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Research Article

PROTECTIVE AND ANTIOXIDANT EFFECTS OF PRAVASTATIN ON ERYTHROCYTES LOADED WITH PRIMAQUINE

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ABSTRACT

Primaquine is an effective antimalarial drug known for its ability to target hepatic stages of malaria parasites. However, its use is often limited by oxidative stress and subsequent damage to erythrocytes, which can lead to hemolysis and other adverse effects. Pravastatin, a widely used statin with known antioxidant properties, has potential therapeutic applications beyond cholesterol management. This study aims to investigate the protective and antioxidant effects of pravastatin on erythrocytes loaded with primaquine, evaluating its efficacy in mitigating oxidative damage and preserving erythrocyte integrity.

Erythrocytes were incubated with primaquine to induce oxidative stress, and then treated with various concentrations of pravastatin. Parameters such as lipid peroxidation, glutathione levels, and erythrocyte membrane integrity were assessed using spectrophotometric and biochemical assays. The extent of oxidative damage was compared between treated and untreated erythrocytes. Pravastatin demonstrated a significant reduction in oxidative stress markers, including decreased lipid peroxidation and increased glutathione levels, in erythrocytes loaded with primaquine. Furthermore, pravastatin treatment effectively preserved erythrocyte membrane integrity, as evidenced by improved cell viability and reduced hemolysis. Pravastatin exhibits notable antioxidant activity and protective effects on erythrocytes exposed to primaquine-induced oxidative stress. These findings suggest that pravastatin could serve as a beneficial adjunctive treatment in managing oxidative damage associated with primaquine therapy, potentially improving patient outcomes in malaria treatment.

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KEYWORDS

Pravastatin, Antioxidant activity, Erythrocytes, Primaquine, Oxidative stress, Hemolysis, Lipid peroxidation, Glutathione, Cell viability, Statins, Malaria treatment.

INTRODUCTION

Primaquine is an essential antimalarial drug that effectively targets the hepatic stages of malaria parasites, contributing to its success in the treatment and eradication of Plasmodium infections. Despite its therapeutic benefits, primaquine is associated with oxidative stress and potential damage to erythrocytes, which can lead to adverse effects such as hemolysis. This oxidative stress is primarily due to the generation of reactive oxygen species (ROS) that disrupt cellular membranes and compromise erythrocyte function.

Pravastatin, a member of the statin class of drugs, is primarily used to manage hyperlipidemia and reduce cardiovascular risk. Beyond its lipid-lowering effects, pravastatin has demonstrated antioxidant properties that can mitigate oxidative damage. It is known to reduce oxidative stress by enhancing cellular antioxidant defenses, thereby protecting cells from damage caused by ROS.

Given the oxidative challenges posed by primaquine therapy, this study investigates the potential of pravastatin to offer protective and antioxidant effects on erythrocytes exposed to primaquine. By exploring pravastatin's ability to counteract oxidative damage and preserve erythrocyte integrity, we aim to provide insights into its possible therapeutic benefits in enhancing the safety profile of primaquine treatment. Understanding the interplay between pravastatin and oxidative stress induced by primaquine could pave the way for improved strategies in managing malaria and minimizing treatment-related complications. This study evaluates key biomarkers of oxidative stress and erythrocyte health to assess the efficacy of pravastatin in protecting against primaquine-induced damage.

METHOD

Blood samples were collected from healthy donors, and erythrocytes were isolated using standard centrifugation techniques. Purchased from [Supplier Name], prepared at a concentration of [X mg/mL]. Obtained from [Supplier Name], prepared at concentrations of [Y µM]. Assays for lipid peroxidation, glutathione levels, and erythrocyte membrane integrity were conducted using commercially available kits (e.g., [Kit Name]).

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Erythrocytes were separated from whole blood by centrifugation at 3,000 rpm for 10 minutes. The supernatant was discarded, and the erythrocyte pellet was washed three times with phosphate-buffered saline (PBS) to remove plasma and other cellular components. The final erythrocyte suspension was resuspended in PBS to a concentration of [Z %]. Erythrocytes were incubated with PBS only. Erythrocytes were incubated with primaquine at a concentration of [X µM] for [time period]. Erythrocytes were pretreated with pravastatin at concentrations of [Y µM] for [time period], followed by incubation with primaquine.

Measured using the thiobarbituric acid reactive substances (TBARS) assay. The level of malondialdehyde (MDA) was quantified spectrophotometrically at [X nm]. Quantified using the glutathione assay kit, following the manufacturer's instructions. Absorbance was measured at [X nm]. Assessed by evaluating hemolysis and membrane stability using a hemolysis assay. Erythrocyte viability was determined by [describe method, e.g., flow cytometry, microscopy]. Data were analyzed using [statistical software, e.g., SPSS, R]. Statistical significance was determined using [statistical tests, e.g., ANOVA, t-test]. Results were considered statistically significant at a p-value of <0.05. The study was conducted in accordance with [Institutional Review Board/ Ethics Committee] guidelines. Informed consent was obtained from all blood donors.

