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Reduction of Body Weight, BMI and Visceral Fat Percentage in Nineteen Non-Diabetic, Obese Patients Having Migraine with Lorcaserin and Topiramate: A Case Series

Sayak Roy[1]* and Abhijnan Ghosh[2]

[1]*Department of Internal Medicine, Medica Superspeciality Hospital, India*

[2]*IPGMER, India*

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***Corresponding author:** Sayak Roy, Consultant Physician, Department of Internal Medicine, Medica Superspeciality Hospital, Kolkata, India

Abstract

Introduction: Obesity and metabolic syndrome have been long inter-linked and it has been found that the cardiovascular (CV) mortality increases steadily with the increase in obesity as defined by increase in body mass index (BMI). The BMI cut-off for defining obesity is different in Asians as compared to Caucasians where we consider BMI 24.9 as normal. In Asians we use a BMI value of 23 as the upper normal due to the increased CV mortality and higher degree of chronic kidney disease (CKD) as defined by decreased age-specific estimated glomerular filtration rate (eGFR) seen in Asians.

Materials and Methods: We analysed the clinic data record of 19 non-diabetic obese patients having migraine (as per standard defining criteria) attending our clinic between November 2019 to 1st February 2020 to see the changes in weight, BMI and visceral fat (VF) from their baseline values using an online software (https://www.calculator.net/standard-deviation-calculator.html) and applied paired t-test for analysis using the online software version available to calculate the values (https://www.graphpad.com/quickcalcs/ttest1/?Format=C). Proper written informed consent was taken from each participating patient so that their clinic records can be used for medical knowledge sharing purpose.

Results: There were 12 females and 7 male patients having an overall baseline age 36.947 years (±13.60%), weight 83.831 kg (±6.15%), BMI 32.615 kg/m2 (±4.60%), eGFR 104.842 ml/min/1.73 m2 (±5.98%), visceral fat 11.342 % (±4.39%) and a mean duration of follow-up of 53.263 days (±4.06%). There were statistically significant changes seen in BMI, weight and visceral fat percentage as reflected by a p value of <0.0001 for each.

Conclusion: Lorcaserin has now been withdrawn after the FDA communication of increased cancer risk on long term use on 13th February 2020 but this case series showed a fantastic reduction in BMI, weight and visceral fat in just 2 month time when topiramate 50 mg is added to standard dose of lorcaserin 20 mg per day. The weight loss with lorcaserin alone in BLOOM trial was 5.8±0.2 kg (approx. 5%) in one year while our case series showed a weight loss average of 3.42% in just approximately 2 months. Although this percentage of weight loss is not the defining criteria for weight loss medication as per FDA but this was used only for 53.263 ±2.161 days. Further short-term trials with larger cohort can be undertaken with increasing dose of topiramate and lorcaserin after the debate of lorcaserin and cancer risk is sorted out as a new weight loss drug regimen since short-term lorcaserin use is not thought to be linked to cancer.

Keywords: Obesity; Metabolic syndrome; Cardiovascular; Topiramate; Lorcaserin; Colorectal; Pancreatic; Non-diabetic; Obese

Abbrevations: CV: Cardiovascular; BMI: Body Mass Index; CKD: Chronic Kidney Disease; eGFR: Estimated Glomerular Filtration Rate; POMC: Pro-Opiomelanocortin; 5HT2C: 5 Hydroxytryptamine Receptor Type 2c; VF: Visceral Fat

Introduction

The average prevalence of obesity and metabolic syndrome is approximately 31% and there is a steep decline in life expectancy with increase in obesity with many times increase risk of CVD, cerebrovascular disease and all-cause mortality [1]. There has been a parallel increase in prevalence in CKD with the epidemic of obesity [2]. The overall body-fat per unit of BMI and truncal fat per kilogram of body fat is higher in Asians as compared to white population [3,4]. The cut-off BMI for obesity in Asian Indians is 23 [5]. Bioimpedance analysis is quite often used as a tool for body composition measurement and it is

used to assess the visceral fat percentage of the patient [6]. The visceral fat is considered as high if it is 10.0 – 14.5 and very high if it is 15 – 30 [7]. Lorcaserin had been licensed as an anti-obesity drug by FDA and as per BLOOM trial it showed a 5% weight reduction in the intervention arm after 1 year [8]. Topiramate is a drug used in migraine and it has shown weight loss property in diabetic patients [9]. Topiramate has also shown reduction in weight when used at a dose of 200 – 600 mg per day in obese affective disorders patients [10]. Topiramate (extended release) has been approved as an anti-obesity drug as a combination with phenteramine since July 2012 [11]. Recently the weight loss medication, lorcaserin, approved by FDA in June 2012 got withdrawn from the market after FDA found an increased signal of various cancers including colorectal, pancreatic and lungs to the tune of 7% from a randomized control trial analysis involving 12,000 patients over 5 years [12]. Our study included patients prior to this announcement and results are based on a short-term use.

Materials and Methods

Our study included 19 patients (12 females and 7 males) having met a primary inclusion criteria of – age 20 years to 60 years, having migraine as per standard diagnostic criteria set by international headache society [13] and on no chronic therapy for that, non-diabetic, obese as defined by BMI >23, non-pregnant, no previous weight-loss medications in last 3 months, no prior history of hospitalisation due to any cause in last 3 months. The baseline characters of the patients are outlined in table 1 and were calculated using the online software https://www.calculator.net/standard-deviation-calculator.html. We used Omron Karada HBF 375 body analyser ® for visceral fat assessment. Paired t-test was applied on baseline and follow-up data to reach statistical analysis using the online software https://www.graphpad.com/quickcalcs/ttest1/?Format=C. All the patients gave their proper written informed consent to share their medical records for medical research and knowledge sharing purpose.

