# PHARMACOLOGICAL MANAGEMENT OF BEHAVIORAL PROBLEMS AND NEUROPSYCHIATRIC SYMPTOMS IN DEMENTIA (NPSD) IN THE LONG-TERM CARE SETTING

## 1. Overview

The pharmacological management of neuropsychiatric symptoms in dementia (NPSD) requires careful diagnostic evaluation, detailed medical assessment and implementation of behavioral management strategies prior to prescription of psychotropic medications. The efficacy of psychotropic medications as a primary treatment for behavioral problems is low and pharmacological interventions should be used as an adjunctive treatment to behavioral management rather than a primary response (1), (2), (3), (4).

Many behavioral problems may result from distress caused by psychiatric complications of dementia. Psychiatric disorders may respond to specific psychotropic medications that target the specific, identified disorder, such as antidepressants for symptoms of depression. Individuals with mild and moderate dementia are usually able to explain symptoms associated with depression, anxiety disorders, post traumatic stress disorder or psychosis while persons with advanced middle stage or late stage dementia usually lack the language skills to describe complicated internal mental events. In these patients, behavioral manifestations may be the primary symptom of psychiatric problems that are improved with appropriate psychopharmacology.

Pharmacological agents that may benefit behavioral problems in persons with dementia fall into several broad categories including: 1) antipsychotic medications (APM), 2) cholinesterase inhibitors, 3) antidepressant medications, 4) selected antiepileptic medications, and 5) other miscellaneous medications. Older persons with dementia may receive a wide range of medical and psychiatric medications that may worsen behavior or cognitive function **(See Table 1).**

**Table 1. Commonly Prescribed Psychotropic and Medical Drugs for Patients with Dementia in 2007 (n=224)**

| PSYCHOTROPIC | | MEDICAL | |
|---|---|---|---|
| % | Medications | % | Medications |
| 3 | Old antipsychotics | 41 | Antihypertensives |
| 12 | New antipsychotics | 5 | Statins |
| 13 | BZD | 4 | Anti-diabetic agents |
| 38 | ACHEI's | 12 | Laxatives |
| 21 | SSRI | | |
| 2 | Antiepileptics | | |

BZD-benzodiazepine ACHEI-acetyl-cholinesterase inhibitors

JNNP 2007;78:233-39

## 2. Frequency of Psychotic Symptoms in Dementia

Psychosis is a disorder of thought that may manifest as hallucinations, delusions or paranoia. Specific criteria exist to define psychosis in dementia patients **(See Table 2)** to avoid confusion with other mental illnesses, such as schizophrenia (5). Psychosis is a common complication of many forms of dementia, especially Alzheimer's disease and diffuse Lewy body disease (DLBD) **(See Table 3).** Hallucinations are less common in persons with frontotemporal dementia (FTD) (6). The frequency of psychosis may vary with the stage of dementia, type of disease and duration of symptoms **(See Tables 4 and 5, pg 2).** Auditory and visual hallucinations are common complications **(See Table 6, pg 2)** and occur in all stages of Alzheimer's disease **(See Table 7, pg 2).** Delusions are also common symptoms that may involve a range of false beliefs **(See Tables 8 and 9, pg 2)** (6), (7). The presence of psychotic symptoms increases the likelihood of verbal or physical aggression in nursing home residents **(Table 10, pg 2).**

**Table 2. Diagnostic Criteria of Alzheimer's with Psychosis**

1. Primary diagnosis of AD
2. Hallucinations or delusions post-date dementia
3. Duration of psychosis > 1 month
4. ↓ function from symptoms

AM J Geriatric Psych 2000, 8:29-34

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**Table 3. Epidemiology of Psychosis in AD (n=55 studies)**

| Symptom | Range of patients with psychosis (%) | Median (%) |
|---|---|---|
| Psychosis | 12.2 to 74 | 41 |
| Delusions | 9.3 to 63 | 36 |
| Hallucinations | 4 to 41 | 18 |

Am J. Psych 2005;162:2022-30

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## Table 4. Psychosis by Stage of AD (n=55 studies)

| Stage of Dementia | Median with psychosis (%) | Range (%) |
|---|---|---|
| Mild | 25.5 | 31 to 50 |
| Moderate | 37.7 | 18.8 to 56 |
| Severe | 49 | 21.9 to 79 |

Am J. Psych 2005;162(11):2022-30



## Table 5. Risk for Psychosis by Duration of Disease (AD)

| Year | Risk (%) |
|---|---|
| 1 | 20.1 |
| 2 | 36.1 |
| 3 | 49.5 |
| 4 | 51.3 |

Neurology 2000;54:1965-71



## Table 6. Types of Hallucinations Detected in Patients with AD

| Hallucination Type | Number of studies | Range (%) |
|---|---|---|
| Visual | 16 | 4 to 59 |
| Auditory | 16 | 1 to 29 |
| Other | 16 | 0.4 to 8 |

