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CLINICAL STUDY

Sibutramine – its impact on health-related quality of life and depression among adult obese non-diabetic patients

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Abstract: *Background:* Obesity is a multifactorial, chronic disorder that has reached epidemic proportions in most industrialised countries and is threatening to become a global epidemic.
Aims: The pilot study evaluates the effect of sibutramine therapy on health-related quality of life and occurence of depression symptoms among adult obese non-diabetic patients.
Patients and methods: This study was prospective and longitudinal. It was conducted at the Department of Hygiene of Faculty of Military Health Sciences in Hradec Králové, Czech Republic. Dates were obtained during year 2007. Twenty two adult obese non-diabetic patients (6 males and 16 females) were treated with sibutramine in dose of 10 mg daily. All of these 22 patients were over 18 years old. The European Quality of Life Questionnaire – EQ-5D Version was used for evaluation of health-related quality of life. The self-assessement Zung-SDS was applied for evaluation of occurrence of depression.
Results: The statistical evaluation demonstrated that health-related quality of life (EQ-5D score and EQ-5D visual analogue scale) presents highly significant statistical dependence on sibutramine therapy ($p<0.05$). The statistical evaluation demonstrated that index of depression (SDS index) presents highly significant statistical dependence on sibutramine therapy ($p<0.05$).
Conclusion: The results show that sibutramine therapy has a highly positive effect on health-related quality of life among adult obese non-diabetic patients. Also, the results show that sibutramine therapy has a highly positive effect on occurence of depresion symptoms among adult obese non-diabetic patients *(Fig. 2, Ref. 10).*
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Key words: sibutramine, health-related quality of life, depression, adult patients, obesity, non-diabetic patients.

Obesity is a multifactorial, chronic disorder that has reached epidemic proportions in most industrialised countries and is threatening to become a global epidemic (1). The prevalence of adult obesity in the states of EU is lower than in the USA: in males between 8–25 %, in females between 8–27 % (2). The highest obesity prevalence is in Central Europe, especially in the Czech Republic (about 25 % of adult male and female population are obese) and in England. The Czech population unfortunately is petting close to the American (2). Clinical management of obese patients is complex and serious doubts have arisen with regard to safety and efficacy of drug therapy (1). Obesity and its associated diseases are an increasing challenge in medicine. A change in lifestyle is usually the first step with modifications in nutrition, physical activity and behaviour. However, most of obese patients are not able to follow such treatment regimen for a longer period of time. If they do not lose >5 % of their initial weight within 3–6 months, pharmacological intervention should be taken into account (3). Pharmacological approaches to the management of obesity can, in broad terms, use distinct strategies: firstly, to reduce energy intake; secondly, to increase energy expenditure; and thirdly, to alter the partitioning of nutrients between fat and lean tissue. Sibutramine is a serotonin-noradrenaline (norepinephrine) reuptake inhibitor indicated for the management of obesity in conjunction with a reduced calorie diet (1, 4, 5). The pharmacological mechanisms by which sibutramine exerts its weight loss effect are likely due to a combination of reduced appetite, feelings of satiety and possibly induction of thermogenesis (1).

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Aims

The study had two aims: 1) to evaluate the effect of sibutramine therapy on health-related quality of life among adult obese non-diabetic patiens during 6 months of this therapy, 2) to

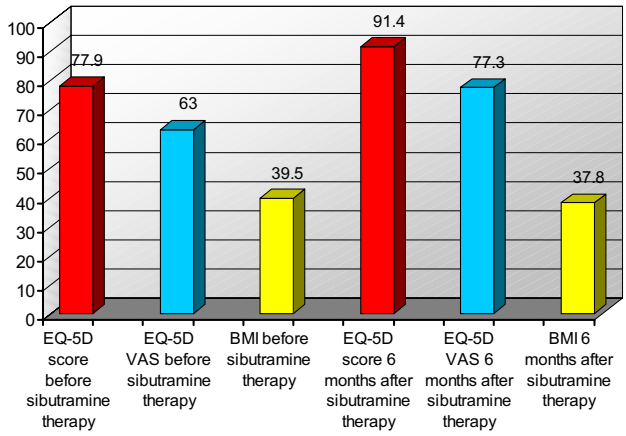

Fig. 1. Comparison of mean values of EQ-5D score, EQ-5D VAS and BMI before and after 6 months of sibutramine therapy (n=22, p<0.05).

evaluate the effect of sibutramine therapy on occurence of depression symptoms among adult obese non-diabetic patients during 6 months of this therapy.

