

Incidence of Statin Induced Diabetes in patient with Hyperlipidemia in Krishna Rajendra Hospital, Mysuru, India

ARMAN ARAB, ADITYA PARASHAR

Department of Pharmacy Practice, Sarada Vilas College of Pharmacy, Mysore, Karnataka, India
Correspondence to Arman Arab, Email: armanarab1986@gmail.com

ABSTRACT

Aim: To carry out a Prospective, Retrospective and Observational study of statin used which induce diabetes in K.R Hospital Mysuru, India and to study of patients with hyperlipidemia, which undergoing statin therapy as anti-cholesterol drug with diabetes mellitus.

Methodology: The investigation was completed for a time of a half year, from September 2017 to March 2018. This study was performed with patients of hyperlipidemia, which undergoing statin therapy as statin drug with diabetes mellitus. All patients meeting the study standard were selected the investigation after obtaining the informed consent. All relevant data of the enrolled patients including demographic details like name, age, gender, body weight, address; clinical data such as diagnosis, laboratory data, past medication history, past history of non-medication adherence and interventions made, co-morbidities, allergy status; therapeutic data such as name of the drug, dose, frequency, route and duration of administration, concurrent medication(s), health care costs, factors influencing noncompliance was collected from various data sources and reported in a reasonably structured information accumulation structure.

Result: In this study assessed the incidence, prevalence, relative risk of hyperlipidemia patient with type 2 diabetes mellitus whose taking statin drug a similar examination among uncovered and non-uncovered gathering. The study observed significant association between the risk factors i.e. statin drugs which are using in the treatment of hyperlipidemia. In this study out of 185 patients 46.48% were male and 53.51% were female. The result shows that rate of occurrence in as high as 98 showing in risk out of 121 patients so of this study was 0.80. Prevalence Measurement of all individuals affected by the disease at a particular timing out of total enroll population, as population at risk so in this study prevalence is 52.972 Incidence is a measure of the probability of occurrence of a given medical condition i.e. diabetes mellitus induced by statin drugs in population. Evolution of risk concept Relative Risk Concept of risk is determining how much risk is associated with any hazards, in relative risk result show that positive correlation of risk calculated relative risk is 4.30 that mean increase risk. Evaluation at statistical significance

Conclusion: In this present study a total number of 185 patients are identified and enrolled according to study procedure and collected all information that are needed for the study from the patient profile and personal interview. In this study result shows that hypothesis of this project is state that there is a relationship and association between diabetes mellitus and statin drugs. This study concludes with that statin which is risk factor for diabetes mellitus of patient with hyperlipidemia, but this is not suggested any way to stop statin drugs or statin drugs are not helpful, but pharmacist play an important role in the calculation of the risk benefit ratio for every patient.

Keywords: Statin, Diabetes mellitus, Hyperlipidemia

INTRODUCTION

Statins are one of the most commonly used drugs in the world base on their potential to prevent adverse cardiovascular events. These cholesterol-bringing down medications got a US sustenance and medication organization cautioning, in February 2012, in regards to expanded danger of episode diabetes and impeded glycemic control in patients who as of now have diabetes. Hypertension is a champion among the most broadly perceived cardiovascular hazard factors in patient with diabetes. It is available in 35% of men and 46% of ladies, and is the reason for 75% of every cardiovascular passing in these patients. In the event that hypertension is ideally controlled, there is potential for a half decrease in the frequency of possibly deadly cardiovascular events¹.

In 90-95% of cases of hypertension, there is no underlying medical disease to cause high blood pressure. this is termed essential hypertension because at one time it was erroneously believed to be an essential compensation

mechanism to maintain adequate circulation. The etiology of essential hypertension is unknown. Genetic factor plays a part as the condition clusters in families with hypertension being twice as common in subjects who have a hypertension parent. Genetic factor account for about one-third of the blood pressure variation between population, although no single gene appears to be responsible except in some rare condition². Hypercholesterolemia and hypertension are as often as possible treated with statin. Statin (HMG-CoA reductase inhibitors) are utilized generally for the treatment of hypercholesterolemia. they restrain HMG-CoA reductase intensely, lessen LDL level more than other cholesterol-bringing down medications and lower triglyceride level in hypertriglyceridemia patients. Statin are very much endured and have a brilliant security record³.

Statins are utilized for essential and auxiliary counteractive action of cardiovascular sicknesses. Different advantages because of statins are not interceded by their lipid bringing properties⁴ but rather due down to its

pleiotropic impacts. In conditions like heart disappointment, cardiovascular arrhythmias, vascular ailment and hypertension the non-lipid bringing down pleiotropic advantages of statins have been observed⁵. These pleiotropic impacts interceded by statins can be because of hindrance of isoprenoid combination which thus restrains intracellular flagging atoms Rho, Rac and Cdc42. The prevalent instrument that has been proposed is restraint of Rho and its actuation to Rho kinase⁶.

