Efficacy of SSRIs for treating depression in Alzheimer's disease

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Introduction

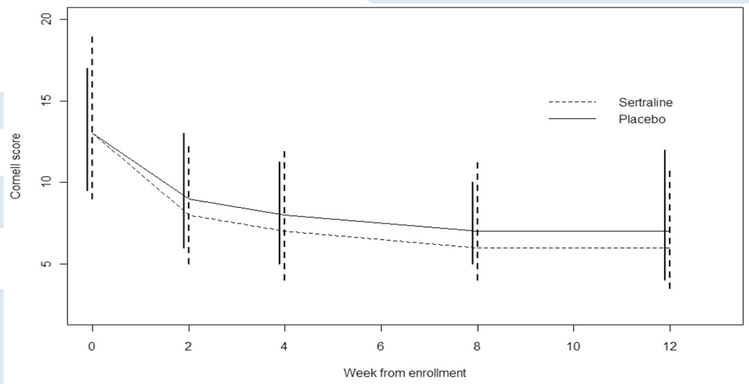
- 5.7 million Americans are living with Alzheimer's disease (AD)[1]
- Depression in AD is associated with greater morbidity and mortality[2,3]
- Societal costs due to AD is around $100 billion per year and are projected to double by 2020 and triple by 2040[4,5]
- This project focuses on the efficacy of selective serotonin reuptake inhibitors (SSRIs) for treating depression in people with AD

Methods

- EBSCO, Google Scholar, and PubMed was searched using the following terms: *depression in Alzheimer's*, *review of SSRI depression Alzheimer's*, *SSRI treatment in Alzheimer's*, *efficacy of SSRI's in Alzheimer's*
- Two randomized controlled trials and a systematic review was also referenced for the clinical review
- Temporary behavioral symptoms of dementia and studies that did not include SSRI's as treatment for AD were excluded
- Cochrane Risk of Bias Tool and the GRADE system was used to evaluate bias

Results

Rosenberg et al., 2010



Notes: The rate of change in the transformed CSDD scores over time did not differ between treatment groups (Likelihood ratio test, $\chi^2 = 0.26$, 3 df, p = 0.97).[6]

CSDD Difference (Placebo – Sertraline) in medians and confidence intervals by visit			
Week 2	**Week 4**	**Week 8**	**Week 12**
0.80 (-1.63, 3.23)	0.80 (-1.75, 3.35)	1.20 (-1.18, 3.58)	1.20 (-1.65, 4.05)

Notes: There was no statistically significant increase in the estimated odds of remission on sertraline treatment compared with placebo (OR = 2.06, 95% CI: 0.84, 5.04, Wald $\chi^2 = 2.55$ with 1 df, p = 0.11), with 33% of sertraline-treated participants achieving remission at week 12 compared with 19% of placebo-treated patients.[6]

mADCS-CGIC Rating	Sertraline n=67	Placebo n=64
7 "much worse"	1 (1.5)	0 (0)
6 "worse"	5 (7.5)	2 (3.1)
5 "a bit worse"	6 (9.0)	9 (14.1)
4 "no change"	10 (14.9)	11 (17.2)
3 "a bit better"	18 (26.9)	18 (28.1)
2 "better"	18 (26.9)	21 (32.8)
1 "much better"	9 (13.4)	3 (4.7)

Notes: Data are presented as n (%). mADCS-CGIC ratings (OR = 1.01 (95% CI: 0.52, 1.97, p=0.98), CSDD scores (median difference at 12 weeks 1.2,[95% CI -1.65, 4.05], p=0.41), and remission at 12 weeks of follow-up (OR = 2.06, [95% CI - 0.84, 5.04], p=0.11) did not differ between sertraline (N=67) and placebo (N=64).[6]

Banerjee et al., 2016

Treatment	Baseline Depression		Week 13 Depression		Week 39 Depression	
	No	Yes	No	Yes	No	Yes
Placebo	-	111	47	48	40	42
Sertraline	-	107	38	40	33	37
Mirtazapine	-	108	42	43	42	34
Total	**-**	***326***	***127***	***131***	***115***	***111***

Notes: Differences in Cornell Scale for Depression in Dementia (CSDD) at 13 weeks from an adjusted linear-mixed model: mean difference (95% CI) placebo-sertraline 1.17 (-0.23 to 2.78; p = 0.102); placebo-mirtazapine 0.01 (-1.37 to 1.38; p = 0.991); and mirtazapine-sertraline 1.16 (-0.27 to 2.60; p = 0.112).[7]

Significant Adverse Events

Rosenberg, et al., 2010

	Sertraline (n=66)	Placebo (n=63)	Sertraline vs. Placebo		
			Unadjusted OR	95% CI	*p*-value
Diarrhea	34	19	2.44	(1.12, 5.52)	0.02
Indigestion	23	11	2.51	(1.04, 6.39)	0.03
Nausea	15	8	2.01	(0.73, 5.97)	0.17
Vomiting	11	4	2.93	(0.81, 13.35)	0.10
Dry Mouth	30	17	2.24	(1.02, 5.07)	0.04
Dizziness	39	19	3.31	(1.52, 7.41)	0.001

Notes: Measures are in numbers of occurrence of significant adverse effects. 66 participants on sertraline and 63 patients on placebo had at least one follow-up visit and provided adverse event data using the symptom checklist. Of these, diarrhea, indigestion, dry mouth, and dizziness were more common in the sertraline group.[6]

Banerjee et al., 2016

Placebo	Sertraline (SSRI)	95% CI	*p*-value
29/111, 26%	46/107, 43%	1.17 (-0.23 to 2.78)	0.102

Notes: Placebo group had fewer adverse reactions (29/111, 26%) than sertraline (46/107, 43%) or mirtazapine (44/108, 41%; *p*=0.017). Measures are in number of participants who reported SAE, not number of occurence.[7]

Conclusions

- No clinically significant findings that suggests SSRI's are effective in treating depression in AD
- In both studies, SSRI's were associated with an increased rate of significant adverse effects
- Limitations were due to small sample sizes from each study
- Issues with generalization of findings because participants do not represent those with AD who are not in specialist care facilities nor the community as a whole
- Larger sample size from different communities is needed
- Further research on this topic becomes increasingly important because of the aging population, as well as the growing number of people who are being diagnosed with AD annually.

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