Is There a Pill that Will Help with Alzheimer’s Dementia Prevention, Progression, or Behaviors Associated with Dementia?

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Medications in 2019
What do we think now?
Objectives

1. What does the current research say about prevention for Alzheimer's Dementia?
   ➤ Are there medications that help prevent dementia?

2. Are there medications that can treat Dementia?
   ➤ If so, how effective are they?

3. Are there medications that can help with the treatment of behaviors associated with Dementia?
   ➤ How beneficial are these medications, and what are the risks of using them?
The Scope of Alzheimer’s Dementia

- Affects 5.8 million adults
- Will affect 14 million adults by 2050
- 1 in 10 adults age > 65 years old
- 1 in 3 adults age > 85 years old
- 2/3 are women
- People are living longer with fewer fatalities from other diseases → More people develop Alzheimer’s Dementia

Alzheimer’s Association data 2019

There are Many Types of Dementias

- Alzheimer’s Dementia
- Multi-infarct Dementia
- Dementia associated with Parkinson’s Disease
- Lewy Body Dementia

Most people have a combination of Dementias

Prevention is based on the cause of the dementia

- Research for the prevention of Alzheimer’s disease and related dementia is prolific and ongoing
- 2 large reviews of the research for the Prevention of Alzheimer’s disease and related dementias were published in the Annals of Internal Medicine and the Lancet in 2017
- There is no magic bullet, but there are things that we can do that may be beneficial by considering the cause of some dementia(s).


Prevention of Alzheimer's Disease and related dementias

► There is no medication or supplement that has been proven through medical research to provide cognitive protection from developing dementia

► There are medications that can treat high blood pressure, diabetes, and heart disease. This in turn decreases the risk of diseases that can lead to some dementias (Stroke, multi-infarct Dementia)


Why is it so Hard to find effective interventions to prevent Alzheimer’s Disease and related Dementias?

► This disease can take decades to show symptoms
► Prevention will need to be studied in people decades before symptoms appear
► Dementia has many causes and combinations in each person → prevention may need to be individualized to the specific person

Prevention of Alzheimer's Disease and related Dementias

Why is it so hard to find effective interventions to prevent Alzheimer’s Disease and related dementia?

The appears to be other factors associated with showing Symptoms of Dementia besides what is in our Brain

- Some people have the brain changes that cause Alzheimer’s Dementia but show few symptoms in real life
- Some countries (USA, Sweden, Canada) have had an unexpected decline in the prevalence of Alzheimer’s disease and related dementias. Other countries, like China, have not had this decline.


Two Schools of Thought for Dementia Prevention

- The Lancet Commission for Dementia Prevention, Intervention, and Care 2017
- The best chance for preventing dementia is a “Life Course” approach
- The National Academy of Medicine found classes of interventions that were encouraging to help prevent dementia, though such interventions were ultimately inconclusive (2017).
  - Blood pressure management
  - Increased physical activity
  - Potentially cognitive training

National Academies of Science, Engineering and Medicine, Preventing Cognitive Decline and Dementia: A way Forward. National Academies PR:2017
So, What does this Mean?

According to the Lancet Commission:
- 35% of potential risk factors for dementia are modifiable from Birth to late life:
  - Hearing Loss
  - HTN
  - Obesity
  - Smoking
  - Physical Activity
  - Depression
  - Social Isolation

Research on Specific Interventions to Prevent Dementia - Hypertension Control

- Hypertension control decreases the risk for a stroke and resultant Dementia
- Hypertension control increases heart and cardiovascular health and decreases micro strokes in the brain
- Current research is also suggestive that hypertension that is well controlled could decrease the risk of multiple kinds of dementia

The SPRINT MIND Investigators for the SPRINT Research Group. Effect of intensive vs standard blood pressure control on probable dementia: a randomized clinical trial [published online January 28, 2019]. JAMA.

