Abstract #654:
Important Clinical Differences Among Alpha Blockers Demonstrated in Post-Marketing Event Rates

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Introduction

Post marketing surveillance is a critical component of evaluating medication safety profiles. Ongoing monitoring of medication adverse events after medication approval can provide a better gauge of adverse events utilizing a larger, more diverse sample size. These strategies can investigate if certain medications have higher rates of adverse events or reveal if there is a particularly concerning adverse event compared to other medications in their class. We sought to understand differences in adverse event rates among medications in the alpha blocker class to better assess each individual medication's safety profile.

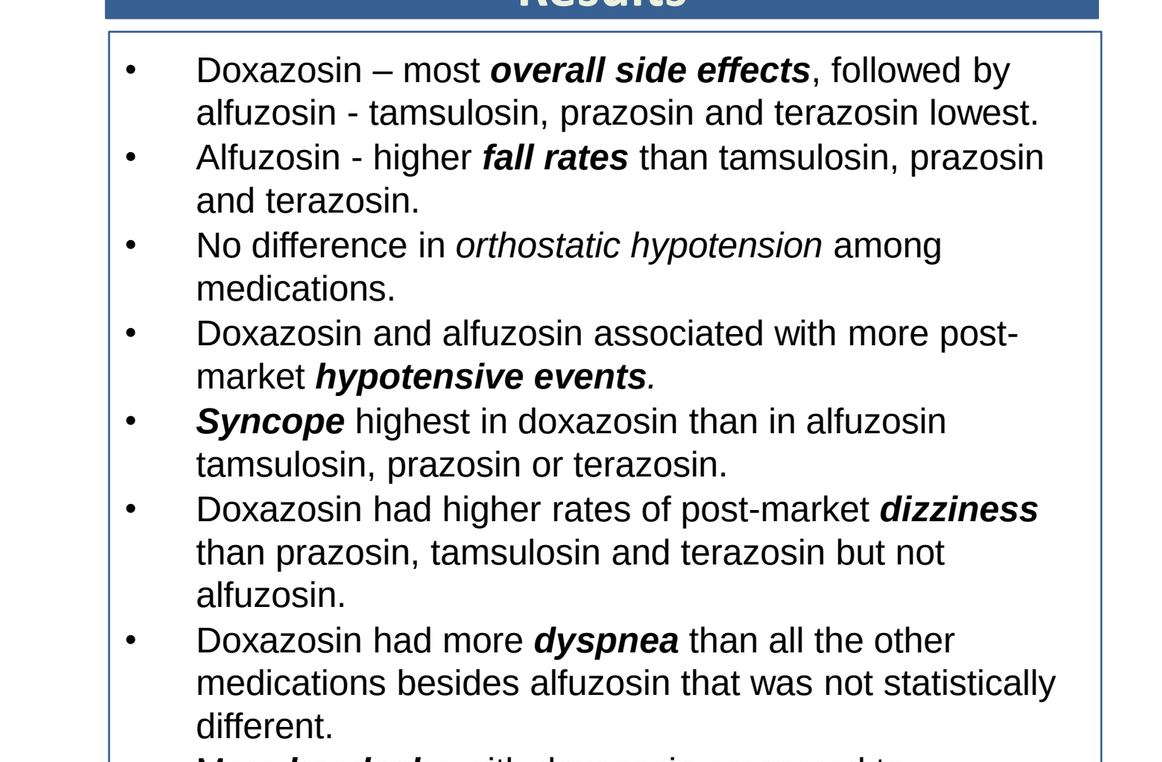
Methods and Materials

- Studied: doxazosin, alfuzosin, tamsulosin, prazosin, terazosin.
- The Food and Drug Administration's adverse event reporting database (FAERS) was used to determine the total number of adverse events reported.
- The U.S. Medical Expenditure Panel Survey was used to record number of patients on each medication.
- Data from 2013 to 2020 were complete for both databases.
- General linear model was used to assess the incidence as a function of drug, type of side effect, and an interaction between drug and side effect.
- Tukey's test was used for multiple comparisons.
- Relative percent and incidence were reported using doxazosin as the reference number 1.
- Data from package inserts (marketing) was compared.