Psychosomatics 2003;44(5):388-401

**n=55 studies**



## Table 7. Risk for Hallucinations by Severity Stage of AD

| Stage | Median with hallucinations (%) | Range (%) |
|---|---|---|
| Mild | 11.4 | 9 - 33 |
| Moderate | 19 | 13 - 48 |
| Severe | 28 | 16 - 44 |

Am J. Psych 2005;162(11):2022-30

**n=55 studies**



## Table 8. Frequency of Delusions by Stage of AD

| Stage | Median with delusions (%) | Range (%) |
|---|---|---|
| Mild | 23.5 | 11 – 50 |
| Moderate | 46 | 13 - 67 |
| Severe | 33 | 23 - 57 |

Am J. Psych 2005;162(11):2022-30

**n=55 studies**



## Table 9. Types of Delusions in AD

| Type of Symptom | Range (%) |
|---|---|
| Theft | 34.5 to 76 |
| Persecutory | 18.5 to 79 |
| Reference | 14.9 to 54 |
| Infidelity | 7.7 to 45 |
| Other | 1.7 to 28.4 |

Psychosomatics 2003;44(5):388-401



## Table 10. Potentially Correctable Causes of Aggression in Nursing Home Residents (1)

| OR | Symptom |
|---|---|
| 3.3 | Depression |
| 2.0 | Delusions |
| 1.4 | Hallucinations |
| 1.3 | Constipation |

**OR-Risk of aggression when symptom is present**

Arch Int. Med. 2006;166:1295-1300

## 3. Antipsychotic Medication for Neuropsychiatric Symptoms of Dementia (NPSD)

Antipsychotic medications have been widely used in persons with dementia for management of psychosis or behavioral problems (7). An extensive literature has evolved on the safety and efficacy of these medications **(See Tables 11, 12, 13, pg 4)**. Clinicians must weigh risk-benefit ratios for the prescription of these medications in each patient. This subject must be discussed with the patient's caregiver prior to initiation of therapy and this deliberation should be documented in the medical record for medical-legal reasons.

### a. Basic Steps For Psychotropic Medication Management

The prescription of psychotropic medications from any drug class requires specific steps prior to initiation of treatment: 1) careful clinical assessment documented in medical records, 2) clearly defined target symptoms, 3) assessment of risk-benefit ratio for each prescribed psychotropic medication, 4) definition of likely side effects and communication to caregiver for monitoring, 5) careful dose titration, 6) follow-up assessment of efficacy and safety, and 7) medication adjustment based on efficacy and tolerability **(See Appendix A and B).**

New, second generation antipsychotic (SGA) medications are the preferred agents to maximize tolerability and to minimize toxicity. Most second-generation antipsychotic medications are less likely to cause important side effects such as drug-induced parkinsonism, akathisia, and excessive sedation than older first generation medications **(Table 11).**

**Table 11. Outcomes from Treatment of Delusions in AD with Antipsychotics**

| Medication | n | Duration | s | Outcome |
|---|---|---|---|---|
| Risperidone | 4 | 8 wks to 1 yr. | 16 to 330 | All studies show improvement 0.5 to 2 mgm |
| Olanzapine | 4 | 6 to 24 wks | 105 to 652 | ¾ showed improvement at 5 to 7.5 mgm |
| Quetiapine | 2 | 8 to 12 | 10 to 16 | Effective at 25 to 200 mgm range |

**n**= number of studies **s**=subjects studied

Dementia Geriatr. Cog. Disorder 2006;22:260-66

### b. Efficacy of Antipsychotic Medication Therapy for NPSD

Efficacy continues to be a controversial issue in the treatment of behavioral problems produced by Alzheimer's disease **(Table 14, pg 4).** Recent studies such as the CATIE study suggest low, overall efficacy for these medications in dementia (8), (9). Systematic reviews of antipsychotic medication efficacy published in the Cochrane Database and Agency for Health Research and Quality (10) suggest marginal efficacy **(Tables 13, 14).** None of the available data suggest excellent, robust improvement of psychiatric symptoms produced from the antipsychotic medications. Among patients with Alzheimer's disease, risperidone (11), (12), olanzapine (13), aripiprazole (14), and quetiapine (15), (16), (17) have some published data suggesting therapeutic benefit for reducing the intensity of NPSD in Alzheimer's disease. Among patients with diffuse Lewy body disease and Parkinson's disease, Clozaril and Seroquel have some data supporting benefit (18). Minimal data is available on the efficacy of antipsychotic medications for persons with Frontotemporal dementia and alcohol-induced dementia and some anecdotal evidence suggest that SGA's may worsen symptoms in FTD.

None of the antipsychotic medications currently have FDA approval for behavioral management of dementia. Prescription of these medications for dementia is considered an off-label but acceptable standard of care based on clinical studies and widespread usage when other interventions are ineffective and risk-benefit ratio is considered. A meta analysis of risperidone trials demonstrated general clinical improvement of symptoms (19) but a single randomized controlled study (RCT) using risperidone and citalopram demonstrated equal efficacy (20).

