



Novel Association between Gemfibrozil and Dyslipidemia: A Case Report

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Authors' contributions

This work was carried out in collaboration between both 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. Both authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Dyslipidemia is a risk factor in many health complications, among them is hypertension.

Case: This report presents a case of a poorly controlled dyslipidemia that could not be managed by medications. A surprisingly and an unexpected factor interfered; the triglyceride-lowering medication caused a significant increase in the appetite toward fat-rich food items which opposed its intended purpose.

Methodology: A dietary intervention and an uncommon drug dose modification were necessary.

Results: The personally designed protocol led to a significant overall improvement and was successful in adjusting the biochemical parameters especially the plasma triglycerides and the total cholesterol and was effective in reversing hypertension and a pre-diabetic state to safer values.

Conclusion: This is the first characterized case in the literature on the involvement of gemfibrozil in poor management of dyslipidemia.

Keywords: Gemfibrozil; dyslipidemia; triglycerides; total cholesterol; hypertension; low-fat diet.

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1. INTRODUCTION

Gemfibrozil (5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoic acid) is an organic compound used as a medication in management of the elevated lipid levels in the blood. Its main intended use is to decrease the concentrations of the triglycerides, the very low density lipoproteins (VLDL), the low density lipoproteins (LDL), and to increase the high density lipoproteins (HDL; good). Gemfibrozil is widely recommended and used in the general clinical practices despite the many recommended precautions. The gemfibrozil mechanisms of action are not completely understood but it is believed that it interferes preferentially in many biochemical processes; production of apolipoprotein-B that is responsible for carrying VLDL, fatty acids uptake by the liver, hepatic VLDL release, lipoprotein triglyceride lipolysis, activation of peroxisome proliferator-activated receptor alpha that is involved in fat metabolism. These interferences enhances many desirable processes; conversion of lipids to energy and other products, decomposition of chylomicrons, conversion of VLDL to LDL, conversion of LDL to HDL, and dumping of lipids into the intestine, which all ultimately lead to a lower blood lipid concentration [1]. In addition to that, numerous studies presented evidences about its potential benefits to correct many other human disorders [2].

Increased cholesterol and triglyceride plasma concentration is a main cause of hypertension and other serious health complications which is one of the common chronic diseases among patients in the primary health care programs [3] that cost money, time, and efforts in the health management program. There are many risk factors for the primary (essential) hypertension like age, obesity, and dyslipidemia, which accounts for majority of the cases. The secondary hypertension might be due to some drugs, kidney disorders, endocrine diseases, and cancer. To diagnose an individual with hypertension it is advisable to document high blood pressure values (blood pressure equal or above 140/90mmHg) for five consecutive days. The potential reasons may be identified by inspecting the personal history and analyzing many biochemical parameters. At early stage, the primary hypertension may be cured completely by adjusting the lifestyle however failure to manage necessitates the addition of one or more medications.

Taking into consideration the patient's history and several high blood pressure readings many biochemical parameters may be inspected depending on the initial primary evaluation of the case; the triglycerides, the total cholesterol, the low density lipoproteins (LDL), the high density lipoproteins (HDL), the thyroid hormones, the kidney function tests, some of the plasma ions, the urine analysis, the complete blood count (CBC), the fasting blood sugar (FBS), and the glycosylate hemoglobin (HbA1c) [4,5]. Upon suspecting a secondary hypertension or a complicated medical condition more specific analyses and examinations are requested at the more-related medical department. In most hypertension cases that we examine and treat the high blood pressure is controlled and lowered using one or combined anti-hypertension drugs. We noticed that the more challenging cases always arise when a patient has higher concentration of plasma lipids than normal. In such cases, lipids lowering medications are prescribed, which eventually support the management of the hypertension successfully.

2. CASE

A 53 years old woman was presented to our clinic for a general checkup especially for the lipids and her main complaint was a feeling of an increase in the blood pressure, which she felt it in her eyes and the upper part of her skull according to her description. She was 166cm height and weighed 75 kg; her body mass index (BMI) was 27.2 kg/m², which classified her as an overweight person. She wasn't a smoker, wasn't alcohol drinker, and used to drink coffee two to three times a day (quantitatively 100-150 ml each). While resting, the blood pressure measurement reading was 155/97 (systolic / diastolic), which indicated that she had a slightly elevated blood pressure in that visit. She illustrated that this feeling became more frequent and more persistent in the last month. In the last week she mentioned that a neighbor measured her blood pressure and the readings were close to that recorded in the clinic. In the consecutive three days her blood pressure readings after overnight (12-hours) fasting were in the same range.

