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Post-Marketing Safety Analysis of Nebivolol In Real-World Settings using Bioinformatics and Disproportionality Analysis with FDA Adverse Event Reporting System (FAERS) Data

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INTRODUCTION

Nebivolol, a selective β1-blocker with vasodilatory properties, is widely prescribed for hypertension management. Despite its clinical efficacy, real-world safety data are limited. Post-marketing pharmacovigilance using the FDA Adverse Event Reporting System (FAERS) and bioinformatics approaches can help identify rare or unreported adverse events and elucidate potential molecular mechanisms.

OBJECTIVE

Cardiovascular diseases remain a major global health burden, with nebivolol widely used for managing hypertension. However, real-world evidence on its safety profile is limited. This study investigates post-marketing adverse events associated with nebivolol using data from the FDA Adverse Event Reporting System (FAERS) and bioinformatics tools.

METHOD

A retrospective pharmacovigilance analysis was conducted using FAERS reports. Signal detection metrics included Reporting Odds Ratio (ROR) and Proportional Reporting Ratio (PRR), with thresholds set at PRR $\geq$ 2, ROR $\geq$ 2, and a minimum of 2 reported cases. Additionally, gene and protein interactions were evaluated using the PubMed Gene database and STRING. Molecular docking simulations were performed using PyRX to assess Nebivolol's binding affinities with inflammatory and regulatory proteins.

RESULTS

Among 29,661,136 total FAERS entries, 4,651 adverse event reports were associated with Nebivolol. Signal detection analysis revealed six notable adverse events: epistaxis (134 cases, PRR 2.5) (Fig 1) , melaena (97 cases, PRR 6.004) (Fig 2), sopor (70 cases, PRR 5.895), diplopia (39 cases, PRR 2.165), bradyphrenia (12 cases, PRR 2.306), and pemphigoid (4 cases, PRR 5.03). Molecular docking revealed strong binding affinities between nebivolol and proteins such as IL6 (-8.9 kcal/mol) (Fig 3), IL1B (-9.1 kcal/mol) (Fig 4), and P53 (-8.7 kcal/mol) (Fig 5), , suggesting possible pathways for these adverse effects.

	Drug(s) of interest	All other drugs	Σ
Adverse event(s) of interest	134	41613	41747
All other adverse events	17629	13750822	13768451
Σ	17763	13792435	13810198

Fig 1

	Drug(s) of interest	All other drugs	Σ
Adverse event(s) of interest	97	12464	12561
All other adverse events	17666	13779971	13797637
Σ	17763	13792435	13810198

Fig 2

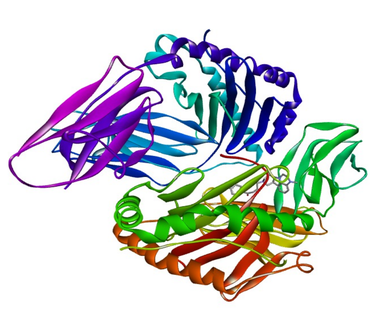

Fig 3

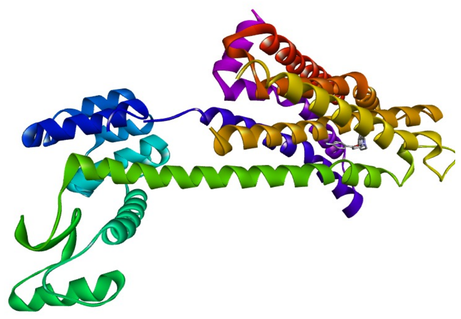

Fig 4

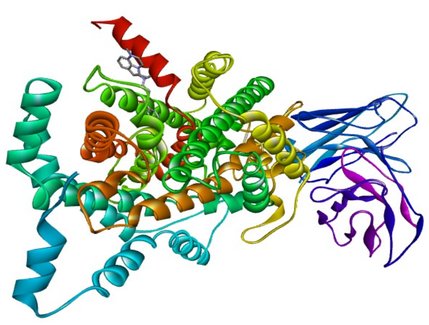

Fig 5

CONCLUSIONS

This real-world post-marketing analysis identified multiple potentially serious adverse reactions to nebivolol, emphasizing the importance of continued pharmacovigilance. The integration of bioinformatics enhances understanding of underlying molecular mechanisms. Further pharmacogenetic studies are warranted to confirm causality and support safer prescribing practices.

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