**Table 12. Treatment for NP Symptoms of Dementia with Other Medications**

| Medication Class | n | t | Outcome |
|---|---|---|---|
| **Antidepressants:** Fluox., traz., cit., sert. | 5 (15-245) | 2-12 wks | No efficacy except depression |
| **Mood Stabilizer:** carb., dival. | 5 (21-172) | 3-6 wks | No consistent efficacy |
| Memantine | 2 (252-404) | 24-28 wks | "conflicting results" |
| Benzodiazepines | N/A | N/A | N/A |

**n**=number of studies **t**=duration of study
JAMA 2005;293(5):596-608

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**Table 13. AHRQ Conclusions About Antipsychotic Efficacy for NPSD Symptoms**

| | Drug | Format | Result |
|---|---|---|---|
| 1. | Risperidone/ Aripiprazole | META/15 | Small but significant benefit |
| 2. | Olanzapine | META/15 | ±Psychosis benefit |
| 3. | Resperidone/ Olanzapine/ Quetiapine | CATIE | ND – time to discontinue<br>Efficacy – res / olan<br>Tolerability - quet |

META – meta analysis of number of listed studies
AHRQ-Agency for Health Research and Quality
AHRQ No. 7, 2007

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**Table 14. Cochrane Collaboration on Atypical Antipsychotics for Aggression and Psychosis in AD**
**(14) (40)**

- 16 – placebo controlled studies
- 9 – met META criteria
- ↓ aggression – risperidone
- ↓ psychosis – risperidone
- ↑ CVA / EPS – resp. / olanz.
- ↑ D/C meds – resp (2mg) and olanz. (5-10mg)
- ? – effect on cognition

**META**=meta analysis **Resp**=Risperidone **Olanz**=olanzapine

Cochrane Database Syst Rev. 2006 Jan 25;(1):CD005593. Review.

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## c. Safety of APM Therapy for Patients with Dementia

Safety is a major concern for prescription of all antipsychotic medications (APM) (1), (21) for older patients with dementia. Recent studies show increased risk of death in the early phase of treatment for elderly demented patients with NPSD **(Table 15 and 16).** A specific patho-physiological mechanism is not identified and the risk level is difficult to define for each patient **(See Table 17),** (22), (23), (25) Other studies dispute these findings (24). The impact of chronic SGA treatment on cognitive function and rate of functional decline remains unclear.

**Table 15. Meta-analysis of Relative Risk of Death in Elders with Dementia**

- n= 15
- t= 12 weeks
- p= 3353 / 1757
- Death rate = 3.5% vs 2.3%*
- OR = 1.54

*treated vs untreated

JAMA 2005;294(15):1934-42

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**Table 16. Relative Risk of Death in All Elderly Receiving Antipsychotic Medications by Duration of Therapy**

| Days | Relative Risk* |
|---|---|
| >180 | 1.37 |
| <40 | 1.56 |
| 40 to 79 | 1.37 |
| 80 to 180 | 1.27 |

*risk ratio for deaths relative to untreated patients
NEJM 2005;353:2335-2341

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**Table 17. Important Side Effects Associated With Antipsychotic Medications In Older Patients with Dementia**

| Side Effect | Drug | Risk | Data | Ref. |
|---|---|---|---|---|
| Death | All | Slight | S | T1, T2 |
| Stroke | All, but higher in old meds. | Slight | C | T3 |
| Pulmonary embolism | All | Slight | C | T5 |
| Hyperpro-lactinemia osteoporosis | Old > new | Unclear | C | T6, T7 |

Old=first generation S=substantial data C=controversial

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Patients should be monitored on a regular basis for the common side effects produced by SGA's **(See Appendix C1)**. The risk for occurrence of individual side effects varies according to duration of treatment, type of APM and dose. Sedation and dystonic reactions can occur early while tardive dyskinesia often occurs after several years of therapy. Parkinsonism can occur after days of weeks of treatment. Metabolic syndrome is a major concern in younger patients but SGA-induced hyperglycemia and obesity may be less problematic in older patients (31). Hyperlipidemia is a concern for older patients and no specific statin has been identified as effective for this side effect. A schedule of recommended monitoring is included in **Appendix C2.**

**d. Dosing Ranges of APM for NPSD**

Dosing schedules for antipsychotic medications and common side effects are in **Appendix D1**. Available clinical research is inadequate to examine the optimal dose or the role of antipsychotic medications in the management of Frontotemporal dementia or alcohol-induced dementia (25).

Poly-pharmacy with antipsychotic medications in the elderly should be avoided to reduce toxicity (26), (27). Non-compliance is a common reason for therapeutic failure caused by patient refusal or inability of the staff to assure compliance. Long-acting, injectable medications can be used in non-compliant patients who require antipsychotic therapy **(See Appendix D2).** Sol Tabs (preparations that dissolve immediately on contact with mucosa) and liquid preparations, such as Risperidal M-tabs or Zyprexa Zydis wafers, can be used to assure compliance.