Research on Specific Interventions to Prevent Dementia - Physical Activity

- Physical Activity
  - Research suggests physical activity in combination with other healthy habits could be helpful to prevent cognitive decline and Dementia
  - Known to decrease heart disease and cardiovascular risk, obesity, and diabetes
  - Can lead to decreased risk of stroke and resulting dementia


Research on Specific Interventions to Prevent Dementia - Physical Activity

- Physical Activity
  - May directly slow cognitive decline through increased blood flow
  - May indirectly intervene by reducing other risk factors (heart disease, diabetes, and obesity)

Specific Physical Activity:
- Aerobic training, resistance training and multicomponent physical activity are all beneficial

as well as DM and Obesity decreased risk with physical activity.

Leslie Eber, 4/14/2019
Research on Specific Interventions to Prevent Dementia  

Cognitive Training

- In older people with normal cognition, training improves cognitive performance in that trained domain.
- Evidence that cognitive training prevents dementia or slows the progression of dementia is insufficient to date.
- Brain training apps or subscriptions are not harmful but are not proven to be helpful.
- Be cautious of expensive opportunities

Research on Specific Interventions to Prevent Dementia - Medication Interventions

- Medications looked at to prevent dementia:
  - Ibuprofen, Aspirin, Estrogen, Lipid lowering Medications (statins), Evista, Aricept (Cholinesterase inhibitors)
  - NO Medications have been proven to prevent dementia

- Over the counter supplements:
  - W3 fatty acids, soy, Ginkgo Biloba, B vitamins, D vitamins + calcium, Vitamin C, B-carotene and multi-ingredient supplements
  - NO supplement was shown to prevent dementia


Medications that can Increase the Risk of Dementia

- Anti-Cholinergic Medications have now been found to increase the risk of dementia
- Examples of medications that have high anti-cholinergic activity:
  - Benadryl, Detrol, Zanaflex and Zyprexa
- The effect is cumulative and for long-term use


Psuedo Medicine: What is it and Why do We Need to Know about It?

Psuedo Medicine:
- Supplements and medical interventions that exist within the law and are often promoted as scientifically supported treatments but lack credible efficacy data

PsuedoMedicine: What Do We Need to Know?

- $2-3$ billion industry
- Uses individual testimonials as established fact
- The supplement is often widely available and appears to gain legitimacy when sold by a major U.S. retailer
- Supplements are not regulated by the FDA
- Some supplements can be harmful and even cause a stroke, lead to dementia, or result in death (Vitamin E)


PsuedoMedicine: What Do We Need to Know?

The Alzheimer’s Association has taken the initiative to highlight these concerns

- Notes these supplements are promoted by testimonies, not science

PsuedoMedicine: What Do We Need to Know?

- Psuedo medical interventions are not ethically, medically, or financially benign
- Effective interventions for common diseases would already be widely used and be the standard of care.


Treatment of Dementia

- There is no current treatment that has been proven to stop the progression of dementia

Medications to Treat Dementia
Aricept, Razadyne, and Exelon (Cholinesterase Inhibitors)
- Symptomatic therapy
- No neuro-protection
- Does not alter the underlying disease trajectory
- Patients with mild to moderate dementia are more likely to respond, but the effect is modest.
- Dementia continues to progress
- Most often, benefits are short-lived (3-6 months)

Side Effects: Gastro-intestinal and Cardiac

target the acetylcholine deficit arising from loss of neurons
Medications to Treat Dementia
Aricept, Razadyne, and Exelon (Cholinesterase Inhibitors) Continued:

- Effectiveness varies person-to-person
- Aricept is also approved for use in severe Alzheimer’s dementia in combination with Memantine
- Effect is variable, short lived and there are many side effects

Reeve E, Farrell B, et al. Evidence-based Clinical practice guideline for deprescribing cholinesterase inhibitors and memantine. Sydney, Australia: University of Sydney;2018

Medications to Treat Dementia
Aricept, Razadyne, and Exelon (Cholinesterase Inhibitors) Continued:

- 2018 guidelines ~30% of prescriptions for these medications are inappropriate
- Up to 80% of patients have adverse drug reactions

