Quality of Evidence in APA Practice Guideline for Alzheimer's Disease

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Abstract

Objective: A recent report[1] indicated that APA practice guidelines for psychiatric disorders are based largely on evidence derived from non-randomized, uncontrolled trials. That report was limited to quantitative analysis of the overall quality of evidence. This study assesses the quality of evidence used in APA Practice Guideline for Alzheimer's disease[2] (AD) by focusing on areas specifically deficient in high quality evidence.
Methods: Evidentiary quality was assessed by identifying citations from (A) randomized-controlled studies, (B) clinical trials, (C) longitudinal studies, (D-G) retrospective/secondary data, and analyzing them according to treatment principles relevant to AD management (psycho-education, psycho-therapy-psychosocial interventions, pharmacological options for cognitive loss, psychosis/agitation, depression, sleep).
Results: On the whole, the distribution of citations was: (A) 25%, (B) 19%, (C) 6%, (D-G) 50%. Distribution of the evidence according to the treatment modalities was: Psychotherapy-psychosocial interventions (A) 20-32%; treatments for: cognitive loss (A) 73-85% (cholinesterase inhibitors, selegiline, ergoloid-mesylates) and (A) 25% (vitamin-E, NSAID, estrogen), psychosis/agitation (A) 35-45%, depression (A) 14%, and sleep (A) 17%, psycho-education (A) 0%.
Conclusions: Results of this study indicate that high quality evidence supporting interventions in AD is specifically deficient in the areas of psycho-education, psychotherapy and psychosocial treatments (behavior and emotion-oriented), disease-modifying treatments with Vitamin-E, NSAIDs, and estrogen, and psychotropic drug treatments for non-cognitive symptoms of AD. Data from new investigations will be required to improve the quality of evidence on which these aspects of AD management are based.

Introduction

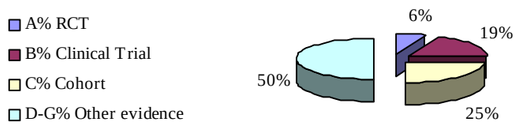
The goal of practice guidelines for the treatment of psychiatric disorders is to establish standards of care against which individual clinical treatments and broad health care policies can be measured. Practice guidelines generally represent a fusion of clinical experience, expert opinion, and research evidence with the aim of making recommendations evidence-based. The current APA guidelines incorporate data coded along a hierarchy of evidence from best (derived from randomized controlled trials) to worst (derived from uncontrolled and often retrospective studies). A recent report[1] showed that, on the whole, APA practice guidelines are based on evidence derived from non-randomized, uncontrolled trials. However, this report was limited to the analysis of overall evidence without pointing to specific areas deficient in high-quality evidence. The *objective* of this study was to identify domains of treatment for dementia that are particularly deficient in high-quality evidence in the APA Practice Guideline for Alzheimer's disease[2].

Methods

Quality of evidence was assessed by identifying citations from:
(A) randomized-controlled trials (RCT),
(B) clinical trials not meeting standards for RCTs,
(C) cohort/longitudinal studies,
(D-G) retrospective/secondary data
The data were analyzed according to the treatment principles that are relevant to the management of Alzheimer's disease. The following categories were analyzed:
- General management issues
- Psychotherapy and psychosocial interventions
- Treatment or delay of cognitive loss
- Treatment of psychosis, agitation, depression and disrupted sleep
- Factors modifying treatment or outcome

Results

On the whole, the distribution of citations according to the hierarchy of evidence was: (A) 25%, (B) 19%, (C) 6%, (D-G) 50%. A domain of evidence was considered specifically deficient if 60% or more of the citations fell into categories (D-G).