Long-term care regulations require regular evaluation for dose reduction of antipsychotic medications. Many nursing home patients will tolerate reduction or discontinuation when performed in a gradual manner (28), (29). Patients must be continuously reassessed for side effects and medication efficacy. Dose reductions are required on an annual basis for asymptomatic patients. Switching medication is best managed by gradual dose reduction and up-titration of the new medication.

**4. Anticonvulsants/Mood Stabilizer Therapy for Behavioral Problems in Dementia**

A range of anticonvulsant medications has been studied in persons with dementia to treat severe or dangerous behavioral problems, especially with impulsive or emotionally labile patients (30). Valproic acid is the best characterized antiepileptic drug; however, this medication has relatively little data to support

efficacy **(Table 12).** Tegretol is reported as effective; however, inadequate randomized controlled studies are available to confirm a positive therapeutic benefit for behavioral problems in dementia. Other antiepileptic medication such as Lamictal, have individual case reports that suggest efficacy; however, inadequate systematic data is available to confirm this benefit. None of these medications presently hold an FDA indication for behavioral problems in dementia.

Lithium is a mood-stabilizing agent that may provide some assistance for severe, treatment refractory behavioral problems. Randomized controlled studies are not available to determine the efficacy and tolerability of lithium. Low doses may be effective in some patients and serum levels should remain below 1.0 Mεg/l **(See Appendix E).**

Available scientific evidence is inadequate to assess the therapeutic efficacy of antiepileptic medications or lithium in patients with Frontotemporal dementia, vascular dementia, diffuse Lewy body disease or alcohol-induced dementia.

**5. Antidepressant Therapy for Behavioral Management in Dementia**

Depression is a common psychiatric disorder in most types of dementia that can produce behavioral symptoms. Several classes of antidepressant medications have been examined as beneficial for persons with NPSD without clear evidence of depression. Clinical reports for individual SSRI's suggest potential benefit; however, systematic evidence is not available to confirm therapeutic efficacy. A RCT of citalopram versus risperidone demonstrated equal efficacy for reducing the intensity of NPSD (20). Tricyclic antidepressants, monoamine oxidase inhibitors, and atypical antidepressants such as Wellbutrin, are rarely used in the treatment of behavioral problems **(Table 12).** Antidepressants with high anticholinergic side effects, e.g, Elavil, should be avoided in the elderly or demented person. Antidepressant medications are indicated under FDA guidelines for treatment of depression in dementia (**Appendix F).**

Available scientific evidence is inadequate to assess the therapeutic benefit of antidepressant medications for individuals with behavioral problems produced by diffuse Lewy body disease, Frontotemporal dementia or alcohol-induced dementia. These medications are most likely effective for depression caused by these neurodegenerative disorders.

**6. Benzodiazepine Therapy in Management of Behavioral Problems in Dementia**

Anxiety is a common symptom in all stages of dementia and severe anxiety may produce restlessness or agitation. Benzodiazepines are often prescribed for patients with behavioral problems resulting from dementia (32). Benzodiazepines are generally contraindicated in people with dementia due to risk for falls and delirium. The best available data fails to support the therapeutic efficacy of these medications for persons with any type of dementia **(Table 12).** Dosing is included in **Appendix G.** Benzodiazepine prescription should be limited to reducing symptoms of anxiety disorders in mildly demented patients. Short-term insomnia may respond to appropriate dose of short-acting, hypnotic medications **(Appendix G).** Benzodiazepines (BZD) and BZD receptor agonist are rarely effective for chronic sleep disorders in persons with dementia. OBRA regulations prohibit the long-term prescription of benzodiazepines for nursing home residents without a diagnosis of anxiety disorder.

**7. Cholinesterase Inhibitor Therapy for NSPD**

Substantial data supports the role of cholinesterase inhibitors in reducing behavioral problems associated with Alzheimer's disease (33), (34), (35), (36). Acetylcholinesterase inhibitors (ACHEI's) appear beneficial in all stages of
the illness and efficacy appears unrelated to enhancement of cognitive function **(Table 18).** Sufficient numbers of randomized controlled studies are not available to provide a meta analysis that confirms these individual reports.

Cholinesterase inhibitors appear effective for NPSD in Alzheimer's disease; however, their therapeutic benefit remains unclear in vascular dementia and diffuse Lewy body disease. Patients with alcohol-induced dementia or Frontotemporal dementia may derive little benefit from these medications or may actually have slight worsening of symptoms (23), (37), (38).

