Rational Medication Use in Dementia

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Objectives

• Discuss the goals of medication use in general, and in dementia.
• Consider the evidence base around benefits and harms of dementia medications.
• Resolve on a reasonable, patient-centered clinical approach.

I have no conflicts of interest to report.

I am an employee of the federal government.

The opinions in this talk are my own.

What are medications supposed to accomplish in general?
What are medications supposed to accomplish in dementia?
How can we ensure that medications produce an overall benefit?
What role can we all play in this process?
SUMMARY:
There is no good reason for general use of medications in dementia.

You can let patients and families know that they have permission not to use medications for dementia.

Ultimately the decision should the patient’s and caregiver’s.

What are medications supposed to accomplish in general?

<table>
<thead>
<tr>
<th>Goal</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eliminate the cause of a disease</td>
<td>Antibiotics</td>
</tr>
<tr>
<td>Reduce unpleasant experience</td>
<td>Medications for itch / pain / mood / gout</td>
</tr>
<tr>
<td>Prevent disease or worsening of disease</td>
<td>Cholesterol medications, diabetes medications</td>
</tr>
<tr>
<td>Improve functioning</td>
<td>Stimulants for ADHD</td>
</tr>
<tr>
<td>Increase lifespan</td>
<td>Cardiac medications</td>
</tr>
<tr>
<td>Emotional benefit</td>
<td>Antibiotics for ear infection</td>
</tr>
</tbody>
</table>

Is the pill accomplishing the goal?

Status

TIME

General Problems

“You have this condition, so you need to take this pill.” (guideline- rather than outcome-based)

All treatments involve costs and risks.

What if there is a tradeoff between goals and costs/risks?

Who gets to choose the goals?
Central problem: Dementia is a **deteriorating** condition.

A **moving target** can justify any conclusions.

Symptoms may be at one **stage** of disease.

Dementia symptoms **fluctuate**.
Therefore: The treatment may not be the reason for improvements.

Medication Types
- Memory medications
- Medications to treat behavioral symptoms
- Medications for other psychiatric symptoms

“Memory” Medications
There are no pills that specifically improve memory.
Cholinesterase inhibitors (donepezil, galantamine, rivastigmine) and memantine are FDA-approved for dementia.
Pills approved for dementia may improve cognitive outcomes in the short term.
These medications are not a cure.
They are nothing like a cure.

“Memory” Medications
There are no pills known to prevent dementia.
There are no medications approved for mild cognitive impairment.
“Memory” Medications

Anticipated optimal effects:
- 0.8 point on a 30-point cognition scale
- About 1 ADL on a 17-point scale

About 1 ADL on a 17-point scale

Memory Medications

“no significant differences were seen between donepezil and placebo in behavioural and psychological symptoms, carer psychopathology, formal care costs, unpaid caregiver time, adverse events or deaths”

The package insert

12. CLINICAL PHARMACOLOGY
12.1. Mechanism of Action
Current theories on the pathogenesis of the cognitive signs and symptoms of Alzheimer’s disease attribute some of them to a deficiency of cholinergic neurotransmission.

Donepezil hydrochloride is postulated to exert its therapeutic effect by enhancing cholinergic function. This is accomplished by increasing the concentration of acetylcholine through reversible inhibition of its metabolism by acetylcholinesterase. There is no evidence that donepezil alters the course of the underlying dementia process.

The ad
Memantine

“Although statistical improvements were noted in the analyses, they do not necessarily translate into clinically relevant benefits for the patients receiving these drugs or for their caregivers.”


Costs

Difficult to estimate exactly
Some medications have become generic
Namenda (memantine): about $300 a month
Total sales in 2014: $1.8 billion

Side Effects

GI upset, diarrhea
Unexpected effects (loss of energy, odd behavior, anxiety)
Most are transitory
Known Long-Term Risks

- Weight loss
- Falls
- Hospitalizations
- Starting medications for urinary overflow (which then counteract the dementia medications)
- Polypharmacy
- Depression

Donepezil and Depression

130 older adults with history of depression
73 no cognitive impairment
57 mild cognitive impairment

Randomized to donepezil or placebo

Cognition and mood outcomes

Those on donepezil had far higher rates of depression recurrence compared to placebo


Explaining Negative Events in Dementia

Most people who have problems during dementia blame them on the DISEASE and not the TREATMENT. Many effects of treatment are delayed (and thus hard to connect to the Rx).

