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Escalating BMI Associated With the Complex Pharmacology of Propranolol: A Case Report

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Authors' contributions

This work was carried out in collaboration among all authors. Author DMSB contributed in acquisition of data, design, analysis and interpretation of data, revising the manuscript and has given final approval of the version to be published. Author TI contributed in design, analysis and interpretation of data, writing the manuscript and has given final approval of the version to be published. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Background: Improving the awareness of the public about the body weight and the body mass index (BMI) criteria is very important as increased body weight may be associated with an increased risk for many dangerous diseases and health complications. Propranolol is generally prescribed for tachycardia while its most common side effects are bradycardia and masking hypoglycemia.
Case Presentation: A tachycardia was diagnosed in a young overweight woman and treated successfully with propranolol but this treatment, unpredictably, was associated with a rapid increase in the weight that classified her as obese.
Discussion: The physical (body weight and heart rate) and the biochemical (blood glucose level) monitoring and analysis including the lifestyle provided a deeper insight into the principal details and helped to design a personalized treatment protocol.
Conclusion: A therapeutic dose of propranolol could be linked to uncommon mounting weight change which was associated with a decrease in the blood glucose level and an appetite enhancement.

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1. INTRODUCTION

Associated with the overweight or the obesity state there are two increasingly spreading diseases: the type-2 diabetes mellitus (T_2DM) and the hypertension. Common among the overweight and the obese individuals, there are elevated concentrations of fatty acids, leptin, and tumor necrosis factors in the plasma, which develop insulin resistance in the various body tissues and consequently T_2DM [1]. Those who are overweight at a younger age are more susceptible to become diabetic later as they become older [2].

Along with the increase in the body mass index there is a higher probability of elevated plasma triglycerides and cholesterol concentrations and also a higher probability of hypertension, which are becoming common among the patients in our health care program and around the world [3]. To a less extent compared to T_2DM and hypertension, the overweight or obese patients may also complain of a noticeable increase in the heart rate. All the health associations around the world support that these health obstacles might be avoided, deferred, reversed, or at least successfully coped with. This requires proper control of the dietary intake [4] and the results will become more positive when accompanied by a lifestyle rich in frequent physical activities.

Propranolol ((R/S)-1-(isopropylamino)-3-(1-naphthyloxy)-2-propanol) is commonly classified as a non-selective beta-blocker (it binds to the beta-adrenergic receptors), was approved as a medication in 1962, and exhibits biomedical activities in various conditions; hypertrophic cardiomyopathy, anxiety, esophageal variceal bleeding, portal hypertension, tachycardia, myocardial infarction, angina pectoris, migraine headaches, capillary hemangiomas, essential tremors, thyrotoxicosis, hyperhidrosis, infantile hemangioma, glaucoma, hypertension, and cancer. However, there is a small probability of minor side effects such as constipation, abdominal pain, and nausea. In coronary artery disease, heart failure, asthma, and liver or kidney problems, it is not a recommended medication. In addition to that, it shows many drug-drug interactions.

2. CASE PRESENTATION

A tachycardia case of a 28 years old woman is presented here. She was 167 cm in height and weighed 75 kg (the body mass index; BMI= 26.9 kg/m^2). She was a working individual (elementary school teacher), did not smoke, did not have a history of alcohol ingestion, and did not take any medication regularly. In the first attendance to our comprehensive health care center she complained of an annoying discomfort in her chest and specified an increase in the heart beating (according to her description). She explained that sometimes this symptom disappears but suddenly comes back and this happens frequently during the day. She could not observe a systematic connection to anything else; a food item, a physical effort, or the psychological status. Also, she illustrated that this symptom developed gradually over the last three years until it became frightening and discomforting.

After resting for 30 minutes her heart rate in that visit was high (115 bpm) but the other primary vital signs were normal. Initially, she was given oral propranolol tablets (2 x 20 mg/day; 12-hours apart) and referred to a cardiologist for consultation, which revealed after extensive investigations that her case was an idiopathic ventricular tachycardia and the cardiologist recommended propranolol; 40 mg in the morning and another 40 mg after nearly 12-hours. Taking into consideration being young suffering a tachycardia the case was uncommon and interesting and therefore she was asked to attend the clinic for a follow up (the BP, the RR, the weight, and the HR) every week for 12-weeks.