Results

- Doxazosin – most ***overall side effects***, followed by alfuzosin - tamsulosin, prazosin and terazosin lowest.
- Alfuzosin - higher ***fall rates*** than tamsulosin, prazosin and terazosin.
- No difference in *orthostatic hypotension* among medications.
- Doxazosin and alfuzosin associated with more post-market ***hypotensive events***.
- ***Syncope*** highest in doxazosin than in alfuzosin tamsulosin, prazosin or terazosin.
- Doxazosin had higher rates of post-market ***dizziness*** than prazosin, tamsulosin and terazosin but not alfuzosin.
- Doxazosin had more ***dyspnea*** than all the other medications besides alfuzosin that was not statistically different.
- More ***headache*** with doxazosin compared to tamsulosin, prazosin and terazosin but not alfuzosin.

Incidence of side effects (Per 100,000 patients)



Comparison of side effects among alpha blockers – package insert and post-marketing (doxazosin set as 1)

Medication/SE	Package Insert (%)	Relative Percent of Package Insert versus Doxazosin	Post Marketing (incidence per 100,000)	Relative Incidence Post Marketing versus Doxazosin	P-values of post marketing Incidence
Headache					
Alfuzosin	3	0.3	0.9	0.25	0.154
Doxazosin	9.9	1	3.5	1	-
Prazosin	7.8	0.78	0.7	0.2	0.040
Terazosin	1.1	0.11	0.3	0.85	0.008
Tamsulosin	19.3	1.94	0.6	0.17	0.038
Dizziness					
Alfuzosin	5.7	0.3	3.5	0.72	0.999
Doxazosin	19	1	4.8	1	-
Prazosin	7.8	0.41	1.9	0.39	0.033
Terazosin	9.1	0.47	1.0	0.2	0.000
Tamsulosin	14.9	0.78	2.1	0.43	0.085
Hypotension					
Alfuzosin	0.4	0.23	5.1	0.75	0.915
Doxazosin	1.7	1	6.8	1	-
Prazosin	1-4	0.58	2.9	0.42	0.000
Terazosin	0.6	0.35	0.5	0.07	0.000
Tamsulosin	0.4	0.23	1.1	0.16	0.000
Syncope					
Alfuzosin	0.2	0.28	2.5	0.45	0.046
Doxazosin	0.7	1	5.5	1	-
Prazosin	1-4	1.42	0.8	0.14	0.000
Terazosin	1	1.42	0.6	0.10	0.000
Tamsulosin	0.4	0.23	1.1	0.16	0.000
Falls					
Alfuzosin	Not reported	Not reported	6.1	2.9	0.000
Doxazosin	Not reported	Not reported	2.1	1	-
Prazosin	Not reported	Not reported	0.9	0.43	0.998
Terazosin	Not reported	Not reported	1.0	0.48	0.819
Tamsulosin	Not reported	Not reported	0.4	0.19	1.000
Dyspnea					
Alfuzosin	Not reported	-	2.5	0.55	0.668
Doxazosin	2.6	1	4.5	1.0-	-
Prazosin	1-4	0.38	0.6	0.13	0.000
Terazosin	1.7	0.65	0.6	0.13	0.000
Tamsulosin	Not reported	-	1.0	0.22	0.001

Conclusions

- Doxazosin had higher rates of headache, dizziness, syncope and dyspnea.
- Alfuzosin had higher than expected probability of dizziness, hypotension, syncope, dyspnea, and falls relative to the other alpha blockers (excluding doxazosin) based on the package insert. Tamsulosin and terazosin had lower than expected relative probability for the same events.
- The findings were unanticipated given that alfuzosin was marketed as a uroselective medication and promoted as having fewer systemic effects.

Future Directions

Better characterization of real-world side effects of alpha blockers will improve personalized patient care by informing selection based on adverse events, comorbidities and patient risk factors.

FAERS is a helpful database for post marketing surveillance. However, it has limitations in that it contains only voluntary reports. Future studies should be conducted in a controlled, prospective manner to most accurately account for difference in drugs.

Future opportunities for study:

- Investigating silodosin and how it compares in adverse events (data not available in the current databases)
- Comparing more side effects such as floppy iris syndrome (insufficient reports in the FAERS database)

References

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