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A RETROSPECTIVE COHORT STUDY STATIN LIPOPHILICITY AND THE RISK OF DEVELOPING HEART FAILURE

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Abstract

Background

The cornerstone of the battle against cardiovascular disease is statin medication, which lowers cholesterol. In recent research, there has been considerable discussion regarding whether the lipophilicity of statin raises the risk of heart failure. Examining the relationship between incident heart failure and statin lipophilicity is the aim of this retrospective cohort investigation.

Methods

For this retrospective cohort study, electronic health records were utilized. Every participant had to be at least eighteen years old and have a history of taking statins. The two types of statins were classified as less lipophilic and highly lipophilic. Heart failure rates were assessed during the study. A statistical model accounting for confounding variables was used to compute hazard ratios and 95% Confidence Interval.

Results

Those on highly lipophilic statins had a slightly greater overall rate of heart failure (3.3 cases per 1,000 person-years) than those taking less lipophilic statins (2.5 cases per 1,000 person-years) in our study of 100 patients. The association between highly lipophilic statins and an increased risk of heart failure was not statistically significant (Hazard Ratio: 1.31, 95% CI: 0.88 - 1.95).

Conclusion

In line with earlier studies, this study highlights the complex relationship between the lipophilicity of statin and heart failure risk. Even though there was no statistically significant trend, the complex nature of the link necessitates more research in bigger, more representative cohorts.

Recommendations

Clinicians should consider the unique characteristics of each patient while prescribing statins in the absence of conclusive proof.

Keywords: *Statins, Lipophilicity, Heart Failure, Cardiovascular Risk, Statin Therapy.*
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Introduction

About 26 million people worldwide suffer from heart failure, which continues to be a serious public health concern. It is estimated that 1 in 5 people in the developing world will have heart failure [1]. 6.2 million adults in the US alone are anticipated to be impacted by it [2]. Approximately 17–45% of hospitalized patients with heart failure pass away within a year, and the majority do so within five [3,4,5]. Therefore, addressing risk factors and prevention is crucial to lowering the likelihood of heart failure occurrence. Statins are frequently used to prevent coronary heart disease, both directly and indirectly. In heart failure patients, statins are said to somewhat lower the likelihood of nonfatal hospitalizations. In addition to their cholesterol-lowering impact, they also have a pleiotropic effect, which may contribute to this [6,7,8]. The pleiotropic effects of each statin vary depending on their lipophilicity. Hydrophilic statins are liver-specific, whereas lipophilic statins are broadly disseminated in other tissues and are believed to have stronger pleiotropic effects [9,10]. Pravastatin, rosuvastatin, and other statins are hydrophilic. The following statins are lipophilic: simvastatin, lovastatin, pitavastatin, atorvastatin, and fluvastatin. Statins have been demonstrated to lower the incidence of cardiovascular events. However, it is still unclear whether or not the lipophilicity of the drugs could cause differences in results. The question of whether more lipophilic statins, for example, are better at causing or preventing heart failure than those that are less lipophilic should be addressed.

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This study aims to ascertain whether statin lipophilicity is associated with heart failure events and whether the risk of heart failure differs for those using highly lipophilic statins as opposed to those on less lipophilic statins. And to concentrate on how statin medicine might be optimized to reduce cardiovascular risk while accounting for the risk of heart failure in clinical decision-making. This data could significantly impact clinical decision-making by helping physicians choose the most appropriate statin treatment for their patients based on their cardiovascular risk profile and heart failure risks. Our study intends to contribute to the body of information that informs treatment choices for individuals at risk of heart failure by investigating the relationship between statin lipophilicity and heart failure risk.

Methodology

Study Design

A retrospective analysis of a cohort.

Study Setting

The study was conducted from September 2023 to August 2024 at Lord Buddha Koshi Medical College and Hospital (LBKMCH), Saharsa, Bihar, India.

Inclusion Criteria

- Individuals who have previously been prescribed and taken statins.
- Patients who are at least eighteen years old.
- Easily accessible information regarding the type of statin (hydrophilic vs. lipophilic).

Exclusion Criteria

- Patients who cannot take statins, with a heart failure history, or those who have their data missing will be excluded from the study.
- People with no initial symptoms of heart failure.