3. DISCUSSION

The patient complied and attended the clinic regularly and each week the BP, the RR, the weight, and the HR were recorded systematically. Here heart rate improved directly and significantly with the specified propranolol dose. Unpredictably, over the 12-weeks follow-up period the patient gained weight gradually and noticeably (Fig. 1). Upon discussing this observation with her she mentioned that she experienced an increase in her appetite in general and specifically an uncontrolled desire toward the sweet food items that may appear sometimes as an uncontrolled sugar rush. Fig. 1 shows that the weight gain was not ascending linearly; it started to stabilize after 8-weeks as suggested and best described by the second order polynomial equation. After six weeks the

weight gain started to become more apparent and she was advised continuously to watch the amount of food she consumes but it appeared that she didn't take this aspect seriously. After the end of the 12-weeks her body mass index reached 30.1 kg/m^2 which rang the warning bell to be classified as an obese person. Many of our patients take propranolol regularly at this dose but it is uncommon to notice this significant increase in the body weight (9kg in three months). Also, the medical textbooks and handbooks do not warn against this as a major or common side effect of propranolol.

In order to understand this rare observation further investigation of the case was continued after the approval of the patient. She was instructed to take propranolol and 250 ml of water (under the medical supervision at the clinic) at the morning of four consecutive days after overnight (12-hours) fasting; 10 mg propranolol was taken (the first day), 20 mg (the second day), 30 mg (the third day), and 40 mg (the fourth day). Blood samples were tested before taking propranolol and every 30 minutes (blood samples were taken through a cannula; 1.0 ml each was sufficient to run the laboratory test). The results of the heart rate (HR) and the biochemical analyses showed noticeable gradual changes and differences in both the HR and the fasting blood glucose (FBG) concentration among the four days, as presented in Figs. 2 and 3. The graph in Fig. 2 shows that the higher dose is more effective but all the doses retained (qualitatively) the pharmacological effect and the HR for nearly four hours. Fig. 3 illustrates that propranolol had a systematic glucose lowering effect but it was mild and the lowest recorded value didn't cross the lower limit of the safety range.

The daily lifestyle was discussed with the patient. She illustrated that she used to take the propranolol dose in the morning before going to work then eat her first meal at the workplace with the other employees (10:00-11:00 am). Taking into consideration the pharmacological performance of propranolol (Figs. 2 and 3), the drug dose was changed to suit her lifestyle; 10 mg of propranolol in the morning before going to work, 20 mg after the first meal, another 20 mg after the evening meal, and 10 mg may be taken during the day only if necessary. Also, she was advised to follow a specific diet to prevent more weight gain and to decrease her body mass index. The obesity dangerous consequences were explained to here to induce and to strengthen the self-commitment. After 4-weeks, she did not have any complaints and started losing weight; lost about 2 kg.

An individual's new weight gain (more IN's, less OUT's) is a complex process and is an interplay among many parameters; age, genetics, environmental factors, amount of the ingested food and its components, metabolism, physical activities, hormones, psychological status, initial body mass index, cognition, gender, insomnia, breastfeeding, socioeconomic, and the medications [5,6]. Many medications are known to associate with an increase in the body weight including beta-blockers [7-10].