Exposing the effects of treatments requires careful and thoughtful examination of large amounts of data.

It has taken time and effort to establish risks.

New Drugs for Alzheimer’s

Many new drugs have been tried.

None has been approved in over 15 years.

No new drugs will be on the market any time soon.

Families and patients may be desperate.
Medications Approved by FDA to Treat Behavioral Symptoms of Dementia:

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All medication use to treat behavioral symptoms of dementia is OFF LABEL

NEWS FLASH: Medical Breakthrough Reduces Risk of Death by 38% in Large Group of Dementia Patients

Antipsychotics in Dementia

1.6 times increased risk of DEATH from antipsychotics compared to placebo.

About 25% of people with dementia in nursing homes are prescribed an antipsychotic
**WARNING: Increased Mortality in Elderly Patients With Dementia-Related Psychosis**

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Analyses of 17 placebo-controlled trials (modal duration* of 10 weeks), largely in patients taking atypical antipsychotic drugs, revealed a risk of death in drug-treated patients of between 1.6 to 1.7 times the risk of death in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group.

Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infections (e.g., pneumonia) in nature. Observational studies suggest that, similar to atypical antipsychotic drugs, treatment with conventional antipsychotic drugs may increase mortality.

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**Antidepressants**

People with dementia often seem apathetic.

Antidepressants are frequently used to address negative mood states or irritability.

But antidepressants often do not work as intended.

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**Antidepressants**

What is the therapeutic value of antidepressants in dementia? A narrative review

Nicolas Farina¹, Lucy Morrell² and Sube Banerjee³

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“the antidepressants tested to date show no convincing advantage over placebo for the treatment of depression in dementia.”

No evidence for use of antidepressants to address cognition, caregiver burden, cognition, psychosis, or apathy.

“We should question the use of antidepressants in dementia.”

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**Even Beneficial Side Effects Are Missing**

Mirtazapine does not improve sleep disorders in Alzheimer’s disease: results from a double-blind, placebo-controlled pilot study

Francisca M. SCORALICK,¹ Luciana L. LOUZADA,¹ Juliana L. QUINTAS,¹ Jureth O.S. NAVES,² Einstein P. CAMARGOS³ and Otávio T. NÓBREGA³

Psychogeriatrics, 2017

→ Psychotropic medications often DO NOT WORK AS EXPECTED in dementia.
Discontinuation

Stopping pills is usually MORE DIFFICULT than starting them.

People often stop medications DURING difficult times -> this does not mean that the stopping caused problems.

When planned carefully, discontinuation usually causes few problems.

The WRONG Way to Use Medications for Dementia

“If you have dementia, you should be taking a pill for it.”

“If a pill exists to treat your condition, you should take it.”

“The pills protect you from getting worse.”

“The pills have very few risks.”

“Pills are the best way to deal with the problems in dementia.”

“If a pill worked at first, you should keep taking it.”

The RIGHT Way to Use Medications for Dementia

“Let us talk about the course of dementia.”

“What is your experience with dementia?”

“Medications can have some benefits, but also can have risks. Let’s discuss them.”

“What are we trying to accomplish? What are your values and preferences?”

“How can we know if the medication is working?”

“Let’s keep re-assessing the effect of the medications.”

“You can try stopping. If things seem worse, you can restart.”
Agitation

Figure out what is going on before turning to medications

Main reasons for agitation:
- Delirium
  → MAIN CAUSE OF DELIRIUM: MEDICATIONS
- Unmet needs
- Conditioning
- Natural response

GIVING PERMISSION

There is a reasonable scientific and ethical case for avoiding medications in dementia, or for stopping those that have been used, focusing instead on behavioral interventions and caregiver support.

You can let people know that they do not have to be using medications for dementia.

Ultimately the decision should be the patient’s and caregiver’s.

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