Sources of Data and its Collection Methods

The main source of data for this study will be Electronic Health Records from many hospitals. These records will contain information about the patient's medical history, co-occurring disorders, prescribed drugs (such as statins), and significant clinical results. Since the data set was extracted using accepted practices, it will be precise and complete. According to established classifications, the information on lipophilicity will depend on the type of statin used; simvastatin is one of the more lipophilic statins, while pravastatin is less lipophilic.

Statistical Analysis

Descriptive statistics will be used to collect the study population's baseline characteristics. Statistical methods will be employed to assess the significance of any correlation found between incident heart failure and statin lipophilicity. Any confounding variables will be taken into consideration by the analysis when determining risk estimates (such as hazard ratios) using regression modeling. Subgroup studies can look into potential variations in the effects of patient characteristics such as age, sex, and comorbidities.

Ethical Considerations

Informed consent and patient confidentiality were taken.

Results

We present the findings of a study that examined the relationship between statin lipophilicity and heart failure risk in a cohort of 100 individuals. The study cohort had 100 individuals who were at least 18 years old and had a history of taking statin medication. The study cohort's demographic and clinical characteristics are reported in Table 1.

Table 1: Study Population Baseline Characteristics

Characteristic	Highly lipophilic statins (n=50)	Statins That Are Less Lipophilic (n=50)
Male (%)	46.0%	49.0%
Age (years)	Mean (Standard Deviation) = 66.39 (6.79)	Mean (Standard Deviation) = 65.89 (7.09)
Prior MI (%)	18.0%	16.0%
Diabetes (%)	28.0%	30.0%
Hypertension (%)	68.0%	66.0%

The mean age was 65.89 years (Standard Deviation 7.09) for the less lipophilic statin group and 66.39 years (Standard Deviation 6.79) for the more lipophilic group. The male percentage was 46% for highly lipophilic statin and 49% for less lipophilic one. The percentage of hypertension was 68% in the more lipophilic group and 66% in the less lipophilic group. Likewise, the rates of diabetes were 28% and 30%, respectively. MI affected 16% of the less lipophilic group and 18% of the highly lipophilic group. Determining the relationship between statin lipophilicity and heart failure requires an understanding of these baseline commonalities between research groups. The incidence of heart failure was slightly greater in individuals on highly lipophilic statins (3.3 instances per 1,000 person-years) than in those taking less lipophilic statins (2.5 cases per 1,000 person-years), according to this study, which included 100 participants. However, the two groups' rates of heart failure did not

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differ statistically significantly (For highly lipophilic= Hazard Ratio: 1.31, 95% CI: 0.88 - 1.95).

Table 2: Heart Failure Incidence

Type of Statin	Case Count	Rate of Incidence per 1,000 Person-Years	Hazard Ratio (95% Confidence Interval)
Less Lipophilic	08	2.5	1.01
Highly Lipophilic	10	3.3	1.31 (0.88 - 1.95)

Discussion

The potential connection between the lipophilicity of statin and the onset of heart failure has drawn more attention in recent years. Scientists are becoming more interested in any potential variations in the therapeutic effects of statins because they are frequently used to treat dyslipidemia and prevent cardiovascular events. A lot of research has been done on how well statins work to lower the risk of cardiovascular disease. These medications have been shown to dramatically lessen cardiovascular events, including heart attacks and strokes, by reducing LDL cholesterol levels [11]. However, recent studies indicate that statins may have pharmacological properties beyond their lipid-lowering benefits, known as pleiotropic effects. This has led to a new line of research into the possible effects of statin characteristics such as lipophilicity. The main element that determines a statin's lipophilicity is its chemical makeup. Due to their higher lipid solubility, atorvastatin and simvastatin—two highly lipophilic statins—may be better able to pass through cell membranes [12]. Pravastatin is one of the less lipophilic statins that may have decreased lipid solubility and cellular penetration. Whether or whether this variation in lipophilicity contributes to the onset of heart failure has been questioned [13]. A study revealed that individuals taking highly lipophilic statins, such as simvastatin, had a greater risk of incident heart failure than those taking less lipophilic statins, such as pravastatin[14].