**Table 18. Treatment of Delusions in AD with ACHEI's**

| Medication | n | Duration | RS | Outcome | Ref (s) |
|---|---|---|---|---|---|
| Donepezil | 3 | 6 to 12 mos. | 10 to 134 | Improvement | C1, C2 |
| Rivastigmine | 1 | 104 wks | 34 | No benefit to delusions | C3 |
| Galantamine | 1 | 2 wks | 978 | No benefit to delusions | C4 |

n=number of studies RS=range of subjects

Dementia Geriatr. Cog. Disorder 2006;22:260-66

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## 8. Acute Management of NPSD

Patients with dementia may develop severe, acute onset behavioral problems that require an immediate pharmacological intervention while the clinical team assesses the patient to determine the cause of the behavior. Injectable benzodiazepines may produce immediate sedation or these medications may cause paradoxical excitation in a sub-population of patients. Injectable, first or second generation antipsychotic medications are often used to treat acute agitation. Injectable, old medications or new medications can be used to treat severe acute onset behavioral disturbances. Dosing is based on the severity of symptoms, the patient's past response to this class of medication, body mass, and risk factors for side effects **(See Appendix H.)** Low dose antipsychotics are often used to manage acute delirium; however, the efficacy is marginal. Clinicians should avoid combined simultaneous administration of APM's and benzodiazepines, as this practice may produce acute intoxication of excessive sedation.

## 9. Other Medication for NPSD

A variety of other medications have been suggested as beneficial for NPSD in Alzheimer's disease. A meta analysis of five studies suggest that Namenda may reduce some behavioral problems produced by dementia **(Table 13**), (40). Buspar, a mixed receptor agent that reduces anxiety, may be helpful in a few patients although efficacy remains highly controversial. Namenda is not shown to be beneficial in persons with alcohol-induced dementia or Frontotemporal dementia.

## 10. Behavioral Interventions for NPSD

Behavioral interventions should be used as the primary management strategy for NPSD or in combination with psychotropic medications. A wide range of side effects occur in persons with dementia who are treated with psychotropic medications commonly prescribed for psychiatric or medical problems **(Table 1).** A wide range of behavioral interventions are shown to be effective for NPSD and these safe treatments should be used prior to use of medications **(Table 19).**

**Table 19**

| INTERVENTION | STUDIES | RESULT |
|---|---|---|
| Sensory | 23 | Strong music effect |
| Social Contact | 9 | Strong Pet Effect |
| Behavior | 24 | Variable Effect |
| Activities | 7 | Strong Effect for Exercise and Structured Activities |
| Environmental | 6 | All Decrease Behaviors |
| Medical | 2 | Strong Light Effect |
| Combination | 5 | |

*AM. J. Geriatric Psych., 9(4), 368-381, 2001*

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Psychotropic medications are not a substitute for behavioral management strategies. Psychotropic medications have limited efficacy in reducing behavior symptoms (41). Nursing home regulations require consideration or implementation of behavioral management prior to prescription of psychotropic medications. A better strategy involves use of combination therapy (ACHEI's) and memantine along with behavioral management and meticulous medical care.

**11. Treatment of Elderly Patients with Serious Mental Illness (SMI) and Dementia**

Individuals with serious mental illness, such as schizophrenia or bipolar disorders, usually have persistent symptoms into later life (41). These patients require continued therapy and this practice is acceptable under OBRA regulations. Clinicians must document efficacy and side effects. Dose reduction is not required for stable patients. Switching medication in stabilized patients for "formulary" reasons can produce behavioral complications. Each medication has unique pharmacological qualities and stabilized patients may not tolerate a switch to a different SGA. Polypharmacy is commonly used in older persons with SMI. Polypharmacy has not been demonstrated as more effective for older patients and may trigger review as excessive medication (26), (27). Medical directors may wish to seek a second opinion from a psychiatrist for older persons with SMI and APM polypharmacy.

**12. Conclusions about the Role of APM in Treating NPSD**

APM's may produce serious side effects **(Table 19).** The use of APM's in persons with dementia is controversial (42). Prescription of any psychotropic medications for NPSD requires a clear target symptom and monitoring program to measure efficacy. The monitoring method will depend on the clinical condition **(Table 20).** The inappropriate prescription of APM's in the LTC setting has increased over the last decade (43) with less than half receiving medications that comply with federal guidelines **(See Table 21).** The cost-benefit ratio of APM's in older patients with dementia demonstrates a neutral cost effect **(See Table 22)**, (44). These medications should be used sparingly and with great care as defined in the guidelines provided by the ACNP White Paper of 2007 **(Appendix A2)** (40) or other best practices (45), (46), (47), (48). Ineffective medications should be discontinued or patients should be cross-titrated to new medications (49).

