

## SIBUTRAMINE AND HEALTH-RELATED QUALITY OF LIFE: FINDINGS OF PROSPECTIVE, LONGITUDINAL STUDY

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### Summary

**Background:** Obesity is a multifactorial, chronic disorder that has reached epidemic proportions in most industrialized countries and is threatening to become a global epidemic. **Aims:** The study evaluates the effect of sibutramine therapy on health-related quality of life of obese patients. **Patients and Methods:** The study is local, prospective and longitudinal. It was carried out at Department of Hygiene of Faculty of Military Health Sciences in Hradec Králové, Czech Republic. Data were obtained during the year 2007. Twenty-two obese patients (6 males and 16 females) were treated by sibutramine in dose of 10 mg/day. All of these 22 patients were aged over 18 years. The European Quality of Life Questionnaire – EQ-5D Version was applied for evaluation of health-related quality of life among obese patients. **Results:** The statistical evaluation demonstrates that health-related quality of life (EQ-5D score and EQ-5D visual analogue scale) presents highly significant statistical dependence on sibutramine therapy ( $p < 0.05$ ). **Conclusion:** The results showed that sibutramine therapy has a highly positive effect on health-related quality of life of obese patients.

**Key words:** Sibutramine; Health-related quality of life; Obese patients.

### Sibutramin, zdraví a kvalita života: Výsledky perspektivní dlouhodobé studie

#### Souhrn

**Základní informace:** Obezita je multifaktoriální chronická porucha, jež dosáhla epidemických rozměrů ve většině vyspělých zemí a je nebezpečí, že se stane celosvětovou epidemií. **Cíle:** Studie hodnotí vliv sibutraminové terapie na zdraví a kvalitu života u obézních pacientů. **Pacienti a metody:** Studie je místní perspektivní a dlouhodobá. Vedena byla v České republice na katedře hygieny Fakulty vojenského zdravotnictví v Hradci Králové. Data byla získávána v průběhu roku 2007. Dvacet dva obézních pacientů (6 mužů a 16 žen) bylo léčeno sibutraminem v dávkování 10 mg/den. Všechny 22 pacientů bylo starších 18 let. Pro hodnocení zdraví a kvality života pacientů byl použit evropský dotazník Quality of Life Questionnaire – verze EQ-5D. **Výsledky:** Statistické vyhodnocení ukazuje, že zdraví a kvalita života (EQ-5D skóre a EQ-5D vizuální analogová škála) vykazuje vysoce významnou statistickou závislost na sibutraminové terapii ( $p < 0.05$ ). **Závěr:** Výsledky ukázaly, že sibutraminová terapie má vysoce pozitivní vliv na zdraví a kvalitu života obézních pacientů.

**Klíčová slova:** Sibutramin; Zdraví a kvalita života; Obézní pacienti.

### Introduction

Obesity is a multifactorial, chronic disorder that has reached epidemic proportions in most industrialised countries and is threatening to become a global epidemic. Clinical management of obese patients is complex and serious doubts have arisen with regard to safety and efficacy of drug therapy (3). 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 behavior. However, most of obese patients are not able to follow such a treat-

ment regimen for a longer period of time. If they do not lose > 5% of initial weight within 3–6 months, pharmacological intervention should be taken into account (10). Pharmacological approaches to the management of obesity can, in broad terms, use different 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 (2, 3, 4). 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 the induction of thermogenesis (3). The quality of life (QoL) is generally defined as “a patient’s subjective evaluation of his health status” (7). The QoL term contains the information on an individual physical, psychological, social and spiritual condition. The QoL evaluation is carried out by means of generic and specific QoL questionnaires (7). Generic QoL questionnaires generally evaluate a patient’s overall condition regardless his disease. Specific QoL questionnaires are designed for the evaluation of a patient’s overall condition in a particular type of disease (7). Modules are often used with these specific QoL questionnaires. These modules are focused on specific symptoms and complaints in a particular type of disease. The areas investigated in QoL questionnaires usually include patient’s physical, psychological and social functions, including his financial situation, his integration into the society, including pain, quality of sleep, spiritual aspects (interests, hobbies) and also symptoms which are specific for a particular disease (7).

### Patients and Methods

The local, prospective and longitudinal study of 22 obese subjects who were treated using sibutramine in dose of 10 mg/day during 2007 (January 1 to December 31) was performed at the Department of Hygiene of Faculty of Military Health Sciences in Hradec Kralove, Czech Republic. The total number of obese subjects was 22 (6 males and 16 females). The mean age for all 22 subjects was 46.5 years (aged 19–72 years). The mean time interval since start of sibutramine therapy was 6 months). The mean Body Mass Index (BMI) for all 22 subjects before start of sibutramine therapy was 39.5 (BMI range: 31–51). The mean BMI for all 22 subjects after 6 months of sibutramine therapy was 37.8 (BMI range: 30.5–50).

