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ORIGINAL ARTICLE

Effect of sibutramine on intraocular pressure

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ABSTRACT

Objective

This study evaluated the effects of sibutramine on intraocular pressure (IOP) and body-mass index (BMI).

Methods

Thirty obese females (body-mass index >30 kg/m^2) treated with sibutramine (10 mg/day) plus diet restriction for 3 months were included in the study. IOP, BMI, and blood biochemical parameters were measured at the beginning and end of the treatment. Results were evaluated statistically by paired t-test, analysis of variance, and least-significant difference test.

Results

A statistically significant decrease was observed in the mean body-mass index ($p < 0.001$) and serum triglyceride ($p < 0.001$), while a statistically insignificant increase was observed in IOP ($p = 0.54$).

Conclusion

While sibutramine provided an effective means for weight loss, it caused a slight increase in IOP, although this was not statistically significant. Nevertheless, it is prudent to monitor IOP in selected obese patients treated with sibutramine.

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IN RECENT years, obesity has become increasingly prevalent worldwide, making it a major public-health problem.[1] The health implications are enormous especially because of complications associated with obesity and overweight. The increase in the prevalence of overweight and obesity results in a subsequent wave of comorbid conditions such as hypertension, cardiovascular diseases, type 2 diabetes mellitus, elevated intraocular pressure (IOP), and several psychosocial complications.[2,3] Because of this, campaigns are being undertaken to advise people to cut down on fat and calorie intake and increase physical activity. A 10% reduction in dietary-fat energy leads to an average weight loss of 5 kilograms over 2 to 6 months in obese subjects. But diet and lifestyle modification alone has not been very successful in many cases. There is a need for more effective treatment programs. Pharmacological treatment with effective and safe compounds is a logical option.[2]

Sibutramine (Reductil, Abbott, Illinois, USA) used in the treatment of obesity, is a novel serotonin and noradrenaline reuptake inhibitor.[4] Sibutramine decreases food intake by increasing satiety, stimulates thermogenesis, and diminishes the weight-loss-induced decline in energy expenditure in humans. The dual effect on energy balance seems to be responsible for the efficient fat loss and weight maintenance achieved in clinical trials involving obese patients.[2]

Serotonin, which is present in the anterior segment of mammalian eyes, acts as a neurotransmitter.[5] Serotonin receptors are regulated by many exogenous and endogenous substances, and the serotonergic transmission system is involved in various physiologic and pathologic processes.[6,7] It is known that adrenergic and serotonergic agents may affect IOP.[8,9]

This study evaluated the effects of sibutramine on IOP and body-mass index (BMI) in obese females.

METHODOLOGY

Thirty obese females (mean age 38.1 ± 5.8, BMI >30 kg/m^2) were treated with sibutramine (10 mg/day) plus diet restriction for 3 months. Patients with obesity of endocrine origin or who had a history of treatment for hypertension, systolic blood pressure (SBP) ≥160 mm Hg, diastolic blood pressure (DBP) ≥95 mm Hg in the seated position with concomitant heart rate ≥100 beats/minute, and type 1 and type 2 diabetes mellitus were excluded.[1]

Assessments were made at baseline and weeks 2, 4, 8, and 12 after administration of sibutramine. At each visit, the investigators recorded the patient's weight to the nearest 0.5 kg with the patient wearing indoor clothing and no shoes. SBP, DBP, pulse rate, IOP, and adverse events were also recorded.[10] BMI was computed as weight in kilograms divided by the square of height in meters.[11] IOP was measured in right eyes between 9:00 and 10:00 AM with a Goldmann applanation tonometer. The mean value of the three IOP measurements was used for analysis. Full ophthalmological examination was performed: slit-lamp biomicroscopy, funduscopy, and ocular refraction. Subjects with glaucoma, IOP ≥22 mm Hg, cup–disc ratio of 0.4 or higher, refractive error >±4 D, or any other type of ocular disease or disorder were excluded. Laboratory investigations (complete blood count, serum glucose, uric acid, creatinine, hepatic enzyme, total cholesterol (TC), triglyceride, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and HDL_3 levels were repeated at baseline and at months 1 and 3.

Results were evaluated statistically by paired *t*-test, analysis of variance (ANOVA), and least-significant difference (LSD) test.