Type 2 diabetes is characterized by hyperglycemia, insulin resistance and insulin deficiency. The insulin resistance contributes to the abnormal lipid profile associated with type 2 diabetes⁷. Dyslipidemia contributes to increased cardiovascular events in patients with type 2 diabetes⁸. A straight relationship exists between cholesterol levels and cardiovascular maladies in diabetics regardless of whether we overlook the gauge LDL⁹. By prevalently bringing LDL-Cholesterol and due down to minor impacts on different lipoproteins, statins seem, by all accounts, to be beneficial⁹. In Heart Protection Study which was done in diabetics, the decline in cardiovascular occasions like first real coronary occasion, stroke was to the tune of 22% when contrasted with placebo¹⁰. It was prescribed by American Diabetes Association that statin treatment ought to be started in people with diabetes and other cardiovascular hazard factors with target LDL cholesterol of 100 mg/dL¹¹. Examiners are likewise of the sentiment that statin treatment ought to depend not on the LDL levels but rather the cardiovascular inconveniences going with diabetes¹². Different investigations which demonstrated decreased coronary occasions with statins in patients with diabetes mellitus are Cholesterol and Recurrent Events and Long-term Intervention with Pravastatin in Ischemic Disease examinations of pravastatin^{13,14}.

MATERIALS AND METHODS

study was conducted at department of general Medicine at Krishna Rajendra Hospital, Mysore which is 1330 bedded teaching hospital, and is a one of largest hospital in Mysore, Karnataka. The investigation was completed for a time of a half year, from September 2017 to March 2018. This study was performed with patients of hyperlipidemia, which undergoing statin therapy as statin drug with diabetes mellitus. All patients meeting the study standard were selected the investigation after obtaining the informed consent. All relevant data of the enrolled patients including demographic details like name, age, gender, body weight, address; clinical data such as diagnosis, laboratory data, past medication history, past history of non-medication adherence and interventions made, co-morbidities, allergy status; therapeutic data such as name of the drug, dose, frequency, route and duration of administration, concurrent medication(s), health care costs, factors influencing noncompliance was collected from various data sources and reported in a reasonably structured information gathering structure. For the incidence, prevalence, relative risk, attributable risk and odd ratio we applied direct formula on collected data by the framed patient consent forms data collection form. data first categorized in category by disease status, for statistical status I applied chi square test.

RESULT AND DISCUSION

In this study assessed the incidence, prevalence, relative risk of hyperlipidemia patient with type 2 diabetes mellitus whose taking statin drug a comparative study among uncovered and non-uncovered gathering. The examination watched noteworthy relationship between the hazard factors for example statin drugs which are utilizing in the treatment of hyperlipidemia. In this investigation out of 185 patients 46.48% were male and 53.51% were female. the patient data is slight dominance of female over male, also the majority population of study belongs to age group 50-70 years (56.75%) and 21.62% of patient.

Statin is as medicine which also called 3-hydroxy-3-methylglutaryl coenzyme A (HMG COA) reductase inhibitor. these medicines act by block an important step in the production of LDL cholesterol in the liver organ and thus cause reduction in the level of LDL cholesterol. Statin also decrease inflammation and taken care health of lining of the arteries. Statins are most commonly used for treatment high LDL cholesterol. The investigation watched noteworthy relationship between the hazard factors for example statin drugs which are using in the treatment of hyperlipidemia. Statin is as medicine which also called 3-hydroxy-3-methylglutaryl coenzyme A (HMG COA) reductase inhibitor. These medicines act by block an important step in the production of LDL cholesterol in the liver organ and thus cause reduction in the level of LDL cholesterol. Statin also decrease inflammation and health of the lining of the arteries. the statin most commonly used for treatment high LDL cholesterol. The procedure of diabetogenesis instrument with statin treatment are hazy, yet deformity insulin affectability and traded off β cell work through increment intracellular cholesterol take-up because of hindrance of intracellular cholesterol amalgamation by statin, just as other system might be included. The statin drugs (atorvastatin, rosuvastatin, simvastatin, fluvastatin) was most recommended medication among all statin drugs.