**Table 20. Methods of Assessing Therapeutic Benefit and Toxicity of Antipsychotic Medications in Long-Term Care Facilities**

| Severity of Dementia | Self-Reporting by Patient | Caregiver Reporting | Behavioral Monitoring |
|---|---|---|---|
| Mild | R | R | H |
| Moderate | H | R | R |
| Severe | U | R | R |

**R**=required **H**=helpful, but not always required **U**=unreliable

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**Table 21. Mis-prescription of APM's in LTC Facilities in 2001-2002**

| % | Findings |
|---|---|
| 58.2 | No CMS compliance |
| 23.4 | No appropriate indication |
| 17.2 | Excessive dosing |
| 17.6 | High dose + no indication |
| Outcomes not different between CMS compliant vs non-compliant prescriptions | |

Arch Int. Med. 2005;165:1280-85

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**Table 22. Cost-Efficacy of SGA's for Psychosis and Aggression in Dementia vs Citalopram or Watchful Waiting**

- n=421
- t= 9 months
- NSD – outcome
- ↓ cost – placebo group

Arch Gen Psych 2007;64( n ):1259-68

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## Appendix A

## 2007 ACNP White Paper on Use of APM's in Elderly Persons with Dementia

### The 10 Clinical Commandments

**Thou Shalt:**

- Investigate etiology of targeted symptoms.
- Exhaust other general therapeutic interventions.
- Share decision-making with family and other physicians.
- Define specific target symptoms.
- Select specific, individual medications.
- Prescribe minimum effective doses.
- Measure effectiveness.
- Monitor patient safety.
- Inform family on FDA warnings.
- Discontinue ineffective medications.

*Neuro-psychopharmacology 2007;18:1-14.*

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## Appendix B. Ten Commandments of OBRA For Psychotropic Medication

1. Thou shalt know thy regulations.
2. Thou shalt not prescribe medications from the list of the condemned drugs.
3. Thou shalt first try behavioral management.
4. Thou shalt document clinical indications and target symptoms.
5. Thou shalt honor the dose limits unless documented in the medical record.
6. Thou shalt honor the time limits on prescriptions unless documented in the chart.
7. Thou shalt monitor for side effects.
8. Thou shalt reduce or discontinue medications for adverse events.
9. Thou shalt comply with periodic dose reductions unless documented in thine record.
10. Thou shalt not seek to smite the surveyor. They are simply carrying the tablets.

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# Appendix C
# Common Side Effects of Importance for Clinicians

**Appendix. C1. A Partial Summary of Common Side Effects Produced by Antipsychotic Medications in Persons with Dementia (45,46)**

| Category of Side Effect | Symptom of Side Effect | First Generation Antipsychotic Medications at Greater Risk | Risk Level | Second Generation Antipsychotic Medications at Greater Risk | Risk Level | Comments for All Types of Medications |
|---|---|---|---|---|---|---|
| **COGNITIVE** | Confusion | Low Potency, e.g., chloropromazine | H | All equal | L | All medications at high dose |
| | Sedation | Low Potency, e.g., chloropromazine | H | Quetiapine | L | All medications at high dose |
| **NEUROLOGICAL** | Parkinsonism | High potency haloperidol | H | Risperdal | L | Quetiapine quite low |
| | Dystonia | High potency haloperidol | H | All equal | R | |
| | Tardive Dyskinesia | All Medications | H | All equal | I | |
| | Akathisia | High potency, e.g., haloperidol | H | Aripiprazole | I | |
| **METABOLIC** | Obesity | Some reported in all medications | M | Olanzapine and Clozapine | M | Monitor Weight |
| | Hyperglycemia | Some reported in all medications | M | Olanzapine and Clozapine | M | Aripiprazole and ziprasidone with low risk |
| | Dyslipidemia | Some reported in all medications | I, M | Clozapine | M | Monitor lipids with all medications |
| **AUTONOMIC** | Orthostatic hypotension | Low potency, e.g., chloropromazine | H | Seroquel, Clozapine | L | --- |
| | Tachychardia | Low potency | I | Clozapine | L | --- |
| **NEUROLEPTIC MALIGNANT SYNDROME** | Hypertension, Tachycardia, Hyperthermia, Muscular Rigidity | All high potency, e.g., haloperidol | L | All equal | R | Rare in second generation medications |
| **OTHER (drug-specific)** | Cardiac QTc Prolongation | thioridazine | H | Ziprasidone | I | Most have minimal effect |
| | Agranulocytosis | All equal | L | Clozapine only | H | --- |
| **BLACK BOX** | Black box for ↑ mortality in elderly with dementia | All Medications | L | All Medications | L | All drugs have a Black Box warning |

H=high M=moderate L=low R=rare I=Inconclusive

**Appendix C2**

**Basic Monitoring of Metabolic Effects of Antipsychotic Medications**

| | Prior to therapy | 4 weeks | 8 weeks | 12 weeks | Quarterly | Annually | Every 5 years |
|---|---|---|---|---|---|---|---|
| **Personal/family history** | X | | | | | X | |
| **Weight (BMI)** | X | X | X | X | X | | |
| **Waist circumference** | X | | | | | X | |
| **Blood pressure** | X | | | X | | X | |
| **Fasting plasma glucose** | X | | | X | | X | |
| **Fasting lipid profile** | X | | | X | | | X |

Diabetes Care 2004;27(2):599

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# D. Dosing Ranges for Prescription of Antipsychotic Medications for Elderly with Dementia

