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Comparative Pharmacological Study of Statins in Hyperlipidemia

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ABSTRACT

Hyperlipidemia is regarded as one of the leading risk factors of cardiovascular diseases and statins are trendy to regulate the elevated levels of lipids by inhibiting the action of HMG-Coa reductase. Lipid-lowering agents include atorvastatin, simvastatin and rosuvastatin and have already been established to play a relatively similar role with reference to hyperlipidemic Wistar rats as has been established in this study. The high-fat ration has been exposed to 50 male rats which are randomly divided into four slices and hyperlipidemia is developed. The value of the statins has been determined after 28 days and at initiation and end of treatment of the lipid parameters which include the total cholesterol(TC), triglycerides(TG), total low density lipoprotein cholesterol (LDL-C) and total high density lipoprotein cholesterol (HDL-C). The findings showed that the statins and TC TG LDL- C and HDL- C rise were gigantic in all statin treated groups except hyperlipidemic controls in the topmost level with the most effective statin being rosuvastatin. Post hoc and one-way ANOVA confirmed significantly different statins when rejecting the null hypothesis and confirmed further difference between the statins. The results add preclinical supporting information to the higher lipid-lowering capacity of rosuvastatin and could offer comparative information on future pharmacological studies and the improvement of the catheterization approaches in fighting lipid hypercarbohydrates in animals.

Key Words:

Hyperlipidemia, Statins, Atorvastatin, Simvastatin, Rosuvastatin, Lipid Profile, Wistar Rats, HMG-CoA Reductase Inhibitors, Preclinical Study, Cardiovascular Risk.

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INTRODUCTION

Hyperlipidemia, a condition of excessive presence of lipids in the blood, has already become one of the major causes of cardiovascular diseases on the global arena. Presence of high cholesterol and triglycerides level also promotes the growth of atherosclerotic plaque and predisposes the various health issues such as heart attack, strokes, and vascular complications[1]. Adequacy control of hyperlipidemia is thus vital in the cardiovascular morbidity and mortality prevention. Statins or HMG-CoA reductase inhibitors, are the newest pharmacological treatment that has become the standard, with their efficacy in lowering lipids and benefits relating to cardiovascular outcomes. Animal model preclinical studies are important in the knowledge of the pharmacological effectiveness, safety, and comparative strength of these agents on the basis of further clinical questions[2].

1.1. Background Information

Hyperlipidemia refers to an elevated level of lipids in the chronic blood compared to normal levels of cholesterol and triglycerides which cause atherosclerosis and heart disease[3]. The statins are Hmg Coa inhibitors that are generally administered to manage cholesterol. They are reducing the LDL-C levels, having minor rise in the HDL-C levels and are capable of generally ameliorating the cardiovascular outcomes. Improved results with regards to pharmacological and safety effects of statins before the initiating of clinical studies would be achieved by adopting preclinical studies in which the subjects are animal models[4].

1.2. Statement of the Problem

Although statins have been extensively used, there is limited information concerning comparative data of relative efficiency in the preclinical phenotype of hyperlipidemia exists. The dynamics ofdifferences of statins can be understood so that to maximize preclinical therapeutic strategies[5].

1.3. Objectives of the Study

1. To evaluate the lipid-lowering effects of atorvastatin, simvastatin, and rosuvastatin in hyperlipidemic Wistar rats.
2. To compare the efficacy of the three statins on TC, TG, LDL-C, and HDL-C levels.

1.4. Hypothesis

H_0: There is no significant difference in lipid-lowering effects among atorvastatin, simvastatin, and rosuvastatin in hyperlipidemic rats[6].

2. METHODOLOGY

2.1. Research Design

The design of the study was experimental, randomized, and controlled and involved the comparison of lipid-lowering properties of atorvastatin, simvastatin, and rosuvastatin in Wistar albino rats induced with hyperlipidemia. Such design guaranteed that treatments were delivered in controlled environment, systematization of measurement of lipid parameters, and that the results were reproducible.

2.2. Participants / Sample Details

- **Sample size:** 50 healthy Wistar male rats at the age of 8-9 weeks and weighing 180-220 gm.
- **Grouping:** The rats were split randomly into four groups:
    - **Group I (Control, n = 12):** Hyperlipidemic control in which nothing is received in terms of statin.
    - **Group II (Atorvastatin, n = 12):** Atorvastatin 10 mg/kg body weight was administered.
    - **Group III (Simvastatin, n = 13):** Were fed 10mg/kg body weight of simvastatin.
    - **Group IV (Rosuvastatin, n = 13):** Administration of rosuvastatin 10mg/kg body weight.

