Second-generation antipsychotics did not improve outcomes and increased costs for patients with Alzheimer disease and psychosis

Rosenheck RA, Leslie DL, Sindelar JL, et al. **Cost–benefit analysis of second-generation antipsychotics and placebo in a randomized trial of the treatment of psychosis and aggression in Alzheimer disease.** Arch Gen Psychiatry. 2007;64:1259-68.

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QUESTION

Do second-generation antipsychotics improve health and reduce costs in patients with psychosis and Alzheimer disease (AD)?

METHODS

Design: Cost–benefit analysis from a randomized placebo-controlled trial (Clinical Antipsychotic Trial of Intervention Effectiveness—AD, [CATIE-AD]) with 9-month follow-up.

Setting: 42 clinical sites in the United States.

Patients: 421 ambulatory outpatients (mean age 78 y, 56% women) who had dementia (Alzheimer type) and clinically severe delusions, hallucinations, aggression, or agitation after onset of dementia; lived at home or in assisted living; scored 5 to 26 on the Mini-Mental State Examination and "moderate" or greater on the Neuropsychiatric Inventory (delusion, hallucination, agitation, or "aberrant motor behavior" items) and Brief Psychiatric Rating Scale (≤ 1 wk before randomization); and had a partner or caregiver (≥ 8 h/wk for ≥ 3 d/wk) able to contribute to assessments. Exclusion criteria included schizophrenia; schizoaffective disorder; delirium; probable vascular dementia; and concurrent use of antipsychotics, antidepressants, anticonvulsants as mood stabilizers, or benzodiazepines.

Intervention: Olanzapine (n = 100), quetiapine (n = 94), risperidone (n = 85), or placebo (n = 142), with flexible dosing schedules. If a treatment was discontinued, patients could be re-randomized to 1 of the other 2 drugs or citalopram.

Outcomes: Health care costs; quality-adjusted life-years (QALYs) assessed using the Health Utilities Index Mark 3; and scores on the AD Related Quality of Life (ADRQOL), AD Cooperative Study Activities of Daily Living (ADCS-ADL), and AD dependence scales. Net health benefits were calculated using estimates of $50 000 and $100 000 per QALY/y minus health care costs.

MAIN RESULTS

Adjusted monthly costs over 9 months were lower for placebo as the initial treatment than for olanzapine, quetiapine, or risperidone (P = 0.02). Placebo was better than olanzapine for activities of daily living; groups did not differ for other outcomes (Table) or for net health benefits of treatment at an estimated value of $50 000 or $100 000 per QALY.

CONCLUSION

In patients with Alzheimer disease and psychosis, olanzapine, quetiapine, and risperidone did not improve outcomes and increased the costs of care.

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Antipsychotics vs placebo over 9 months in patients with Alzheimer disease (AD) and psychosis or aggression*

Outcomes †	Initial treatment (adjusted mean scores)				*P* value
	Olanzapine	Risperidone	Quetiapine	Placebo	
QALYs	0.12	0.16	0.15	0.14	0.42
ADRQOL	72.44	71.08	72.19	72.12	0.88
ADCS-ADL	30.4	33.27	33.79	34.4	0.03‡
AD dependence	3.73	3.69	3.7	3.62	0.66

*ADCS-ADL = AD Cooperative Study Activities of Daily Living scale; ADRQOL = AD-Related Quality of Life scale; QALY = quality-adjusted life-year.
†Higher scores better for all scales except AD dependence.
‡Favors placebo compared with olanzapine.

COMMENTARY

Behavioral and psychological symptoms of dementia (BPSD) are common and challenging to manage. Atypical antipsychotics are frequently prescribed for BPSD, although a recent large, randomized, controlled trial (1) adds to the growing literature that efficacy may be outweighed by adverse effects. Accordingly, the findings of Rosenheck and colleagues, that atypical antipsychotics are not a cost-effective intervention for community-dwelling older adults with AD and significant BPSD, are not surprising.

Although their analysis provides important information about direct health care expenditures, potential indirect costs and benefits were not measured. Management of BPSD accounts for a substantial proportion of all costs associated with dementia care (2), much of which is related to indirect costs of informal caregiver activities provided by family members (3).

Some trials of psychosocial interventions for dementia (4) have shown both efficacy and cost-effectiveness; guidelines and education on alternative management strategies for BPSD are needed. Guidelines should emphasize nonpharmacologic approaches as initial interventions for BPSD when possible (5), and clinicians should minimize use of antipsychotics.

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