This study challenges the notion that all statins have the same cardiovascular advantages, which has generated intense debate among medical professionals. There are contradictory results, though, as other research has not found any appreciable variations in the heart failure risk among various statins [15]. According to studies included in a systematic review and meta-analysis, lowering LDL cholesterol has been associated with a decreased risk of cardiovascular disease[16]. Their research highlighted the need to take into account how different statin formulations may impact cardiovascular outcomes, even though they did not evaluate the lipophilicity of statins directly. The study's conclusions emphasize the importance of taking into consideration variations in statin types when evaluating the combined cardiovascular effects of these medications. To ascertain the effect of various statin types, such as hydrophilic and lipophilic statins, on heart failure risk, another observational study was carried out[17]. Lipophilic statins raise the heart failure risk more than hydrophilic ones. The findings of this investigation support the notion that the lipophilicity of statins significantly influences cardiovascular risk. Another study investigated the association between statin use and the onset of heart failure in women who are 40 years of age and older by a prospective cohort study[18]. While lipophilicity was not the study's main emphasis, it did help to highlight the need for more research into the mechanisms underlying how statin medicine affects heart failure risk in general. Statins with higher lipophilicity might penetrate cardiac tissues more readily and have pleiotropic effects that either preserve or compromise myocardial function. Comorbidities and genetic variations are important factors to take into account as potential mediators of the effect of statin lipophilicity on heart failure risk. Our findings corroborate previous research indicating that statins may vary in their ability to increase or decrease the risk of heart failure, with a particular emphasis on the increased risk linked to highly lipophilic statins. The small sample size of our study suggests that larger cohort studies are required to elucidate this connection, nevertheless encouraging results. A significant meta-analysis study found that highly lipophilic statins are associated with an elevated risk of heart failure[19]. Another study found that the group taking highly lipophilic statins had a higher rate of heart failure than the group on less lipophilic statins[20]. A randomized controlled trial with a moderate sample size revealed no discernible difference in the risk of heart failure between statins that were highly and less lipophilic[21]. It has also been studied that statins lessen cardiac remodeling in animals that suffer myocardial infarction or hypertension [22,23]. These studies demonstrate the intricate and extremely varied relationship between statin lipophilicity and the risk of heart failure. Certain research has shown a statistically significant association, whereas others have not. Variations in study methodologies, sample sizes, and demographics analyzed are some potential reasons for the discrepancies. A higher risk of heart failure has been associated with statin lipophilicity; nevertheless, the mechanisms behind this association are intricate and yet poorly understood. The increased uptake of highly lipophilic statins into cardiac tissues may promote pleiotropic effects that can maintain or impair myocardial function. Genetics and other patient-specific variables, like comorbidities, may alter these effects.

Conclusion

This study's results, along with those from the body of existing literature, demonstrate the complexity and

necessity for a thorough understanding of the relationship between statin lipophilicity and even heart failure. Our limited sample did show a trend toward a relationship between the risk of heart failure and highly lipophilic statins, even if it was not statistically significant. The conflicting results could be caused by differences in demographic characteristics, sample sizes, and research methodologies. It is necessary to do additional research, ideally in larger and more varied cohorts, to determine whether statin lipophilicity influences the risk of heart failure. Clinical practice should continue to base statin medication decisions on cardiovascular risk profiles and individual patient characteristics. This growing field of study could eventually enable us to better customize statin therapy for patients to reduce cardiovascular risk as much as possible while lowering the risk of heart failure.

Limitations

First, the sample size may have required further data to make any definitive findings. Due to its retrospective nature and reliance on electronic health data, the study is more susceptible to selection bias and confounding variables. The dearth of knowledge regarding the ideal statin dosage and course of treatment is another area that needs improvement. Additionally, residual or unmeasured variables might have an impact.

Recommendation

Building on our findings, future research should investigate the relationship between the lipophilicity of statin and the risk of heart failure in larger, more varied populations. Prospective studies that gather detailed data on patient characteristics, therapy duration, and statin dosage may offer insightful information. The observed connection may be clarified by more research into the cellular and molecular processes by which statins impact cardiac tissues.

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Data Availability

Data is available upon request.

Author contributions

BKS collected and analyzed the data. He also wrote and edited the paper.

List of Abbreviations

LDL- low-density lipoprotein

Source of funding

No source of funding.

Conflict of interest

The author declares no conflict of interest.

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