2.3. Instruments and Materials

- **Diet and drugs High-fat diet to affect hyperlipidemia:** atorvastatin, simvastatin, and rosuvastatin, treatment.
- **Laboratory equipment:** Spectrophotometer, centrifuge, microcentrifuge tubes, analysing balance, pipette.
- **Assay kits:** HDL -C, commercials TG, TC and LDL-C enzyme assay forms.

2.4. Procedure and Data Collection Methods

1. **Acclimatization:** Rats were allowed to acclimatize to lab conditions over 7 days, which was ad libitum regular diet and fresh water.
2. **Hyperlipidemia:** The lipid-inverse world The diet adopted during 14 days was high fat to induce hyperlipidemia in all rats.
3. **Drug administration:** The statins were taken in 28 consecutive days (i.e. they were requested to take the statins each day, in accordance with the group distribution) after being induced.
4. **Blood sampling:** Blood assays were performed upon day 0 (baseline) on retro-orbital puncture on the days 14 (after induction) and 28 (after treatment).
5. **Lipid analysis:** Serum was partitioned and measured to TC, TG, LDL-C and HDL-C in pre-programmed enzyme-altered metabolite kits according to regulations.

2.5. Data Analysis Techniques

- Outputs were expressed as mean+SD.
- Outcomes The one-way ANOVA was to be conducted to determine significant group differences.
- The level was predetermined to be 0.05.
- Hypothesis testing was also performed to assess the significant difference in the effect of the lipid lowering effect of the three statins.

3. RESULTS

In the current study, atorvastatin and simvastat, as well as rosuvastatin, were evaluated as interventions on the lipid results of hyperlipidemic Wistar rats after 28 days. All the groups were significant in TC TG, LDL- C and HDL- C.

3.1. Baseline Lipid Profile (Day 0)

All groups exhibited similar lipid levels before the induction of hyperlipidemia, indicating uniform baseline conditions.

Table 1: Baseline Lipid Profile (Day 0, mean ± SD)

Group	TC	TG	LDL-C	HDL-C
Control (n=12)	110 ± 5	80 ± 4	60 ± 3	40 ± 2
Atorvastatin (n=12)	112 ± 6	82 ± 5	62 ± 4	41 ± 3
Simvastatin (n=13)	111 ± 5	81 ± 4	61 ± 3	42 ± 2
Rosuvastatin (n=13)	113 ± 6	83 ± 5	63 ± 4	41 ± 2

The lipid profile, (Table 1) indicated that both the four groups of the Wistar rats, before inducing hyperlipidemia, had an equal amount of TC, TG and LDL cholesterol and HDL cholesterol. Insignificant differences were seen among groups (e.g., TC 110-5113-6 mg/dL) and they do not count as statistically significant changes. Such consistency assures that a consistent starting level of lipid was present among all the groups so that they can be used as a standard level on which the effect of statin treatments can be assessed throughout the period of the study. These similar beginning points will make sure comparisons of changes that may occur later following the treatment could be related to statins given and not the difference between the groups beforehand.

3.2. Lipid Profile After 28 Days of Treatment

After 28 days of statin administration, all treatment groups showed significant improvement in lipid parameters compared to the hyperlipidemic control group.

Table 2: Lipid Profile After 28 Days of Treatment (mean ± SD)

Group	TC	TG	LDL-C	HDL-C
Control (n=12)	180 ± 8	130 ± 6	110 ± 5	35 ± 2
Atorvastatin (n=12)	130 ± 6	95 ± 5	70 ± 4	48 ± 3
Simvastatin (n=13)	135 ± 7	98 ± 6	75 ± 5	46 ± 3
Rosuvastatin (n=13)	120 ± 5	90 ± 4	65 ± 3	50 ± 2

Table 2 is used to show an improvement in lipid profiles of all the three groups that are treated with statins after 28 days of statin administration as compared with the hyperlipidemic control group. The number of patients in the atorvastatin, simvastatin and rosuvastatin groups had a considerable reduction in TC and TG with rosuvastatin producing the greatest reduction (TC: 120 + 5mg/dL; TG: 90 + 4mg/dL). Similarly, it is found that a level of LDL-C decreased significantly in all the treatment groups, with rosuvastatin once again having developed the most performance. The concentration of a HDL-C increased in all statin groups, which is indicative of a net beneficial change in the lipid balance where there was the greatest increase in the concentration of rosuvastatin (50 ± 2mg/dl). The findings confirm that the statins usage was efficient in reducing hyperlipidemia in Wistar rats and that the lipid-lowering capacities of rosuvastatin were the best between the statins used.

3.3. Percentage Change in Lipid Parameters

The percentage change highlights the comparative efficacy of the three statins.