About the statin habit of patients more number of male patient 49(26.48%) with chowing tobacco, female patient 25(13.51%) having this social habit. out of total enrolment 10.21% are alcoholic, 17.29% are smokers, 11.89% are having other social habits. whose as 60% patient have any social habits. Enrolment in the different categories of disease are in hyperlipidemia with type 2 diabetes mellitus have highest 98(52.97) enrolment, 23(12.43%) have hyperlipidemia, 43(23.24%) have type 2 diabetes mellitus and 21(11.35) patient with hypertension. The results show that the 53(28.64%) patient have some co-morbidities condition like thyroid, cancer, anemia like disease and 132(71.35%) patient doesn't have any other co morbid condition other than study criteria.

Assessment of result for the Incidence, Prevalence, Relative risk we applied direct formula on collected data by the prepared patient consent forms cum data collection form. Data first categorized in different categories by enrollment, gender, disease status etc., for statistical significance applied chi square test, hypothesis testing tool. **Evaluation of incidence and prevalence** Incidence: The result shows that rate of occurrence in as high as 98 showing in risk out of 121 patients so of this study was 0.80.

Prevalence Measurement of all individuals affected by the disease at a particular timing out of total enroll population, as population at risk so in this study prevalence is 52.972 Incidence is a measure of the probability of occurrence of a given medical condition i.e. diabetes mellitus induced by statin drugs in population (hospital patient with specified period of time (6 months) (Table 2)

Evolution of risk concept Relative Risk Concept of risk is determining how much risk is associated with any hazards, in relative risk result show that positive correlation of risk calculated relative risk is 4.30 that mean increase risk (Table).3

Attributable risk The cases attributable and avoidable to this exposure in relation to all cases.so result show that calculated attributable is 17.05 that show the occurrence of the disease on exposure status.

Odd ratio The result show that odd ratio of study was 2. 080.thisdemonstrate that relationship between an introduction and a result .it higher the 1 odd ratio shows that control is better than intervention.

Evaluation at statistical significance The observed frequencies are those observed in the sample and the expected frequencies are calculated by chi square test and result shows that null hypothesis is rejected due to calculated value (4.403) is higher than tabulated (chi squire table) value 3. 874.that is based the degree of freedom. It clearly shows that the attributes statin drugs and type 2 diabetes mellitus are not independent (Fig. 1).

Table 1: Details of gender and disease distribution of patients

Disease	Male	Female	Total
Hyperlipidemia with Type II Diabetes Miletus	47	51	98
Hyperlipidemia	8	15	23
Type II Diabetes Miletus	19	24	43
Hypertension	12	9	21
Total	86	99	185

Fig. 1: Chi square test

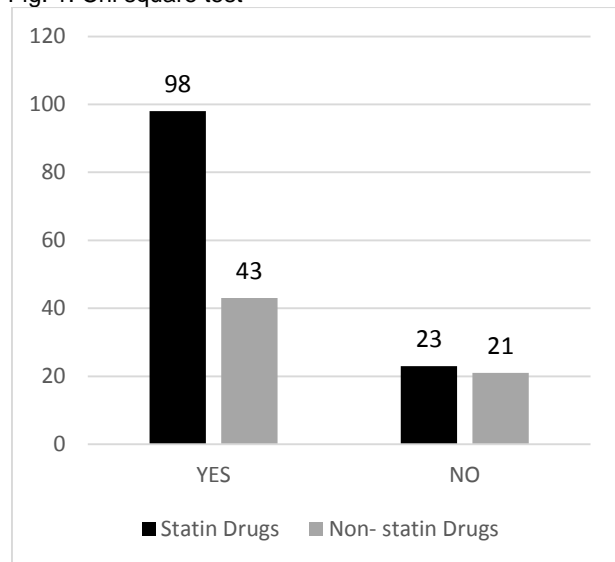


Table 2: Details of Incidence and Prevalence disease:

Gender	Incidence	Incidence Rate	Prevalence
Male	9	16.36%	54(96% CI 51.91-57.38)
Female	14	21.21%	51.51(95% CI 48.51-54.08)
Total	23	19.00%	52.97 (95% CI 50.33-55.61)

Table 3: Relative risk and Attributable risk

TYPE II Diabetes Mellitus	Yes	No	Total
Statin Drugs	98	23	121
Non- statin Drugs	43	21	64
Total	141	44	185

