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Evaluating a Potential Link Between Alprazolam and Intracranial Aneurysm: A Pharmacovigilance and Bioinformatics Approach Through FAERS and Molecular Docking

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INTRODUCTION

Alprazolam, a widely prescribed benzodiazepine, is primarily used for the management of anxiety and panic disorders. While its common adverse effects are well-documented, rare and serious events such as intracranial aneurysm have not been systematically explored.

Signal detection using large pharmacovigilance datasets can help identify previously unrecognized adverse drug reactions (ADRs).

OBJECTIVE

This study aimed to investigate the potential association between alprazolam use and intracranial aneurysm, utilizing the US FDA Adverse Event Reporting System (FAERS) database from 1998 to 2024. An intracranial or cerebral aneurysm is a ballooning of a weak spot on a blood vessel in the brain that can cause symptoms like a sudden, severe headache, vision changes, or facial numbness.

METHOD

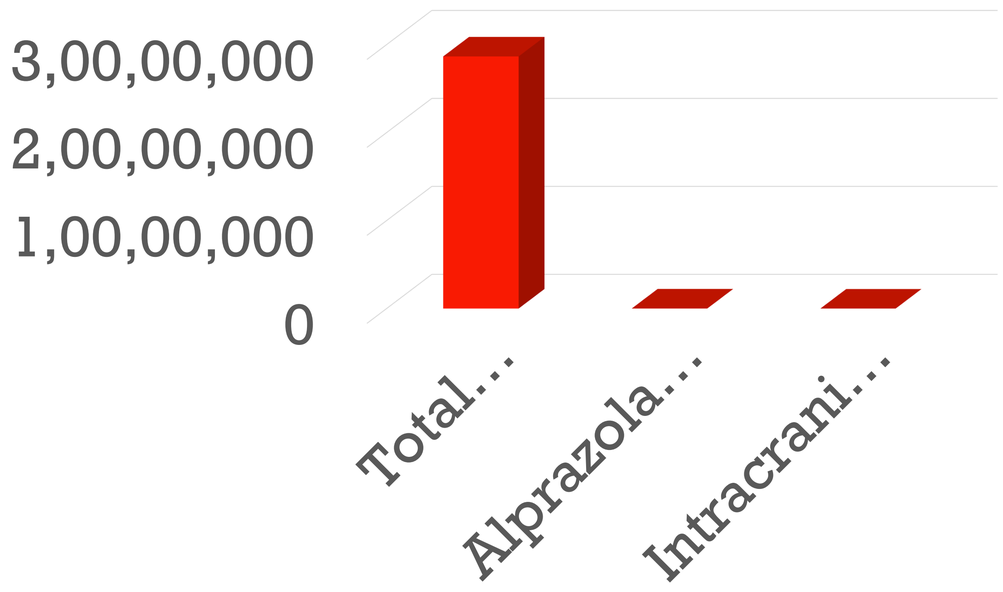
FAERS data were analysed to detect novel signals linking alprazolam to intracranial aneurysm. Disproportionality analysis was performed using data mining algorithms such as Proportional Reporting Ratio (PRR) and Reporting Odds Ratio (ROR), with data extracted via the Open Vigil platform. Positive signals were defined as PRR ≥ 2, ROR-1.96SE > 2, and chi-square > 4, with at least three reported adverse events. Relevant genes and proteins implicated by molecular docking studies with alprazolam using BIOVIA Discovery Studio and related intracranial aneurysm pathophysiology were identified using bioinformatics resources including STITCH, STRING, and HuGE Navigator.

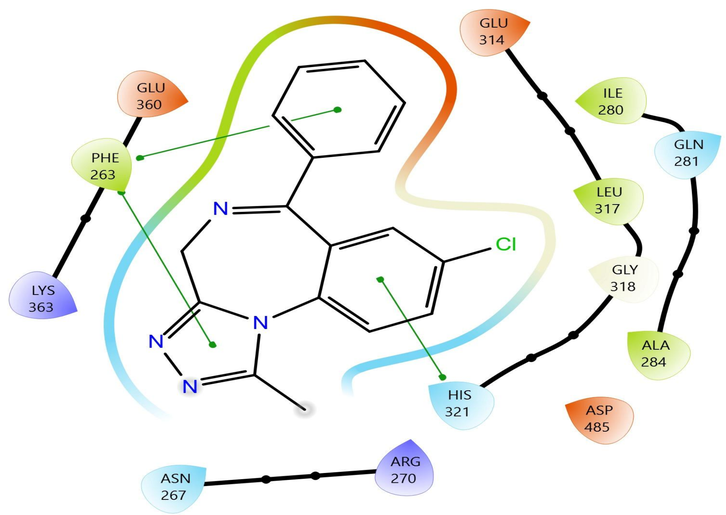
RESULTS

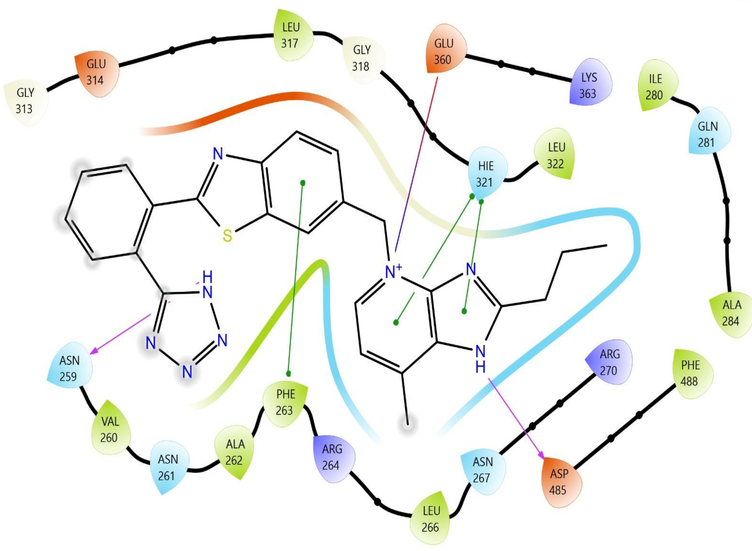
Out of 28,655,483 reports in the FAERS database, 7,214 were associated with alprazolam, of which 9 cases were reported for intracranial aneurysm.

Disproportionality analysis demonstrated a positive safety signal with a PRR of 2.19, ROR of 2.10, and a chi-square value of 4.70. The highest binding affinity was observed for PDB ID 7X11, with a docking score of –11.2, followed by the progesterone receptor, PDB ID 3HQ5, with a docking score of –9.5, supporting a mechanistic association.

Data Mining Results	Values
Total FAERS Reports Analysed	28,655,483
Atorvastatin Reports	7,214
Total Adverse Events Reported for Hilar lymphadenopathy	9
Highest docking score	-11.2
Reporting Odds Ratio (ROR)	2.10
Proportional Reporting Ratio (PRR)	2.19







CONCLUSIONS

This study revealed that intracranial aneurysm is likely to occur among patients administered with alprazolam.

The authors conclude that healthcare practitioners should exercise caution and monitor for potential vascular complications in patients receiving alprazolam therapy.

Further large-scale epidemiological studies and clinical investigations are warranted to validate this novel pharmacovigilance signal and elucidate the underlying molecular mechanisms.

REFERENCES

Huang F, San X, Liu Q, Zhu H, Xu W. Signal mining and risk analysis of Alprazolam adverse events based on the FAERS database. Scientific Reports. 2024 Mar 29;14(1):7489.

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