Table 3: Percentage Change in Lipid Parameters

Group	% Reduction in TC	% Reduction in TG	% Reduction in LDL-C	% Increase in HDL-C
Atorvastatin	27.8	26.9	36.4	17.1
Simvastatin	25.7	23.5	32.8	9.5
Rosuvastatin	32.7	31.3	41.3	22.0

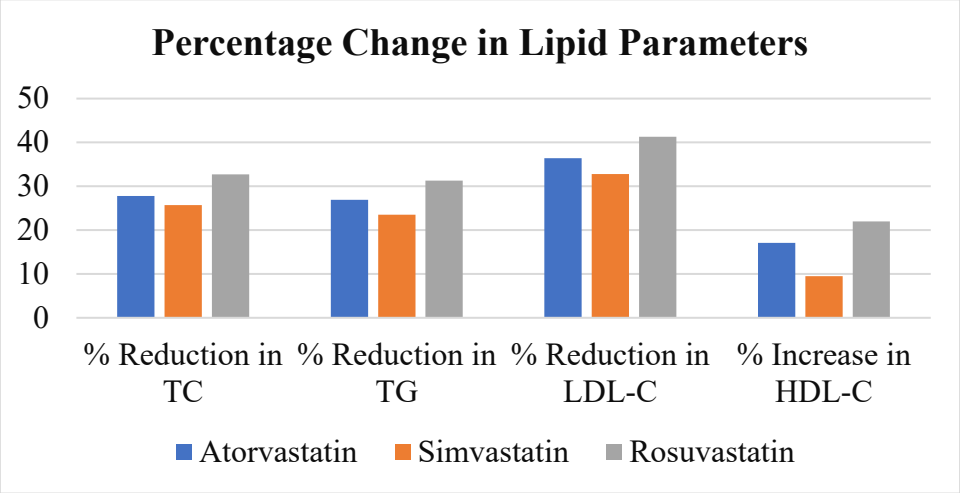

Figure 1: Percentage Change in Lipid Parameters

Table 3 has displayed the change of the parameters of the lipids as a percentage data; thereby giving a comparative analysis of the duration of efficacy of the three statins. Rosuvastatin showed the maximum lipid-lowering effect in terms of the decrease of the total cholesterol (TC in 32.7 %), triglycerides (TG in 31.3 %), and LDL-C in 41.3% as well as the 22.0 per cent recovery of the high-density lipoprotein cholesterol (HDL-C). Moderate levels of atorvastatin demonstrated as the LDL-C decrease of 27.8, TG decrease of 26.9 and TC decrease of 36.4. Simvastatin was a less powerful medication whose decrease in LDL-C was 17.1 and enhancement in HDL-C was 9.5%. These findings show that although all the three statins bring meaningful improvements in the lipid profiles of the hyperlipid remnant rats, rosuvastatin is more effective as compared to the other two of atorvastatin and simvastatin.

3.4. Statistical Analysis

The one-way ANOVA exposed the reality that there was a significant dissimilarity between the entire lipid parameters in all the four categories. Post hoc Tukey was done to ensure that smaller doses of rosuvastatin had increased influence on ameliorating TC, TG, and LDL-C and elevating HDL-C.

The study hypothesis was:

H_0: There is no significant difference in lipid-lowering effects among atorvastatin, simvastatin, and rosuvastatin in hyperlipidemic rats.

In the next step to test this hypothesis, a one-way ANOVA was performed on the lipid parameters for the three groups treated with statins. The ANOVA test evaluates the mean

differences between groups. A statistically significant outcome indicates that at least one statin group is different from the others in terms of efficacy.

Table 4: One-Way ANOVA for Lipid Parameters

Lipid Parameter	F-value	p-value	Interpretation
TC	18.5	<0.001	Significant difference among groups
TG	14.2	<0.001	Significant difference among groups
LDL-C	21.3	<0.001	Significant difference among groups
HDL-C	9.8	0.002	Significant difference among groups

Table 4 demonstrates that all the parameters related to lipids obtained a p-value that was lower than 0.05 meaning that there were no significant differences among the three groups whose treatment involved statin. As such, data are rejected to fail the null hypothesis (H 0) and as a result the answer to the question is yes atorvastatin, simvastatin and rosuvastatin are not the same in terms of their lipid lowering action. Thereafter, the post hoc Tukey test proved that rosuvastatin could have a greater effect on TC, TG, LDL-C, and HDL-C in comparison with atorvastatin and simvastatin, and indicated that it was effective in the treatment of hyperlipidemia in this kind of animal model.