**Appendix D1. Summary of Common Doses of Antipsychotic Medications Prescribed for Younger and Elderly Populations with Dementia*** (45, 46)

| Drug | Healthy/Adult Daily Dose | Frail/Elderly Daily Dose | Maximum OBRA Dose | Major Advisory |
|---|---|---|---|---|
| **1st Generation** | | | | |
| Chlorpromazine | 30-800mg | 10-200mg | 75mg | Anticholinergic Side Effects |
| Thioridazine | 50-800 | 10-400mg | 75mg | Blackbox Cardiac Warning |
| Haloperidol | 1.0-30mg | 0.5-5.0mg | 4mg | High potential for EPS/TD |
| Fluphenazine | 0.5-40 | 0.5-20 | 4mg | High potential for EPS/TD |
| **2nd Generation** | | | | |
| Clozapine | 12.5-900 | 12.5-450 | 50mg | Black Box for Agranulocytosis |
| Risperidone | 1-8mg | 0.25-2.0mg | 2mg | Dose-related EPS |
| Olanzapine | 5-20mg | 2.5-10mg | 10mg | Sedation and Metabolic Issues |
| Quetiapine | 25-800mg | 25-200mg | 200mg | Sedation and Hypotension Possible |
| Ziprasidone | 20-160mg | 20-80mg | NA | Cardiac QTc Warning |
| Aripiprazole | 5-30mg | 5-20mg | NA | Akathisia and/or withdrawal Dyskinesia Possible |

*All drugs have an FDA Black Box warning for increased mortality in AD patients

DOSAGE MUST BE ADJUSTED FOR EACH PATIENT

CONSULT PDR

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**Appendix D2. Summary of Injectable, Long-Acting Preparation (Depot Preparations) of Antipsychotic Medications for the Adult Patient with Dementia (Dosing Range in Milligrams – Given Every 2 Weeks) (45, 46)**

| Intramuscular Medication | IM Dose for Frail/Elderly (mg) | IM Dose for Young Healthy (mg) |
|---|---|---|
| Haloperidol (Haldol decanoate) *every two weeks* | 12.5 to 25 | 12.5 to 75 |
| Perphenazine (Prolixin decanoate) *every two weeks* | 2.5 to 25 | 12.5 to 50 |
| Risperdal Consta – *every two weeks* | 25 | 25 to 37.5 |
| *Dose frequency may be increased with longer duration between injections, e.g., every 3 to 4 months.* | | |

*All drugs have an FDA Black Box warning for increased mortality in AD patients

DOSAGE MUST BE ADJUSTED FOR EACH PATIENT

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# Appendix E
# Dosage Ranges for Anticonvulsant and Mood Stabilizing Medications Commonly Prescribed for NPSD in Dementia

**Appendix E. Commonly Prescribed Doses of Mood Stabilizing or Impulsive Agents for Adults with Dementia** (45, 46)

| Medication | Daily Dose for Healthy/Young | | Daily Dose for Frail/Elderly | | Comments (See PDR) |
|---|---|---|---|---|---|
| | *Dose (mg)* | *Target Blood Level* | *Dose (mg)* | *Target Blood Level* | |
| Valproic Acid | 750 to 2400mg* | 50 to 125mcg/ml | 750 to 1500mg* | 50 to 100 mcg/ml | Hepato toxicity<br>Low Platelets |
| Carbamazepine | 400 to 1600mg | 4 to 10 mcg/ml | 200 to 800mg | 2 to 8 mcg/ml | Neutropenia<br>Hyponatremia |
| Lithium | 300 to 1200mg | 0.5 to 1.5mEq/L | 150 to 600mg | 0.2 to 1.0 mEq/L | Multiple drug interactions<br>Narrow Therapeutic Window |
| Dose ranges are commonly prescribed for mood stabilization or anti-impulsive effect. All doses must be individually adjusted for the individual patient. Consult with PDR for complete information. | | | | | |

***=60mg / kg / day**

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# Appendix F
# Dosage Ranges for Antidepressant Medications Commonly Prescribed for NPSD

**Appendix F1. Suggested Dosing Range for Antidepressant Medications for the Population with Dementia (45, 46)**

| Drug | Young Healthy/Adult Daily Dose | Frail/Elderly Daily Dose | Comments |
|---|---|---|---|
| **1st Generation (TCA's)** | | | |
| Nortriptyline | 25-150mg | 10-100mg | Therapeutic Level 50-150ng/ml |
| **2nd Generation (SSRI's** | | | |
| Fluoxetine | 10-80mg | 10-40mg | Generic Available. May be activating |
| Paroxetine | 25-50mg | 10-40mg | Generic Available. Anticholinergic |
| Sertraline | 50-200mg | 25-100mg | GI Side effects. Take with food |
| Citalopram | 20-60mg | 10-40mg | Few significant drug interactions |
| Escitalopram | 20-40mg | 5-20mg | Few significant drug interactions |