1. General Management Issues

	Quality of evidence								
	Total # Refs	A	% A	B	% B	C	% C	D-G	% D-G
Safety: wandering	3	0	0	3	100	0	0	0	0
Safety: driving	14	0	0	1	7	2	14	11	79
Resources for Care	11	1	9	3	27	1	9	6	55
Psycho-Educ (Pt & Family)	11	0	0	0	0	1	9	10	91

2. Psychotherapy and Psychosocial Interventions

	Quality of evidence								
	Total # Refs	A	% A	B	% B	C	% C	D-G	% D-G
Targeting Behavior	3	0	0	0	0	0	0	3	100
Targeting Emotions	10	2	20	3	30	0	0	5	50
Targeting Cognition	19	6	32	12	63	0	0	1	5
Controlling Stimulation	5	1	20	3	60	0	0	1	20

3. Treatment or Delay of Cognitive Loss

	Quality of evidence								
	Total # Refs	A	% A	B	% B	C	% C	D-G	% D-G
Cholinesterase inhibitors	11	8	73	0	0	2	18	1	9
Vitamin E	5	1	20	0	0	0	0	4	80
Selegiline	14	11	79	1	7	0	0	2	14
Ergoloid mesylates	13	11	84	1	8	0	0	1	8
NSAIDs	5	1	20	0	0	1	20	3	60
Estrogen	8	0	0	2	25	1	12	5	63

4. Treatment of Psychosis, Agitation, Depression, and Disrupted Sleep

	Quality of evidence								
	Total # Refs	A	% A	B	% B	C	% C	D-G	% D-G
Antipsychotics	20	7	35	3	15	0	0	10	50
Benzodiazepines	11	5	35	0	0	0	0	6	65
Anticonvulsants	7	1	14	2	29	0	0	4	57
Other agents*	17	2	12	4	23	0	0	11	65
Antidepressants	14	2	14	6	43	0	0	6	43
Treatments for disrupted sleep	12	2	17	4	33	0	0	6	50

* Other agents include b-blockers, buspirone, lithium, medroxyprogesterone, and trazodone.

5. Factors Modifying Treatment or Outcome

	Quality of evidence								
	Total # Refs	A	% A	B	% B	C	% C	D-G	% D-G
Co-morbid conditions*	7	2	29	0	0	0	0	5	71
Enviornment**	17	0	0	3	17.5	3	17.5	11	65
Fixed factors (age, gender, ethnicity)	9	1	11	0	0	0	0	8	89

* include: general medical conditions, delirium, Parkinson's disease, stroke.
** include: home, day care, long-term care, hospital.

Conclusions:

This study outlines the status of evidence used in APA Practice Guideline for Alzheimer's disease.
- On the whole, 50% of the evidence used in the practice guideline originates from retrospective and/or secondary data and is classified in the lower-quality categories.
- Specific areas of deficit, i.e. more than 60% of the evidence originated from retrospective and non-randomized studies, were in:
  - General management
    - Behavior-oriented interventions (100%)
    - Psycho-education (91%)
    - Driving safety (79%)
  - Factors modifying treatment or outcome
    - Fixed factors (89%)
    - Co-morbid conditions (71%)
    - Environmental factors (65%)
  - Drugs targeting cognitive loss and disease progression
    - Vitamin E (80%)
    - NSAIDs (60%)
    - Estrogen (63%)
  - Psychotropic drug therapies
    - Benzodiazepines and "Other" drugs (65%)
- The strongest evidence, i.e. evidence originating from RCTs and clinical trials (A-B), comes from studies of:
  - Cognition-oriented therapies, including drugs and psychosocial treatments (95%)
  - Ergoloid mesylates (92%)
  - Selegiline (86%)
  - Stimulation-oriented psychosocial therapies (80%)
- Our data point to two unusual patterns:
  - With a few exceptions (studies of cholinesterase inhibitors, ergoloid mesylates, and selegine), the evidence about pharmacological treatments mostly originates from non-randomized, uncontrolled studies. One would expect that most high-quality evidence would come from studies using these forms of treatment, yet controlled trials of classical psychotropic agents are rare.
  - A substantial proportion of evidence about psychotherapy and psychosocial interventions derives from controlled clinical trials and therefore falls in the higher range of quality. This is surprising, given the traditional difficulty of conducting controlled trials of such interventions.
- New data from well-designed investigations are required to improve the quality of evidence on which most aspects of Alzheimer's disease management are based. Some have begun to appear, including a large RCT of risperidone for the treatment of psychosis and aggression in demented nursing home patients[3], and two controlled trials of caregiver-focused interventions to manage depression[4] and delay nursing home placement[5] in Alzheimer's disease. No mechanism currently exists for regular updating of the Alzheimer's disease or other psychiatric practice guidelines as better-quality evidence emerges, a problem promoting rapid obsolescence of the guidelines as they are currently conceived.

References:

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