Table 1: Baseline patient characteristics.

	Age (Years)	Duration of Follow-Up (Days)	eGFR (ml/min/1.73m2)	Baseline Weight (kg)	Baseline BMI (Weight in kg/Height in m²)	Baseline Visceral Fat (%)
Average	36.947	53.263	104.842	83.831	32.615	11.342
95% CI	36.947 ±5.024 (±13.60%)	53.263 ±2.161 (±4.06%)	104.842 ±6.265 (±5.98%)	83.831 ±5.156 (±6.15%)	32.615 ±1.501 (±4.60%)	11.342 ±0.497 (±4.39%)

CI: Confidence Interval; eGFR: Estimated Glomerular Filtration Rate; BMI: Body Mass Index

Results

Topiramate 50 mg per day when used simultaneously with lorcaserin 20 mg per day reduced the weight, BMI and visceral fat significantly as reflected by a p value of <0.0001 for each of the three. The results of paired t-test are summarised in table 2. A linear regression analysis (https://www.graphpad.com/quickcalcs/linear1/) showed that baseline BMI did not affect the outcome BMI and there was a significant linear relation between the two (Figure 1). After dividing the baseline BMI into two groups, one having BMI 27 – 34 and the other having BMI 34.1 – 41, and using the percentage change of each group to calculate One-Way ANOVA (https://www.socscistatistics.com/tests/anova/default2.aspx), we found that the baseline BMI did not decide the final BMI as the p value is 0.128 and the reduction in BMI across various baseline BMI was constant.

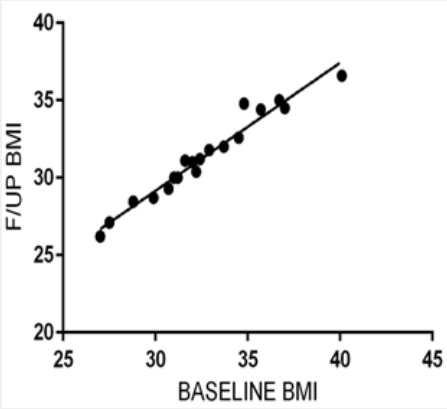

Figure 1: Baseline BMI.
BMI: Body Mass Index; F/UP: Follow-Up

Table 2: Paired t-test values of the various parameters.

	Weight		BMI		Visceral Fat	
	Baseline Weight (kg)	Follow-Up Weight (kg)	Baseline BMI (Weight in kg/Height in m²)	Follow-up BMI (Weight in kg/Height in m²)	Baseline Visceral Fat (%)	Follow-Up Visceral Fat (%)
Mean	83.832	80.968	32.6158	31.3242	11.342	10.079
SD	11.467	11.085	3.338	2.8196	1.106	0.769
SEM	2.631	2.543	0.7658	0.6469	0.254	0.176
P value	<0.0001*	<0.0001*	<0.0001*			
95% CI	[1.979, 3.748]	[0.9017, 1.6815]	[0.759, 1.767]			

*statistically significant; SD: Standard Deviation; SEM: Standard Error of Mean; CI: Confidence Interval

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Discussion

The south Asian population has a body composition which is different than the white people with the same BMI since they have a lower skeletal muscle mass and higher body fat with increased abdominal adipocity and liver fat content. All of these lead to increased CVD and increased propensity to cause type 2 diabetes [14]. Lorcaserin is a weight loss medication approved by US-FDA in 2012 and acts as an agonist at 5 hydroxytryptamine receptor type 2c (5HT2C) present in hypothalamus to reduce the appetite [15]. Stimulating the 5HT2C receptors of pro-opiomelanocortin (POMC) neurons of the arcuate nucleus leads to release of alpha-melanocortin-stimulating hormone which acts in the paraventricular nucleus area causing suppression of appetite [16]. The approval for topiramate dates back to 1995 when it was approved in UK as an adjunctive medication for adult patients with partial-onset seizures [17]. Topiramate acts by blocking voltage-dependant calcium and sodium channels [18, 19] as well as enhances the inhibitory effects of gamma aminobutyric acid [20]. The anti-migraine mechanism of this molecule is still not clearly understood. In one prospective trial (N 38) topiramate was investigated to find out the people who will respond to its weight loss property and found that decreased food intake was responsible for the early phase of weight loss and higher BMI showed better weight loss [21]. Our case series showed a significant decrease in weight in just 53.263 ±2.161 days follow-up using 20 mg per day lorcaserin and 50 mg topiramate tablets. Though we had a significant linear correlation in BMI but on applying One-Way ANOVA analysis we found that the baseline BMI does not decide the outcome BMI and there is a constant reduction in BMI over a range of baseline BMI. This regimen if tried over short period on a larger cohort can give us valuable information on weight loss physiology and new regimens can be used if it is seen that lorcaserin does not increase cancer risk over short-term use.

Conclusion

Obesity is a major health issue not only in developed countries but also in developing countries and needs to be tackled urgently and efficiently. The new regimen using a combination of lorcaserin and topiramate as a short-term indication for weight management might be investigated taking a larger cohort once the lorcaserin controversy is settled. Lorcaserin and topiramate combination seems to reduce weight, BMI and visceral fat modestly and thereby addresses the long-term complications of obesity.

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