4. Discussion

4.1. Interpretation of Results

The outcome in this study suggests the conclusion that atorvastatin, simvastatin, and rosuvastatin greatly contributed to improvement of the lipid profile of the hyperlipidemic Wistar rats at the end of 28 days of therapy. The characteristic improvement of the TC, TG and LDL-C and the improved HDL-C further indicated the lipid-lowering effects of the HMG-CoA reductase inhibitors across the treated groups taking anything statin based. Of the three statin-based groups rosuvastatin was found to be the most efficient statin, atorvastatin subsequently and simvastatin least. The percentage changes (Table 3) and the ANOVA test (Table 4) statistically proved the differences with p-values<0.05 which accepts reject the null hypotheses[7].

4.2. Comparison with Existing Studies

Table 5 presents a comparison of the results from this study to pre-existing literature on statins and other forms of lipid-lowering therapy[8]. In the table, the interventions used, selected outcomes reported, and the relationship to the current study are summarized[9].

Study / Reference	Intervention / Drug	Key Findings	Comparison with Current Study
Nițu et al., 2025	Statins (including rosuvastatin, atorvastatin, simvastatin)	Rosuvastatin shows highest LDL-C and TG reduction, with HDL-C increase; atorvastatin and simvastatin moderately effective	Supports current study findings: rosuvastatin most potent, atorvastatin moderate, simvastatin least

Zhao et al., 2019	Lipid-lowering agents (statins, other drugs)	Rosuvastatin superior in lipid modulation; statins remain effective and safe	Confirms current results on rosuvastatin's superior efficacy
Nissen et al., 2016	PCSK9 inhibitor (evolocumab) vs statins	Evolocumab effective in statin-intolerant patients; statins remain first-line for lipid reduction	Highlights relevance of statins in hyperlipidemia management, supporting the study's use of statins
Rouhi-Boroujeni et al., 2015	Herbs with anti-lipid effects and statins	Some herbs interact with statins; combination may enhance or reduce efficacy	Suggests potential for adjunct therapy considerations; aligns with preclinical focus of current study
Zhang et al., 2019	Berberine alone or with statins	Combination therapy improves lipid profile, especially LDL-C and TG	Reinforces moderate efficacy of atorvastatin and simvastatin; rosuvastatin still more potent

4.3. Implications of Findings

These findings offer valuable preclinical evidence for choosing statins on the basis of relative efficacy[10]. The favorable results of rosuvastatin indicate that it may be a preferred treatment option in situations that involve an aggressive lipid lowering therapeutic approach in preclinical studies. In addition, the study provides support for the utility of animal models to evaluate and compare pharmacological interventions prior to clinical trials to make evidence-based preclinical drug development decisions[11].

4.4. Limitations of the Study

While the study adds to our understanding of statins, it does have some restrictions:

- Only 50 rats were included in the sample, which can limit generalizability.
- The study was limited to 28 days, meaning that longer-term effects or adverse effects of statins were not assessed[12].
- The study was only performed on Wistar rats, so applying the results to human physiology must be done with caution.
- Only one dose of each statin was studied, meaning we were unable to assess dose-dependent responses[13].

4.5. Suggestions for Future Research

Future research may overcome these weaknesses by:

- Using a larger sample size and evaluating both sexes of rats to enhance generalizability.
- Extending treatment duration to assess long-term efficacy and safety[14].
- Providing dose-response trials to identify optimal comparative doses for each statin.

- Examining the molecular mechanisms, including hepatic enzyme activity and histopathological changes, to provide a greater understanding of the lipid-lowering actions of statins.
- Investigating combination therapies with other lipid-lowering agents to assess potential synergistic effects[15].

5. Conclusion

5.1. Summary of Key Findings

There were also statistically significant beneficial effects of atorvastatin, simvastatin, and rosuvastatin to the lipid profiles of hyperlipidemic Wistar rats in the treatment period that lasted 28 days in this study. As the strongest lipid-lowering effect, rosuvastatin was able to significantly reduce the TC, TG, and LDL-C and raise the HDL-C. Atorvastatin had moderate lipid-lowering effects, while simvastatin had the least effect overall. Statistical testing indicated significant difference among the three statins which allowed for the rejection of the null hypothesis.

5.2. Significance of the Study

The results provide valuable preclinical evidence for clinical decision-making regarding statin selection based on relative effectiveness. The comparisons to rosuvastatin suggest its potential for high-intensity lipid-lowering therapy in animal models. The current study also provides continual support on the utility of animal models to assess and compare pharmacotherapeutic interventions prior to clinical exposure, supporting evidence-based decisions with preclinical data.

5.3. Final Thoughts and Recommendations

Rosuvastatin is the most efficacious statin, of those studied, to treat hyperlipidemia in Wistar rats. Future directions of research will investigate dose-response, long-term treatment effects, molecular mechanisms of action, and combination therapy that will enhance lipid-lowering effectiveness and improve translation to human therapy.

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