VMAT-2 inhibitors in the Treatment of Tardive Dyskinesia

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Background & Purpose

Tardive dyskinesia is a movement disorder involving abnormal, repetitive, involuntary movements that is a chronic condition with an insidious onset.[1] Antipsychotics make up 20-35% of the cases of tardive dyskinesia after being on the medication for at least 3 months.[2] People greater than 50 years old are 3 to 5 times more likely to develop tardive dyskinesia than younger patients and patients over 65 years old are 5 to 6 times more likely to develop tardive dyskinesia.[3]

Purpose:

Removing the antipsychotic from a patient's treatment regimen can worsen the underlying psychiatric condition; therefore, the use of VMAT-2 inhibitors in addition to the antipsychotic medications has been widely used for treatment of tardive dyskinesia.[4] The goal of this research is to determine if there is an effect of treatment with VMAT-2 inhibitors on antipsychotic-induced tardive dyskinesia using a reduction of points in the Abnormal Involuntary Movement Score (AIMS) scale compared to placebo medication.

PICOT

In patients taking antipsychotic medications, do VMAT-2 inhibitors result in effective treatment of antipsychotic-induced tardive dyskinesia using reduction in AIMS scores compared to placebo medications?

Design & Methods

Keywords:
Deutetrabenazine, valbenazine, tardive dyskinesia, antipsychotic, VMAT-2 inhibitor, AIMS scores, vitamin E

Inclusion:
Only studies published after 2018; only studies involving antipsychotic-induced tardive dyskinesia; only studies including patients older than 18 years old; studies must include research on either Deutetrabenazine, valbenazine, or both

Exclusion:
Studies examining other causes of tardive dyskinesia; studies older than 2018; studies that were not in English; studies including patients younger than 18 years old

Table 1: Summary of Evidence of Search

Database	Yielded	Reviewed	Included in Analysis
Google Scholar	366	21	8
Pubmed	13	5	2
Summon	8	3	2
Total:	387	29	12

Table 2: Synthesis of Evidence

	Google Scholar	Pubmed	Summon	Total
Systematic Review	4	1	1	6
Meta-Analyses			1	1
Placebo-Controlled Trial	1	1		2
Cross Sectional Study	1			1
Assessment Manual	1			1
Prospective Study	1			1
Total:	8	2	2	12

Results:

Table 3: Deutetrabenazine

Studies	Reduction in AIMS score of Deutetrabenazine compared to placebo
Solmi et al.[5]	❖ 1.4 points lower for Deutetrabenazine (p = 0.019) ❖ 1.9 points lower in 36mg dose (p = 0.003) ❖ 1.4 points lower in 24mg dose (p = 0.001)
Khorassani et al.[6]	❖ 3.3 points lower in 36mg dose ❖ 3.2 points lower in 24mg dose ❖ 2.1 points lower in 12mg dose **Both 36mg and 24mg dose are statistically significant
Ricciardi et al.[4]	❖ 1.9 points lower for 36mg dose (p < 0.001) ❖ 1.8 points lower for 24mg dose (p < 0.001)

❖ Regarding side effects of deutetrabenazine, the most common side effects were headache, anxiety, and diarrhea as examined by Arya et al.[2]

Table 4: Valbenazine

Studies	Reduction in AIMS score of Valbenazine compared to placebo
Solmi et al.[5]	❖ Endpoint of 50% reduction in scores: 48.9% reached this for valbenazine and 18.2% for placebo (p < 0.001) ❖ 40.0% lower for 80mg dose ❖ 23.8% lower for 40mg dose ❖ 8.7% lower for placebo **Both 80mg and 40mg doses are statistically significant
Khorassani et al.[6]	❖ 3 points lower for 40mg dose (p < 0.001) ❖ 4.8 points lower for 80mg dose (p < 0.001)
Ricciardi et al.[4]	❖ 2.4 points lower for valbenazine (each patient was on individualized doses) (95% CI = -3.7 to -1.1)

❖ Arya et al. examined side effects of valbenazine in a study of 234 patients showing the most common side effects were somnolence, dry mouth, and akathisia.[2]

Best Practice

Discussion:

- ❖ Both VMAT-2 inhibitors, deutetrabenazine and valbenazine, reduced AIMS scores significantly more than the placebo.
- ❖ No increased risk of serious adverse events were found between a placebo and VMAT-2 inhibitors. Side effects include headache, anxiety, and diarrhea for deutetrabenazine and somnolence, dry mouth, and akathisia for valbenazine.[2] These were not found to be significantly worse than those in the placebo group.
- ❖ Parkinsonian side effects of tardive dyskinesia treatment were less common with deutetrabenazine and valbenazine compared to the placebo.[5, 7]
- ❖ For a 30-day supply cost (average wholesale): deutetrabenazine costs between $6,208 and $9,270 and valbenazine costs between $7,176 and $7,740.[6] The high cost of there medications may limit their use even for patients with insurance.

Limitations/Further study:

- ❖ There are no studies comparing the efficacy of valbenazine and deutetrabenazine directly.
- ❖ Many trials involve a limited course of treatment. As these medications are taken long-term, longer follow-up is needed to establish further safety and efficacy.[8]
- ❖ Not all studies use the same scales to measure symptoms of tardive dyskinesia which may skew the results of comparing different trials, although the majority of the studies in this review utilized AIMS scoring.

Conclusion:

Through the research, it appears that VMAT-2 inhibitors, specifically deutetrabenazine and valbenazine, do provide treatment of tardive dyskinesia which is seen through a statistically significant decrease in AIMS scores across multiple studies. However, further research needs to be conducted comparing valbenazine and deutetrabenazine directly regarding efficacy of the two treatments compared directly to each other and a placebo as well as research involving longer treatment periods. Overall, the PICOT question was answered through this research; however, even though both VMAT-2 inhibitors are effective in the treatment of tardive dyskinesia, access to the medications is limited due to the cost of the medication.

References:

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