The patient's history was obtained on the first attendance. Nine months ago the patient had high plasma triglycerides and total cholesterol and her blood pressure readings were fluctuating upper the normal limit (there wasn't access to the exact readings). She was given oral medications;

atorvastatin (20 mg/day at night), and gemfibrozil (600 mg/day in the morning). She described, quickly by time the blood pressure became within the normal range and the lipids improved only over a period of three months. She continued these medications but one month ago she experienced annoying headache and high blood pressure despite the strict commitment to the daily drug dose. She acted independently and treated herself by paracetamol (2 x 500 mg) to get rid of the headache. The same feelings continued and arose frequently which pushed her to seek a medical advice; her first attendance to the clinic. Her case was interesting and needed in-depth investigation and the details of her treatment are presented in the discussion section.

3. DISCUSSION

The elementary blood analysis was performed after overnight (12-hours) fasting and the results are presented in Table 1. The blood glucose and the glycosylated (glycated) hemoglobin data are slightly above the normal range and indicated that she was pre-diabetic. Primarily, she was advised to decrease the consumption of carbohydrate-rich food items, all kinds of deserts, and to decrease the consumption of table sugar and replace it with a natural low-calorie sweetener, if available. The results also indicated elevated plasma lipids, sodium, and chloride concentrations while low potassium and magnesium concentrations. The values in Table 1 were consistent with the dyslipidemia and the high blood pressure readings and suggested two probabilities. The patient did not take her medications regularly and/or she had an unbalanced dietary regimen [6,7]. The patient ascertained that she took her medications every day on the same time and didn't miss any dose. Therefore, primarily it was necessary to examine her average food intake for any suspicious contributor.

While discussing any possible causes behind the uncontrolled lipids concentrations and the development of the fluctuating hypertension, the patient noticed a very crucial point, her appetite for fried food items, chocolates, deserts, snacks, and nuts increased noticeably after she started taking the triglycerides and the cholesterol medications. Her family income allowed to fulfill her desires. Investigating her recent consumption of food per week revealed that she had an unbalanced mix of food types and sources. She consumed nearly 1500 g/week of fast food

chicken meals, 500 g/week of lamb and goat meat, one 300 g/week of a fried fish-based meal, about 500 mg of salted mixed nuts per week, and two fried eggs/day while her consumption of cooked vegetables and salads was minor and negligible. The patient illustrated that she consumed the chicken, the lamb, and the goat meats without taking off the white tissues. All these meals are noticeable sources of triglycerides and cholesterol and other steroids. Aging and the high lipid food sources are main factors in decreasing the vascular flexibility and promoting the water retention and consequently the development of the chronic hypertension despite of using the medications [8].

The regular consumption of coffee is well-known to contribute in raising the systolic and the diastolic blood pressure components. In addition to that the patient was not a worker, lived a sedentary lifestyle, and involved only in the everyday house work duties, which is another factor participated in her persistent dyslipidemia and the development of the hypertension. It is known that the daily programmed exercising is useful in correcting the lipid profile and therefore in decreasing the probability of hypertension and cardiovascular diseases [9].

It was suspected that the nature of her diet, including many lipid-rich food components, is the major cause of her medical condition [10]. Therefore after discussing the strict commitment to a specific dietary intervention, she was given the following instructions to be followed for three months. She was asked to avoid table salt as possible [11], to remove the white parts from the red meat as possible, to decrease the total consumption of the red meat to 200 mg/week (on two to three separate occasions per week), to decrease the chicken consumption to two boneless skinless chicken breasts (boiled or grilled with or without seasoning), to consume a maximum of 100 mg/week of un-salted mixed nuts (not one specific type), to enrich the daily meals with vegetables [12], to decrease the coffee consumption, and to decrease the total eggs consumption to two eggs per week. Also she was asked to decrease the gemfibrozil dose (to 300 mg/day; half a tablet in the morning) while keeping the atorvastatin dose unchanged (20 mg/day in the evening). In addition to that, the patient illustrated that she can buy exercising walking machine, she was instructed to start to train 30 min/day (3 x 10 min/day; the first day) and to increase it to 60 min/day (3 x 20 min/day; in the tenth day up to 90-days) and to try to

maintain this program at gentle walking speed that she can handle.

Her blood pressure was monitored in the clinic every week over a period of twelve weeks while her fasting blood glucose, the glycosylated hemoglobin (HbA1c; %), the plasma triglycerides and the total cholesterol were measure every month over a period of three months. The graph in Fig. 1 illustrates a gradual decrease in both the systolic and the diastolic pressure values and after twelve weeks the reading was 132/81 (with the lipid medications). After three months the patient weighed 69kg (lost 6 kg; BMI= 25 kg/m²), the fasting blood glucose and the HbA1c readings were closer to the ideal normal ranges (97 mg/dL and 5.7%, respectively). On the other hand, the triglycerides, the total cholesterol, sodium, potassium, magnesium, and chloride concentrations improved significantly [13,14].