CONCLUSION

Diabetes mellitus, disorder of carbohydrates metabolism, due to impaired ability of pancreas cell to produce sufficient insulin to response sugar to maintain proper dimension of glucose in the blood. Diabetes mellitus is a champion among the most generally perceived metabolic issue.it has public health importance in all over world. But as India has become a capital of diabetes, it shows a blur picture of our healthcare, which is as my topic for this project is a discussed with a risk factors to develop diabetes mellitus in the patient who have hyperlipidemia and also taking any statin drugs. This study supports the theory that statin causes diabetes by altering glucose homeostasis. Actually glucose is most important signal for insulin release but during the cholesterol synthesis so many other metabolites (Isoprenoid, Farnesyle pyrophosphate and Ubiquinone) also release from cholesterol synthesis that are affect insulin secretion as action adversely. In this present study a total number of 185 patients are identified and enrolled according to study procedure and collected all information that are needed for the study from the patient profile and personal interview. In this study result shows that hypothesis of this project is state that there is a relationship and association between diabetes mellitus and statin drugs. This study concludes with that statin which is risk factor for diabetes mellitus of patient with hyperlipidemia, but this is not suggested any way to stop statin drugs or statin drugs are not helpful, but pharmacist play an important role in the calculation of the risk benefit ratio for every patient. Diabetes mellitus, disarranges of starches digestion, because of disabled capacity of pancreas cell to deliver adequate insulin to reaction sugar to keep up legitimate dimension of glucose in the blood. Diabetes mellitus is a champion among the most generally perceived metabolic issue. it has general wellbeing significance in all over world. But as India has become a capital of diabetes, it shows a blur picture of our healthcare, which's as my topic for this project is a discussed with a risk factors to develop diabetes mellitus in the patient who have hyperlipidemia and also taking any statin drugs. I have already discussed this All in detail in the project study. This study supports the theory that statin causes diabetes by altering glucose homeostasis.

REFERENCES

1. David J. Maron, Sergio Fazio, MacRae F. Linton. Current Perspectives on Statins, *Circulation*. 2000; 101:207-213.
2. Roger walker, Churchill Livingstone elsevier, clinical pharmacy and therapeutic. 2012; 295,389,686
3. Ruggenenti, P., Perticucci, E., Cravedi, P., Gambarà, V., Costantini, M., Sharma, S. K., & Remuzzi, G. (2008). Role of remission clinics in the longitudinal treatment of CKD. *Journal of the American Society of Nephrology*, 19(6), 1213-1224.
4. Wang, C. Y., Liu, P. Y., & Liao, J. K. (2008). Pleiotropic effects of statin therapy: molecular mechanisms and clinical results. *Trends in molecular medicine*, 14(1), 37-44.
5. Mihos, C. G., Pineda, A. M., & Santana, O. (2014). Cardiovascular effects of statins, beyond lipid-lowering properties. *Pharmacological research*, 88, 12-19.
6. Zhou, Q., & Liao, J. K. (2010). Pleiotropic effects of statins. *Circulation Journal*, 74(5), 818-826.
7. Adiels, M., Olofsson, S. O., Taskinen, M. R., & Borén, J. (2008). Overproduction of very low-density lipoproteins is the hallmark of the dyslipidemia in the metabolic syndrome. *Arteriosclerosis, thrombosis, and vascular biology*, 28(7), 1225-1236.
8. Brunzell, J. D., Davidson, M., Furberg, C. D., Goldberg, R. B., Howard, B. V., Stein, J. H., & Witztum, J. L. (2008). Lipoprotein management in patients with cardiometabolic risk: consensus statement from the American Diabetes Association and the American College of Cardiology Foundation. *Diabetes care*, 31(4), 811-822.
9. Stamler, J., Vaccaro, O., Neaton, J. D., Wentworth, D., & Multiple Risk Factor Intervention Trial Research Group. (1993). Diabetes, other risk factors, and 12-yr cardiovascular mortality for men screened in the Multiple Risk Factor Intervention Trial. *Diabetes care*, 16(2), 434-444.
10. Heart Protection Study Collaborative Group. (2003). MRC/BHF Heart Protection Study of cholesterol-lowering with simvastatin in 5963 people with diabetes: a randomised placebo-controlled trial. *The Lancet*, 361(9374), 2005-2016.
11. American Diabetes Association. (2004). Dyslipidemia management in adults with diabetes. *Diabetes care*, 27(suppl 1), s68-s71.
12. Eldor, R., & Raz, I. (2009). American Diabetes Association indications for statins in diabetes: is there evidence? *Diabetes care*, 32(suppl 2), S384-S391.
13. Lewis, S. J., Sacks, F. M., Mitchell, J. S., East, C., Glasser, S., Kell, S., & Pfeffer, M. A. (1998). Effect of pravastatin on cardiovascular events in women after myocardial infarction: the cholesterol and recurrent events (CARE) trial. *Journal of the American College of Cardiology*, 32(1), 140-146.
14. Keech, A., Colquhoun, D., Best, J., Kirby, A., Simes, R. J., Hunt, D., ... & Tonkin, A. (2003). Secondary prevention of cardiovascular events with long-term pravastatin in patients with diabetes or impaired fasting glucose: results from the LIPID trial. *Diabetes care*, 26(10), 2713-2721.