Patients and methods

This was a pilot prospective and longitudinal study among 22 adult obese non-diabetic patients who were treated with sibutramine in dose of 10 mg daily during 2007 (January 1 to December 31) at the Department of Hygiene of Faculty of Military Health Sciences in Hradec Králové, Czech Republic. The total number of all obese respondents was 22 (6 males and 16 females). The mean age for all 22 respondents was 46.5 years old (age range 19–72 years old). The mean time interval since start of sibutramine therapy was 6 months. The mean Body Mass Index (BMI) for all 22 respondents before the start of sibutramine therapy was 39.5 (BMI range: 31–51). The mean BMI for all 22 respondents after 6 months of sibutramine therapy was 37.8 (BMI range: 30.5–50).

The study was approved by the Ethics Committee of the Charles University Hospital and Faculty of Medicine in Hradec Králové, Czech Republic.

Instruments

The Czech version of an international generic European Quality of Life Questionnaire – EQ-5D Version was applied for evaluation of health-related quality of life among obese patients (6, 7). This questionnaire evaluates 2 indicators, objective and subjective. The objective indicator includes 5 dimensions of QoL: mobility, self-care, usual activities, pain/discomfort, anxiety/depression. Three kinds of answers which express the degree of complaints are offered to each question (no complaints, mild complaints, severe complaints). Totally 243 (35) combinations of health condition exist. The outcome is EQ-5D score (dimensions of quality of life) which has the values from 0 to 1 (0 – the worst health condition, 1 – the best health condition). Subjective indicator includes visual analogous scale (the value of 100 – the best health condition, the value of 0 – the worst health condition). The respondent marks his subjectively perceived health condition at the thermometer scale. The outcome is EQ-5D VAS (a subjective health condition) which has the values from 0 to 100 (6, 7).

The Czech vision of self-assessement Zung-SDS was applied for evaluation of occurrence of depression among obese patients (8, 9). The Zung self-rating depression scale is a short self-administered survey to quantify the depressed status of a patient. There are 20 items on the scale that rate the four common characteristics of depression: the pervasive effect, the physiological equivalents, other disturbances, and psychomotor activities. There are ten positively worded and ten negatively worded questions. Each question is scored on a scale of 1–4 (a little of the time, some of the time, good part of the time, most of the time). The scores range from 25–100. 25–49 Normal Range. 50–59 Mildly Depressed. 60–69 Moderately Depressed. 70 and above Severely Depressed (8).

Data collection, statistical methods

The evaluation of quality of life questionnaires was carried out by means of descriptive analysis in accordance with European Quality of Life Group Method. Statistical analysis was performed by means of analysis of variance (ANOVA) and the paired t-test. $p<0.05$ were considered significant. The statistical analysis was conducted using the StatSoft Statistica Base software package, version 7.1.

Results of study

1) The results show that sibutramine therapy has a highly positive effect on health-related quality of life among adult obese non-diabetic patients. The mean EQ-5D score (dimension of quality of life) before sibutramine therapy for all 22 obese respondents was 77.9 %. The mean EQ-5D VAS (subjective health condition) before sibutramine therapy for all 22 obese respondents was 63 %. The mean EQ-5D score (dimension of quality of life) 6 months after sibutramine therapy for all 22 obese respondents was 91.4 %. Mean EQ-5D VAS (subjective health condition) 6 months after sibutramine therapy for all 22 obese respondents was 77.3 %. The statistical evaluation showed that sibutramine therapy has a highly positive effect on health-related quality of life among adult obese non-diabetic patients ($p<0.05$) (Fig. 1).

2) The results show that sibutramine therapy had a highly positive effect on occurence of depresion symptoms among adult obese non-diabetic patients. The mean index of depression (SDS index) before sibutramine therapy for all 22 obese respondents was 51.6 (minimal or mild depression symptoms). The mean SDS index 6 months after sibutramine therapy was 43.6 (without depression symptoms). The statistical evaluation demonstrated that