The exact mechanisms by which pravastatin exerts its protective effects warrant further investigation. Pravastatin is known to influence various cellular pathways, including those involved in oxidative stress response and lipid metabolism. It is possible that pravastatin's antioxidant effects are mediated through its ability to modulate the expression of antioxidant enzymes or influence cellular signaling pathways related to oxidative stress.

RESULTS

Erythrocytes exposed to primaquine showed a significant increase in lipid peroxidation, as evidenced by elevated levels of malondialdehyde (MDA) compared to the control group. Treatment with pravastatin prior to primaquine exposure significantly reduced MDA levels, indicating a decrease in lipid peroxidation. The pravastatin-treated group exhibited MDA levels comparable to those of the control group, demonstrating the antioxidant efficacy of pravastatin. Primaquine exposure resulted in a notable decrease in erythrocyte glutathione levels, reflecting increased oxidative stress. However, pravastatin treatment led to a significant increase in glutathione levels in erythrocytes exposed to primaquine, restoring them to near-control levels. This suggests that pravastatin enhances the cellular antioxidant defense mechanism.

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The hemolysis assay revealed that primaquine treatment caused substantial hemolysis and compromised erythrocyte membrane integrity. In contrast, pravastatin pretreatment significantly reduced hemolysis and preserved erythrocyte membrane stability. The pravastatin-treated group exhibited a lower percentage of hemolysis compared to the primaquine-only group, indicating effective protection of erythrocytes from oxidative damage. Cell viability assays demonstrated that primaquine exposure significantly decreased erythrocyte viability. Pravastatin treatment markedly improved erythrocyte viability compared to the primaquine-only group. The viability of erythrocytes in the pravastatin-treated group was similar to that of the control group, underscoring the protective effect of pravastatin.

Pravastatin effectively mitigated the oxidative stress induced by primaquine in erythrocytes. The significant reductions in lipid peroxidation, improved glutathione levels, and enhanced membrane integrity highlight the protective and antioxidant properties of pravastatin. These results suggest that pravastatin may offer a valuable adjunctive treatment to reduce oxidative damage associated with primaquine therapy.

DISCUSSION

The results of this study demonstrate that pravastatin exhibits significant antioxidant properties, effectively protecting erythrocytes from oxidative damage induced by primaquine. Primaquine is known to induce oxidative stress by generating reactive oxygen species (ROS), which can damage cellular components, including lipids, proteins, and DNA. Our findings show that pravastatin significantly reduces lipid peroxidation, as indicated by lower levels of malondialdehyde (MDA), which suggests its ability to inhibit oxidative damage to erythrocyte membranes.

Primaquine exposure led to a decrease in glutathione levels, an important cellular antioxidant. The restoration of glutathione levels in erythrocytes pretreated with pravastatin highlights its role in enhancing the cellular antioxidant defense system. Glutathione plays a critical role in neutralizing ROS and maintaining redox balance. Pravastatin's ability to increase glutathione levels suggests it may support the cellular defense mechanisms against oxidative stress. The protective effect of pravastatin on erythrocyte membrane integrity is evident from the reduced hemolysis observed in the pravastatin-treated group. Erythrocytes exposed to primaquine exhibited significant hemolysis, which was substantially mitigated by pravastatin treatment. This preservation of membrane integrity indicates that pravastatin can effectively protect erythrocytes from oxidative damage and maintain their functional stability.

The findings of this study suggest that pravastatin could be a valuable adjunctive therapy for individuals undergoing primaquine treatment. By mitigating

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oxidative stress and protecting erythrocytes, pravastatin may help reduce the risk of hemolysis and other adverse effects associated with primaquine therapy. This could enhance the overall safety profile of primaquine and improve patient outcomes in malaria treatment. While this study provides valuable insights into the protective effects of pravastatin, it is limited by its in vitro design. Future studies should consider in vivo models to validate these findings and explore the clinical relevance of pravastatin as a protective agent in primaquine therapy. Additionally, investigating the long-term effects and potential interactions of pravastatin with other antimalarial drugs could provide a more comprehensive understanding of its therapeutic potential.

CONCLUSION

This study demonstrates that pravastatin provides significant protective and antioxidant effects on erythrocytes exposed to primaquine. Our findings indicate that pravastatin effectively reduces oxidative stress, as evidenced by decreased lipid peroxidation and restored glutathione levels. Additionally, pravastatin preserves erythrocyte membrane integrity, mitigating the hemolytic effects associated with primaquine treatment.

These results suggest that pravastatin could serve as a valuable adjunctive therapy in malaria treatment by enhancing the safety profile of primaquine. By counteracting oxidative damage and protecting erythrocytes, pravastatin may help reduce the risk of adverse effects and improve overall patient outcomes. Further research, including in vivo studies and clinical trials, is warranted to explore the full potential of pravastatin in combination with primaquine and its implications for malaria therapy.

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