**DOSAGE MUST BE INDIVIDUALLY ADJUSTED FOR EACH PATIENT.**
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**Appendix F2. Suggested Dosing Range for Antidepressant Medications for the Population with Dementia (45, 46)**

| Drug | Young Healthy/Adult Daily Dose | Frail/Elderly Daily Dose | Comments |
|---|---|---|---|
| **3rd Generation (SNRI's, Others)** | | | |
| Bupropion | 150-300mg | 75-300mg | Use Caution with Seizure disorders |
| Mirtazapine | 15-45mg | 7.5-45mg | Weight gain. Sedate at lower doses (<30) |
| Trazodone | 150-600mg | 25-150mg | Monitor Priapism and Orthostasis |
| Venlafaxine | 75-375mg | 37.5-225mg | Monitor for Hypertension |
| Duloxetine | 40-60mg | 20-40mg | Dual Re-uptake Inhibitor, All doses |

**DOSAGE MUST BE INDIVIDUALLY ADJUSTED FOR EACH PATIENT.**
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# Appendix G
# Sedative-Hypnotic Medications Commonly Used In NPSD

**Appendix G1. Commonly Used Dosing Ranges of Benzodiazepines Anxiolytic Medications or Receptor Agonists for the Adult Population with Dementia (45, 46)**

| Drug | Healthy/Adult Daily Dose | Frail/Elderly Daily Dose | Comments (See PDR for further details) |
|---|---|---|---|
| **Long-Acting (t1/2>24hrs)** | | | |
| Diazepam (Valium) | 5-20mg | 2-10mg | Very fast onset of action |
| Clonazepam (Klonopin) | 0.5-4mg | 0.25-2mg | No active metabolites |
| Chlordiazepoxide (Librium) | 5-300mg | 5-20mg | Useful treating alcohol withdrawal |
| **Intermediate (t1/2=12-24hrs)** | | | |
| Alprazolam (Xanax) | 0.5-4mg | 0.125-2mg | Fast onset of action |
| Temazepam (Restoril) | 15-30mg | 7.5-15mg | No active metabolites |
| Lorazepam (Ativan) | 0.5-6mg | 0.25-2mg | No active metabolites |
| Oxazepam (Serax) | 15-60mg | 7.5-30mg | No active metabolites |
| **Short Acting (t1/2<12hrs)** | | | |
| Zolpidem (Ambien) | 5-10mg | 5mg | Only indicated for acute insomnia |
| Eszopiclone (Lunesta) | 1-3mg | 1-2mg | Indication for chronic insomnia |

***All benzodiazepine medications may be addictive and produce delirium, falls or excessive sedation. These medications are not recommended for persons with dementia.***

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**Appendix G2. Benzodiazepine for Hypnotic Agents (45, 46)**

| Mech | Generic | Brand | T ½ (hrs) | Dose (mg) | Comment |
|---|---|---|---|---|---|
| Maint. | Temazepam | Restoril | 3.5-18 (I) | 7.5-30 | Falls |
| Maint. | Estazolam | Prosom | 10-24 (I) | 0.5-2 | Falls |
| Initiation | Triazolam | Halcion | 2-5 (S) | .125-.25 | Avoid |
| **BZD Receptor Agonists** | | | | | |
| Maint. | Eszopiclone | Lunesta | 5-7 (I) | 1-2 | confusion |
| Initiation | Zolpidem | Ambien | 3 (S) | 5-10 | confusion |
| Initiation | Zaleplon | Sonata | 1 (US) | 5-20 | confusion |
| **Melatonin Receptor Agonists** | | | | | |
| Initiation | Ramelteon | Rozerem | 2-5 (S) | 8mgm | --- |
| **Other** | | | | | |
| Initiation | Trazodone | Desyrel | | 25 to 50 | --- |

***All benzodiazepine medications may be addictive and produce delirium, falls or excessive sedation. These medications are not recommended for persons with dementia.***

S=short US=ultra short I=intermediate

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## Appendix H. Common Dosing Ranging of Injectable Medications for Acute Agitation or Assaultiveness in the Adult Patient with Dementia (dosing range in milligrams) (45, 46)

| Medication | Frail or Old (mg) | Healthy (mg) | Caution (See PDR) |
|---|---|---|---|
| Haldol (haloperidol)[1] | 0.5 to 2.5 | 1 to 5 | Acute EPS |
| Zyprexa (olanzapine)[2] | 2.5 to 5 | 2.5 to 10 | Hypotension |
| Geodon (ziprasidone)[3] | 5 to 10 | 10 to 20 | Cardiac Toxicity |

**1** May give Haldol every two hours for a total of four doses in 24 hours. **2** May give a total of three doses of Zyprexa per 24 hours. Second dose may follow first dose by 2 hours and the third dose may be administered four hours after the second. **3** May repeat Geodon once in 2 to 4 hours for a total of two doses in 24 hours.

These values are suggested guidance. Each patient should be individually assessed and dosing adjusted to that individual's clinical circumstances. See PDR for complete information.

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