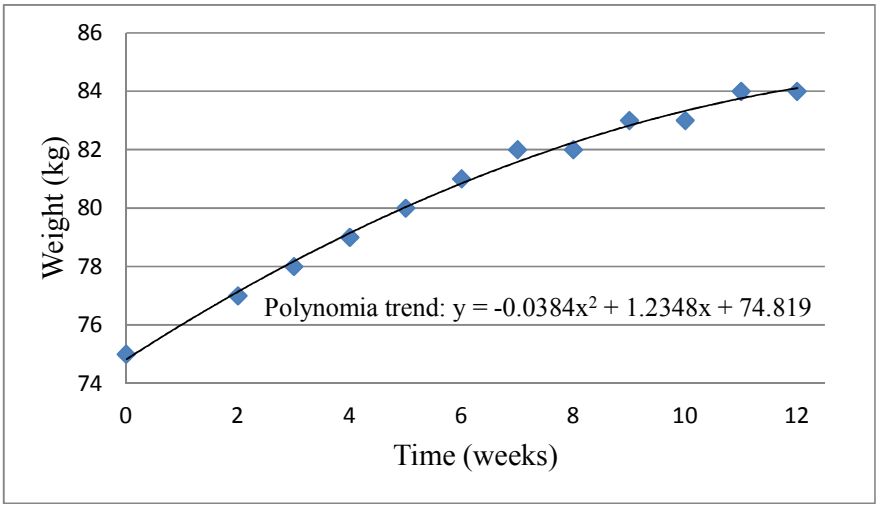

Fig. 1. The weight (kg) change over the 12-weeks period

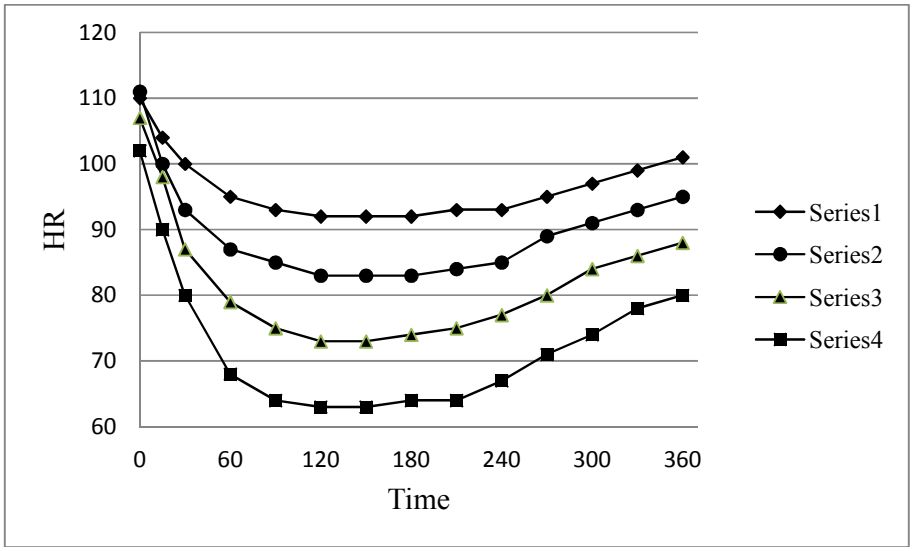

Fig. 2. The change in the heart rate (HR, beats per min; bpm) with time (min) concerning the value before taking propranolol at different propranolol doses; 10 mg (series 1; day-1), 20 mg (series 2; day-2), 30 mg (series 3; day-3), and 40 mg (series 4; day-4)