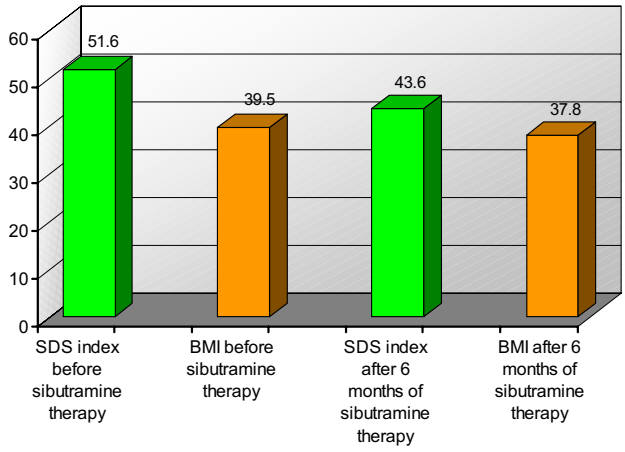

Fig. 2. Comparison of mean values of SDS index and BMI before and after 6 months of sibutramine therapy (n = 22, p<0.05).

occurence of depression symptoms (SDS index) presented highly significant statistical dependence on sibutramine therapy ($p<0.05$) (Fig. 2).

Discussion

We confirmed that the sibutramine therapy in dose of 10 mg/day has a highly positive effect on health-related quality of life among adult obese non-diabetic patients. Also, sibutramine therapy has a highly positive effect on individual dimensions of quality of life evaluated in European Quality of Life Questionnaire EQ-5D Version (mobility, self-care, usual activities, pain/discomfort, depression/anxiety). We confirmed that sibutramine therapy in dose of 10 mg/day has a highly positive effect on occurence of depression symptoms among adult obese non-diabetic patients.

The results of our prospective study support Nisoli•s and Carruba's review work (1). The efficacy of sibutramine for inducing initial weight loss and the subsequent maintenance of weight loss is well proven in short- and long-term clinical trials of up to 2 years' duration. Most individual placebo-controlled trials and pooled estimates found that the drug produced statistically significantly greater weight loss than placebo at all observed endpoints (weighted mean difference for weight change at 8 weeks: -3.4 kg; mean difference range for weight change at 6 months: -4.0 to -9.1 kg; and at 1 year: -4.1 to -4.8 kg). The most frequent dosage regimen in these trials was 10–20 mg daily. These findings suggested a dose-effect relationship in terms of weight loss. Sibutramine was also associated with better weight maintenance relative to placebo (statistically significant difference). Results from mainly small trials showed that sibutramine produced more favourable outcomes in terms of loss of fat mass, reduction in body mass index and loss of •5–10 % of initial body weight (1).

The author Wilfley et al (10) performed a study which it evaluates the efficacy of sibutramine in binge eating disorder. The total number of 304 participants who met DSM-IV criteria for binge eating disorder were randomly assigned to 24 weeks of double-blind sibutramine (15 mg) or placebo treatment. The outcome measures included the frequency of eating binges (primary outcome), binge day frequency, body mass index, body weight, global improvement, response categories, associated eating pathology, and quality of life. The primary analysis for continuous measures was the difference between groups in the change from baseline to endpoint using analysis of variance (ANOVA) with the last observation carried forward. The results were compared with subjects receiving placebo, participants who received sibutramine had a significantly greater reduction in weekly binge frequency (sibutramine group mean = 2.7 [SD = 1.7], placebo group mean = 2.0 [SD = 2.3]); weight loss (sibutramine group mean=4.3 kg [SD = 4.8], placebo group mean = 0.8 kg [SD = 3.5]); reduction in frequency of binge days; reduction in body mass index; global improvement; level of response, including the percentage of abstinence from binge eating (sibutramine group: 58.7 %; placebo group: 42.8 %); and reduction in eating pathology (cognitive restraint, disinhibition, and hunger). The change in quality of life scores was not significant. Sibutramine was associated with significantly higher incidence of headache, dry mouth, constipation, insomnia, and dizziness. This trial demonstrated the efficacy of sibutramine in reducing binge eating, weight, and associated psychopathology (10).

Conclusion

In summary, our study is the first investigation of the effect of sibutramine therapy among obese non-diabetic patients on health-related quality of life and occurence of depression symptoms in our country. Our study is one of the few of such studies carried out in countries within the former Eastern European bloc. Our findings represent a contribution for dietist and general practitioners because this physicians must think on quality of life of their obese patients. Also, they must think about the possibility of occurence of depression and its relevance among the obese patiens.

Limitations

We are also aware of the fact that our study can be limited by a few other factors: the relatively small number of our adult obese non-diabetic patients and the relatively short period after sibutramine therapy.

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