Also, the patient illustrated that her appetite for the fatty food decreased significantly and she didn't struggle with the diet modification.

Appetite as a desire and the consequential action (eating food) is a result of a complex chemistry in the brain that depends on the concentration and the signaling of many bio-molecules from various parts of the body. In medical practices, it is seen among the patients that appetite may increase or decrease depending on many factors; the hormonal changes, the medical condition, the psychological condition (stress, anger, mode swings), and some drugs. There are strong evidences in the literature that appetite is regulated by specific hormones and affected directly by dietary fat and protein [15,16]. It appears that there are many challenges encounter the research in this area therefore the clinical information about the effect of drugs on

Table 1. The laboratory blood analysis results; the initial and after three months

Test	Normal range	Initial	After 3-months
Glucose (mg/dl)	70-100	109	97
HbA1c (%)	4.0-5.6	6.4	5.7
Triglycerides (mg/dL)	< 150	290	141
Total Cholesterol (mg/dL)	< 200	249	193
Creatinine (µmol/L)	53-97	59	67
Sodium (mmol/L)	136-145	144	139
Potassium (mmol/L)	3.5-5.1	3.5	5.1
Magnesium (mmol/L)	0.66-1.07	0.67	0.99
Calcium (mmol/L)	2.2-2.5	2.3	2.3
Chloride (mmol/L)	95-110	108	98

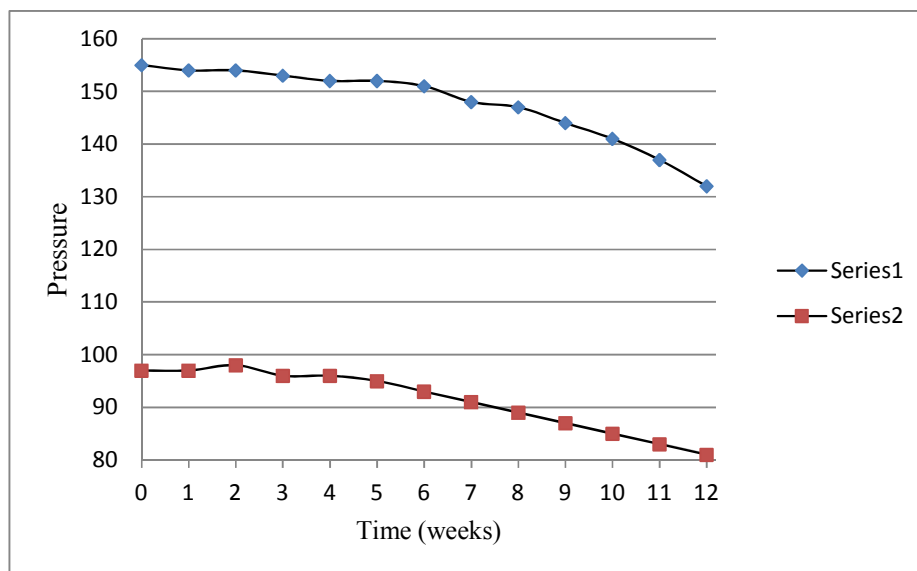


Fig. 1. A graph presenting the change in the pressure components (mmHg); systolic (series 1) and diastolic (series 2) with time (in weeks)

the appetite are rather scattered and not integrating. In the context of the patient's case the medication, gemfibrozil, has not received any considerable attention. We hypothesize that at the beginning gemfibrozil and/or its effect (lower plasma lipid concentration) increased one or more of the appetite hormones which stimulated the appetite toward the fulfilling fatty food items. We believe that, later on in this case, this response merged as a habitual behavior without a careful attention to the amount of the consumed triglycerides and cholesterol [17]. The second hypothesis depends on triggering the fatty food memory-retailed biochemical reactions and the associated brain signaling after decreasing the plasma lipid concentration by the medication which in turn stimulated a mindless compensation by excessive ingestion that happens without full cognitive control of the dietary composition [18].

4. CONCLUSION

Investigating the patient's history and the laboratory analyses revealed that gemfibrozil induced the appetite toward fat-rich food items which opposed the medications intended purpose which indirectly maintained high plasma concentrations of lipids and consequently increased the hypertension significantly. Gemfibrozil dose was decreased from 600 to 300 mg/day, not a common recommended therapeutic dose but was found necessary and reserved a reasonable effectiveness. To lower the plasma lipids the fat content in the diet was decreased largely. It must be explained clearly to the patients that taking anti-lipid medications, despite of probable appetite stimulation, doesn't permit excessive ingestion of fat-rich food items. This is the first evidence in the literature on the association between gemfibrozil and dyslipidemia and development of hypertension.

CONSENT

Written informed consent was obtained from the patient for publication of this Case Report.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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