The study evaluated the effect of sibutramine therapy on health-related quality of life of obese patients during 6 months this therapy. The Czech version of European Quality of Life Questionnaire EQ-5D Version was applied for evaluation of quality of life in these patients (6–8). The Czech version of an international generic European Quality of Life Questionnaire – EQ-5D Version was applied for evaluation of HRQoL (6, 8). This questionnaire evaluates two 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). 243 ( $3^5$ ) combinations of health condition exist in total. The outcome is EQ-5D score (dimensions of QoL) 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 (6–8).

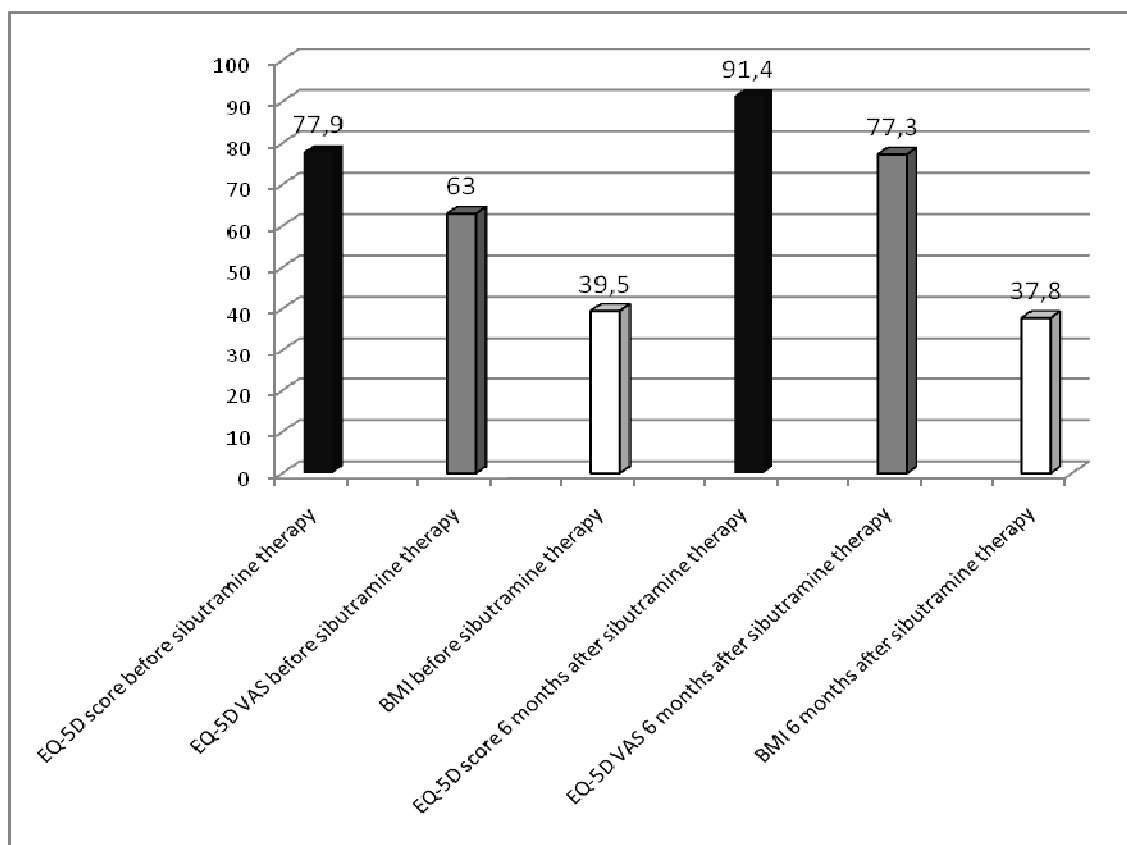
Statistical analysis was performed by means of analysis of variance (ANOVA) and the paired t-test. P values < 0.05 were considered significant. The statistical analysis was conducted using the StatSoft Statistica Base software package, version 7.1.

### Results

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

### Discussion

We confirmed that the sibutramine therapy in dose of 10 mg/day has a highly positive effect on health-related quality of life of obese patients. Also, we confirmed that the sibutramine therapy has a highly positive effect on individual dimensions of quality of life evaluated by means of European Quality of Life Questionnaire EQ-5D Version



Graph 1: Comparison of mean values of EQ-5D score, EQ-5D VAS and BMI before and after 6 months of sibutramine therapy (N = 22,  $p < 0.05$ )

(mobility, self-care, usual activities, pain/discomfort, depression /anxiety).