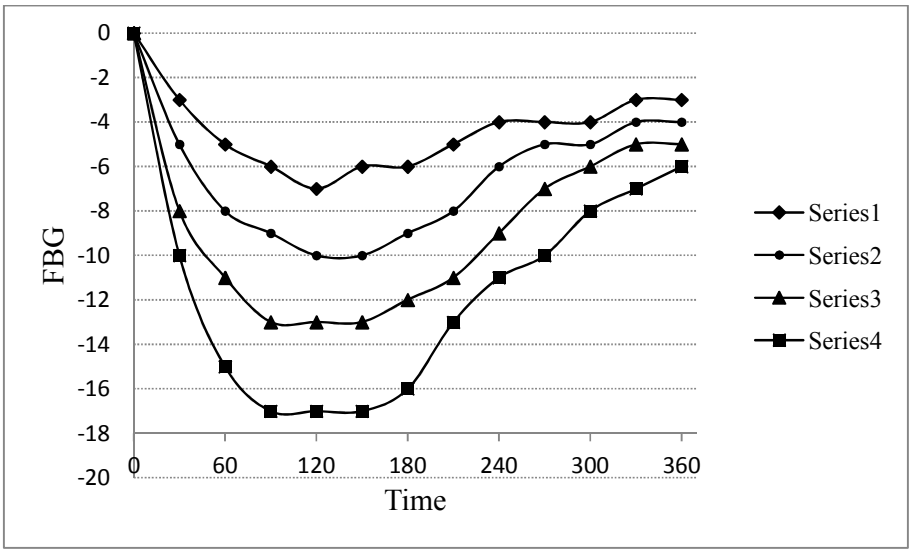

Fig. 3. The decrease in the fasting blood glucose level (FBG; mg/dl) with time (in minutes) with respect to the value before taking propranolol (FBG= 103-105 mg/dl) at different propranolol doses; 10 mg (series 1; day-1), 20 mg (series 2; day-2), 30 mg (series 3; day-3), and 40 mg (series 4; day-4)

The variety in the characterized physiological effects (positive or negative) of propranolol confirms its complex biochemistry and its ability to interact and affect many sites in the body including the brain. Despite being a sixty years old medication the image of the molecular mechanisms is not well structured [11, 12].

The effect of propranolol on the body weight was studied in a randomized double blind trial that included a placebo component [13]. The study was based on a large sample; 3837 men and women, and for a long trial duration; forty months. It was noticed that the patients who were treated with propranolol could burn more energy through physical activities, which was

expected to decrease the body weight (compared to the control group), on the contrary of that, they gained more weight; 2.3 kg compared to 1.2 kg of the placebo group, which indicated that the weight difference could be higher. This result appeared in both genders and in all ages regardless of the physical activity or using other medication. The weight gain happened slowly but these findings confirmed that it is directly related to propranolol consumption.

The exact pathological, physiological, and biochemical mechanisms behind the weight gain with propranolol use are not well-defined in the literature therefore the following is hypothesized regarding the present case.

1. Fig. 3 shows that propranolol had a mild hypoglycemic effect. Consistent with this finding, previous studies confirmed that propranolol can participate in reducing the blood glucose level in conjunction with insulin or metformin anti-hyperglycemic therapies through decreasing the Tnf and PKA protein expression and increasing the expression of Slc2a4 and the glucose transporter-4 (GLUT4) and therefore increases the glucose cellular uptake [14, 15].
2. According to her daily routine, this effect might have increased while going to work until her first meal (10:00-11:00). Going to work, for sure, involved a higher energy expenditure compared to that while resting in the clinic during the data acquisition. This caused the sugar-rush or the enhanced appetite episodes, and triggered the uncontrolled eating. This condition could be corrected or suppressed by a small portion of the chosen food item, instead of that, she used to consume the whole item without recognizing that she consumed folds of the needed calories. Most of the available fast food meals and snacks are in fact fat-rich, too, which implies that unnecessary fat is deposited in her body tissues every day and accumulated repeatedly.
3. We believe that another point played a crucial role in the rapid weight gain. This daily scenario might have turned quickly into a continuous tendency and a habitual behavior that is triggered always by the continuous desire to gain more of the "rewarding feeling of pleasure" associated with eating.
4. The patient mentioned that images of food items that she enjoyed appeared in her mind frequently (as if she is fasting) until she eats a meal. This may indicate that propranolol affects the complex chemistry and signaling that intercede among the gastrointestinal tract, the adipose tissues, hypothalamus, the limbic system, and the cortex [16].

4. CONCLUSION

A case of tachycardia that had normal health signs was diagnosed and responded successfully to treatment with propranolol. Unexpectedly, the patient experienced an escalating increase in BMI. The biochemical investigation revealed that appetite activation was triggered by a glucose-lowering effect of the medication. A drug dose modification and a dietary plan correction appeared to be promising. It is recommended to educate the overweight and obese patients to be careful about any appetite increase and uncontrolled food intake because that might turn into habitual behavior, a hidden reason for a gradual increase in BMI and potential health problems.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by the personal efforts of the authors.

CONSENT

The patient consent was obtained to publish the information.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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