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Real-World Pharmacovigilance of Metoprolol: A Disproportionality Analysis of Adverse Events using US FDA Adverse Event Reporting System (FAERS) and Bioinformatics

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INTRODUCTION

Metoprolol, a widely used β1-blocker for cardiovascular diseases, requires ongoing post-marketing surveillance to identify rare adverse events. Real-world pharmacovigilance and bioinformatics analyses provide valuable insights into its safety and underlying molecular mechanisms.

OBJECTIVE

Cardiovascular diseases remain a major global health burden, with metoprolol widely used for hypertension management. This study investigates rare or unreported adverse drug reactions (ADRs) of metoprolol through data mining of the FDA Adverse Event Reporting System (FAERS).

METHOD

A retrospective disproportionality analysis was performed using FAERS data. Signal detection algorithms, including Proportional Reporting Ratio (PRR) and Reporting Odds Ratio (ROR), were applied with thresholds of PRR ≥ 2, ROR ≥ 2, and at least 2 reports. Additional investigation of associated genes and proteins was conducted using the PubMed gene database and STRING. Molecular docking studies were performed to evaluate the interaction of metoprolol with identified targets using PyRX, PYMOL, BIOVIA Discovery Studio, and Swiss PDB Viewer.

RESULTS

Among 29,661,136 reactions recorded in FAERS, 32,160 cases were linked to Metoprolol. Signal detection identified three novel adverse events: 36 cases of epicondylitis (PRR 3.62) (Fig 1), 49 cases of areflexia (PRR 2.484) (Fig 2), and 17 cases of solar lentigo (PRR 2.68). Docking studies revealed strong binding affinities between metoprolol and proteins DYSF (PDB ID: 9B8K, docking score -8.8) (Fig 3) and TRP1 (PDB ID: 5M8O, docking score -9.5) (Fig 4) suggesting a plausible molecular basis for the observed events.

	Drug(s) of interest	All other drugs	Σ
Adverse event(s) of interest	36	754	790
All other adverse events	179450	13629958	13809408
Σ	179486	13630712	13810198

Fig 1

	Drug(s) of interest	All other drugs	Σ
Adverse event(s) of interest	49	1498	1547
All other adverse events	179437	13629214	13808651
Σ	179486	13630712	13810198

Fig 2

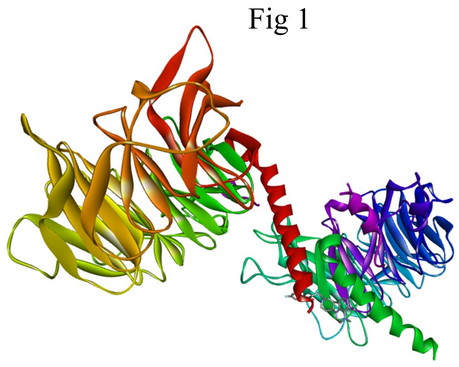

Fig 3

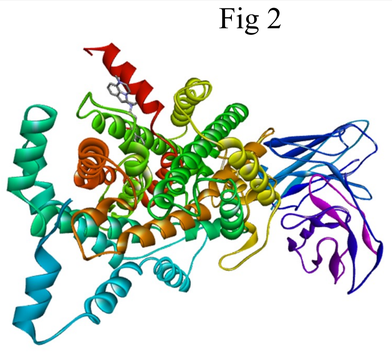

Fig 4

CONCLUSIONS

Post-marketing pharmacovigilance data revealed new safety signals associated with metoprolol that warrant further investigation. The integration of bioinformatics and molecular docking enhances understanding of potential drug-protein interactions. Further pharmacogenetic and pharmacoepidemiological studies are necessary to validate these findings and inform clinical risk mitigation strategies.

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