The results of our prospective and longitudinal study support Di Francesco's overview work (1). The author performed double-blind randomized trial on 309 outpatients (51 males, 258 females; age 41.8  $\pm$  10.9 years, BMI 35.0  $\pm$  3.1 kg/m<sup>2</sup>) (10) randomized to sibutramine (n = 154) or to placebo (n = 155) treatment. A combination of sibutramine 10 mg or matching placebo and a balanced hypocaloric diet was given for 6 months with monthly evaluations. The main outcome measures were weight loss, the impact of weight on QoL, BMI, and waist circumference. The author presents the mean weight reduction was 8.2 kg in the sibutramine group and 3.9 in the placebo group at 6 months ( $p < 0.01$ ). 40 % of the sibutramine subjects and 14 % of the control subjects lost  $\geq$  10 % of their body weight ( $p < 0.01$ ). The improvement in the impact of weight on QoL was statistically significant only in the sibutramine group at 6 months (mean -12.5 vs. -4.5 points;  $p < 0.01$ ). In the sibutramine group the reduction in BMI (-3.1

vs. -1.4 kg/m<sup>2</sup>) (2) and waist circumference (7.7 vs. 3.5 cm) was significantly greater ( $p < 0.001$ ). The incidence of adverse events was low and similar to the placebo. This study confirmed that sibutramine significantly enhances the effect of diet on weight loss, BMI and waist circumference reduction, and showed a significant improvement of QoL (1). Author Warren et al. (9) performed a study which it reports incremental cost-utility of sibutramine compared to diet and lifestyle advice for the treatment of obesity. The model estimates the costs and quality of life benefits associated with weight loss itself and the reduced incidence of coronary heart disease (CHD) and diabetes in the "healthy obese." The key source of effectiveness data is 2 randomized controlled trials over 12 months. Utility gain per kilogram lost is analyzed using Short Form-36 data from sibutramine trials. The impact on CHD is estimated using the Framingham risk equation, which relates age/sex/body mass index to risk of heart disease. The reduced incidence of diabetes due to weight loss is estimated from published literature. A life tables approach was used to calculate the

cost per quality-adjusted life year (QALY) of 1 year's treatment with sibutramine compared to diet and lifestyle advice. The author (9) presents that the incremental cost per QALY of sibutramine is 4,780 UK pounds. Sensitivity analyses show that this result is sensitive to utility associated with weight loss and the frequency of monitoring. Sibutramine is a cost-effective treatment for obesity when combined with diet and lifestyle advice (9).

### Conclusion

It is common in the clinical practice to evaluate a patient's health condition and the success of the treatment based only on one type of markers, the most often by means of somatic, laboratory or detecting markers (7). But the trend in modern clinical medicine is to evaluate a patient's health condition in a more complex way, using other aspects. The QoL means more dimensional evaluation of a number of life aspects. Different aspects can be affected in a different way in a different phase of the disease and its treatment. That is why this information enriches our knowledge concerning patient's needs and it can significantly contribute to the medical treatment improvement. It can also help us to reveal the mechanisms which modify the origin and the course of disease (5–7).

In summary, our study is the first investigation of effect of sibutramine therapy on health-related quality of life of obese patients in our country. Our study is one of the few such studies carried out in countries within the former Eastern European bloc.

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### References

1. Di FRANCESCO, V. – SACCO, T. – ZAMBONI, M., et al. Weight loss and quality of life improvement in obese subjects treated with sibutramine: a double-blind randomized multicenter study. *Ann. Nutr. Metab.*, 2007; vol. 51, p. 75–81.
2. LUQUE, CA. – REY, JA. The discovery and status of sibutramine as an anti-obesity drug. *Eur. J. Pharmacol.*, 2002, vol. 440, p. 119–128.
3. NISOLI, E. – CARRUBA, MO. A benefit-risk assessment of sibutramine in the management of obesity. *Drug Saf.*, 2003, vol. 26, p. 1024–1048.
4. PAYER, J. – HAINER, V. – ONDREJKA, P., et al. Sibutramine in obesity treatment (multicenter, open, prospective 12-month-long study). *Vnitř. Lék.*, 2004, vol. 50, p. 825–829.
5. SLOVÁČEK, L. – BOHUTÍNSKÁ, H. – KAŠLÍKOVÁ, M., et al. Occurrence of depression symptoms in peripheral arterial occlusive disease. *Voj. zdrav. Listy*, 2008, roč. 77, s. 29–32.
6. SLOVACEK, L. – SLOVACKOVA, B. – CHOVANEC, V. The effect of femoral and popliteal percutaneous transluminal balloon angioplasty on patients quality of life. *Sao Paulo Med. J.*, 2007, vol. 125, p. 250–252.
7. SLOVACEK, L. – SLOVACKOVA, B. – JEBAVY, L. Global Quality of Life in Patients Who Have Undergone the Hematopoietic Stem Cell Transplantation: Finding from Transversal and Retrospective Study. *Exp. Oncol.*, 2005, vol. 27, p. 238–242.
8. THE EUROQol GROUP. EuroQol – a new facility for the measurement of health-related quality of life. *Health Policy*, 1990, vol. 16, p. 199–208.
9. WARREN, E. – BRENNAN, A. – AKEHURST, R. Cost-effectiveness of sibutramine in the treatment of obesity. *Med. Decis. Making*, 2004, vol. 24, p. 9–19.
10. WIRTH, A. Weight loss via drug therapy. *Internist (Berl.)*, 2003, vol. 44, p. 359–366.

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