RESULTS

At three months posttreatment, participants achieved a mean weight loss from baseline of 8.46%. While a statistically significant decrease was observed in the mean BMI ($p < 0.001$), and serum triglyceride ($p < 0.001$), a significant increase was found in serum HDL ($p < 0.001$) and HDL_3 levels ($p < 0.001$). There were no statistically significant changes between pretreatment and posttreatment values in serum glucose, TC, LDL, SBP, DBP, or pulse rate (Table 1). Only one of the patients experienced tachycardia, and no one discontinued treatment.

A slight increase from baseline was seen in the mean IOP values (Table 2), but there were no statistically significant differences by ANOVA ($p = 0.54$) during the

Table 1. **Profile of patients treated with sibutramine.**

Parameters	Baseline (Mean)	3 Months (Mean)	Paired-*t* test
BMI (kg/m^2)	38.1 ± 5.8	34.4 ± 5.5	0.000
IOP (mm Hg)	16.1 ± 2.2	16.7 ± 2.3	0.346
SBP (mm Hg)	128.6 ± 19.9	125.0 ± 19.9	0.062
DBP (mm Hg)	86.5 ± 11.9	83.6 ± 13.3	0.084
Pulse rate (/min)	89.1 ± 8.1	88.9 ± 9.2	0.943
Glucose (mg/dl)	101.4 ± 23.1	99.8 ± 24.9	0.528
Total triglyceride (mg/dl)	186.2 ± 94.4	126.0 ± 50.1	0.000
TC (mg/dl)	180.1 ± 34.8	185.7 ± 29.7	0.340
HDL (mg/dl)	39.1 ± 7.6	43.7 ± 8.6	0.000
HDL_3 (mg/dl)	25.7 ± 7.7	31.4 ± 7.1	0.000
LDL (mg/dl)	94.1 ± 38.8	95.7 ± 21.7	0.849

Table 2. **Mean IOP at baseline and follow-up visits.**

Study period	Mean IOP (mm Hg)
Baseline	6.13 ± 2.17
Week 2	7.13 ± 1.98
Week 4	16.81 ± 2.38
Week 8	16.75 ± 2.43
Week 12	16.68 ± 2.26

follow-up visits. LSD test showed no significant differences in the mean IOP between visits (Table 3).

DISCUSSION

Low sympathetic activity may be a causal factor in obesity. Obese subjects have lower noradrenaline levels than nonobese subjects, which suggests that a proportion of obese subjects may have a lower sympathetic activity.[2]

Sibutramine possesses anorectic properties attributable to both noradrenergic and serotonergic effects. Sibutramine causes a negative fat balance and weight loss by a dual-action mechanism. Sibutramine causes weight loss in laboratory animals through effects on both food intake and metabolic rate. In this study, a statistically significant decrease was observed in the BMI.

In our study, sibutramine did not elevate either SBP or pulse rate despite findings in some studies associating sibutramine treatment with increases in these parameters.[4] Nonetheless, weight loss generally has a predictable effect in reducing blood pressure. Heart rate is not thought to be influenced by overweight or by weight loss.[1]

Hanotin et al. determined that plasma triglyceride and cholesterol levels decreases with sibutramine treatment, but the decrease was not statistically significant.[1] In our study, sibutramine produced statistically significant increases in serum HDL and HDL_3 levels, and statistically significant decreases in triglyceride levels.

Increased serotonin levels in the anterior chamber of the eyes produce an increase in IOP. Topical application of serotonin to rabbit eyes has been reported to increase IOP.[12] In our study, sibutramine treatment produced a slight increase in IOP, but this was not statistically significant. Although IOP was expected to decrease along with weight loss, an increase was noted instead, which may be related to the indirect mechanism of increasing serotonin on noradrenalin activity and secondary activation of β-adrenoreceptors.[13]

Table 3. **Mean IOP changes between baseline and follow-up visits.**

Compared groups	Mean difference	*p*
Baseline v. week 2	-1.0000	0.088
Baseline v. week 4	-0.6833	0.242
Baseline v. week 8	-0.6167	0.291
Baseline v. week 12	-0.5500	0.346

In conclusion, sibutramine treatment plus diet restriction may produce a significant weight loss over a 12-week treatment period in obese subjects. While sibutramine used for treatment of obesity provided an effective means for weight loss, it might cause a slight increase in IOP, but not changes in SBP and pulse rate. The increase, however, is not statistically significant. Nevertheless, it is prudent to monitor IOP in selected obese patients treated with sibutramine.

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