six weeks each. RMANOVA revealed no statically significant (p>0.05) decrease in body mass index suggesting that psychoeducational methods with naltrexone were as ineffective in reducing obesity as psychoeducational methods alone. The limitations of the study and implications for future research are discussed.

Key words - Obesity, naltrexone, endorphinergic mechanisms.

There is ample evidence regarding the role of endorphinergic mechanisms in the modulation of eating behaviour (Cooper & Sanger, 1984; Reid, 1985; Morley, 1987; Cooper et al., 1988; Levine & Billington, 1989; Bakshi & Kelley, 1993a & 1993b; Cooper & Kirkhan, 1993; Halmi, 1995). However, the use of opioid receptor antagonists in eating disorders including obesity has given conflicting results (Sullivan, 1980; Cooper & Sanger, 1984; Cohen et al., 1985; Fantino et al., 1986; Jonas & Gold, 1986, 1988; Mitchell et al., 1986, 1989; Cooper et al., 1988; Levine & Billington, 1989; Bertino et al., 1991; Benjamin & Buot-Smith, 1993; Clearly et al., 1996). Heterogeneity of the various diagnostic entities may be an important reason for such conflicting findings and it may be more rewarding to conduct studies on small subgroups of well delineated eating disorders (Fard & Bankum, 1996). We came across a family in which six members had hypochondriacal disorder with well investigated primary hyperphagic obesity thereby providing us with an opportunity to evaluate the role of naltrexone in weight-reduction in such patients.

MATERIAL & METHOD

The population of the study consisted of six siblings (male 2, female 4, age range 23-41 years) from one family. All the six patients were obese with Body Mass Index (BMI)>35 Kg/m² at the time of recruitment in the study. They also had a persistent belief in the presence of cardiac disorder ("heart-attack") despite normal clinical examination, negative investigations & reassurance from cardiologists and physicians, thus satisfying the criteria for hypochondriacal disorder according to ICD-10 (World Health Organization, 1992). None of the patients had a history of anorexia or bulimia nervosa. All of these patients had been evaluated intensively in India and abroad for risk-factors for heart disease and were found to have none except obesity, occasional drinking, smoking, hypertriglyceridemia (secondary to obesity) in all the six siblings and use of oral contraceptives in the four female sibs. The patients had normal
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EKGs, Holter monitoring, treadmill test, Doppler scan, ejection fraction, radionucleotide, cardiac scan, creatinine clearance test, glucose tolerance test, lipid profile (except increased triglycerides secondary to obesity) thyroid function test, dexamethasone suppression test but had evidence of increased fat mass on total body electrical conductivity and computerised split conduction adipometry during the past one year. The patients were included in a 12 week study protocol after informed consent. Throughout this period a trained dietician made twice a week domicilary visits for dietary guidance, exercises, counselling, cognitive cue feedback therapy (recording by family members of the mood state and environmental factors preceding the desire to eat so that they may be apprised the relationship between the former & latter) and cognitive visual profile feedback (showing the patients their computer generated pictures at various projected body weights so as to enhance their motivation to reduce). The patients were kept drug free during the first six weeks but were given naltrexone hydrochloride 50 mg orally daily during the later six weeks of the study. Throughout the study period, the patients were advised to reduce their total calorie intake but no restrictions were made on frequency or type of food taken. Body Mass Indices (weight in Kg/height in meters$^2$) of the patients calculated at the beginning of the study, after 6 weeks after 12 weeks are shown in table.

**RESULTS**

The mean body mass index of the group at three time points (baseline, 6 weeks and 12 weeks) was not statistically significantly different from each other on Repeated Measures Analysis of Variance (RMANOVA) suggesting the naltrexone with psychoeducational measures (dietary guidance & counselling + cognitive cue feedback therapy + cognitive visual profile feedback therapy) was as ineffective in reducing body mass index of our patients as psychoeducational measures alone.

| Patient no. | Body Mass Index at Beginning (Kg/Meter$^2$) | After 6 Weeks | After 12 Weeks |
|-------------|--------------------------------------------|---------------|---------------|
| 1           | 36.47                                      | 36.45         | 36.44         |
| 2           | 38.40                                      | 38.42         | 38.40         |
| 3           | 39.43                                      | 39.44         | 39.45         |
| 4           | 40.82                                      | 40.77         | 40.81         |
| 5           | 36.55                                      | 36.62         | 36.61         |
| 6           | 37.33                                      | 37.36         | 37.34         |

**TABLE**

| Patient no. | Body Mass Index (Kg/Meter$^2$) |
|-------------|---------------------------------|
| 1           | 36.18±1.57                     |
| 2           | 38.17±1.50                     |
| 3           | 38.17±1.50                     |
| 4           | 38.17±1.50                     |
| 5           | 38.17±1.50                     |
| 6           | 38.17±1.50                     |

Statistical Significance F=0.164, p>0.05 (RMANOVA)

**DISCUSSION**

Because of differences in methodology and patient sample, our findings cannot be compared with other studies which evaluated the role of naltrexone in obesity (Cohen et al., 1985; Fantino et al., 1986; Bertino et al., 1991; Benjamin & Buot-Smith, 1993). The findings of inefficacy of naltrexone in our study should be interpreted in the light of the limitations of the study viz small number of patients (n=6), open nature of trial, absence of placebo-control and absence of quantitative adipometric evaluation after 6 & 12 weeks of trial. The patients had comorbid hypochondriacal disorder and we have not been able to find any literature regarding endorphinergic mechanisms in their disorder. This raises a question which can not answer at the moment "Would our patients have responded differently to naltrexone if they did not have comorbid hypochondriacal disorder?". In addition, we have adopted a free food choice procedure for the patients which did not take into consideration certain important variables like meal size, meal duration, meal frequency, inter-meal interval, preferential ingestion of micronutrients, change of taste, etc., which may be selectively affected by endorphinergic mechanisms (Bertino et al., 1991; Parker & Rennie, 1992; Clearly et al., 1996; Gosnell &
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Levine, 1996). Endorphinergic mechanisms modulated appetite probably by their action on mesolimbic (ventral tegmental-nucleus accumbens) dopaminergic system leading to altered reward-value and motivation-incentive towards food (Cooper & Sanger, 1984; Bakshi & Kelley, 1993a, 1993b; Badiani et al., 1995; Berridge, 1996; Kelley et al., 1996; Zhang & Kelley, 1997). Psychoeducational techniques (e.g., cognitive visual profile feedback therapy) also can modify the reward-value and motivation of an individual towards food, hence the simultaneous use of such techniques in this study may act as a confounding variable. There is need for a placebo controlled double blind study with crossover design to evaluate the role of naltrexone in a large population of well investigated primary hyperphagic obese patients without any comorbidity. If such a study replicates the findings of the present study, we should seriously consider the alternative possibility proposed by Walsh & Devlin (1998) that endorphinergic abnormalities may be the consequence rather than the cause of obesity.

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