Reeve E, Farrell B, et al. Evidence-based Clinical practice guideline for deprescribing cholinesterase inhibitors and memantine. Sydney, Australia: University of Sydney;2018

Medications to Treat Dementia
Aricept, Razadyne, and Exelon (Cholinesterase Inhibitors) Continued:

- Particular concern: if a patient take these medications in combination with a class of medications called Anticholinergics (used for urinary leakage), muscular spasms or seasonal allergies could result
- These 2 types of medications work directly opposite one another and can both negatively affect Dementia medication and cause harm

Adverse Drug Reactions: slow heart rate, drug to drug interactions, like anticholinergics, diarrhea

Leslie Eber, 4/20/2019
Medications to Treat Dementia

Since these medications only help for a while, what is the RIGHT way to stop them after starting?

- Tapering these medications to off is not “giving up”
- It is assessing if this medication is helping and weighing the risk/benefit of the medication
- Do Not Stop Abruptly: This can lead to worsening cognition, behavior, and withdrawal symptoms

Reeve E, Farrell B, et al. Evidence-based Clinical practice guideline for deprescribing cholinesterase inhibitors and memantine. Sydney, Australia: University of Sydney; 2018

Namenda (NMDA Receptor Antagonist)

- For moderate Alzheimer’s Dementia patients
- Again, modest effect for 3-6 months
- Question of benefit when combined with Cholinesterase Inhibitors
- Studies find this medication to be less effective than Cholinesterase Inhibitors
- There was no statistical signs of effectiveness at 12 months

LE3  1/2 the medication every 4 weeks with close monitoring, Trial discontinuation
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LE4  Note: discontinuation deteriation may also be due to the progression of the disease it's self
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EBE1  what kind of behaviors???
Eber, Benjamin E., 4/21/2019
Behaviors Associated with Dementia

What are some of the behaviors associated with dementia?

- Agitation, anxiety, irritability, depression, apathy, disinhibition, delusions, hallucinations, and sleep or appetite changes, refusal of care
- These behaviors are also called behavioral and psychological symptoms of dementia

Kezia Scales, PhD Sheryl Zimmerman, PhD et al. Evidence-Based Nonpharmacological Practices to Address Behavioral and Psychological Symptoms of Dementia. The Gerontologist, Volume 58, Issue suppl_1, February 2018, Pages S88–S102

Are There Medications that Can Help with These Behaviors?

Medications that have been tried:

- Benzodiazapines (Ativan, Klonapin, Valium)
- Atypical antipsychotics (Seroquel, Zyprexa, Respidal)
- Antipsychotics (Haldol)

- None of these medications have been showed to be helpful to decrease behaviors
- They can ALL be harmful


Are There Medications that Can Help with These Behaviors?

There have been many studies on medications to see if they can help with the behaviors associated with dementia

None have been successful
Are there Medications that can Help with these Behaviors?

- There are now national, federal, and international initiatives to discourage the use of these medications for dementia behaviors
- Because of their harm and lack of effectiveness
- There is now a **BLACK BOX** warning on the use of some medications like Seroquel, Resperdal and Zyprexa
- Increased risk of diabetes and mortality.


Behaviors with Dementia: What can we do?

Alzheimer’s Association Tools

- **Person-centered Care**
- **Sensory practices**: aromatherapy, massage, multisensory stimulation, bright light therapy
- **Psychosocial practices**: validation therapy, reminiscence therapy, music therapy, pet therapy, meaningful activities
- **Structured care protocols**: bathing, mouth care

Kezia Scales, PhD, Sheryl Zimmerman, PhD et al. Evidence-Based Nonpharmacological Practices to Address Behavioral and Psychological Symptoms of Dementia. The Gerontologist, Volume 58, Issue suppl_1, February 2018, Pages S88–S102

Behaviors with Dementia: What can we do?

Alzheimer’s Association Tools: undesirable behavior observed

**Detect**: Who is involved?
- What is happening?
- Where is this happening?
- When is it happening? What time?
- Why do you think it is happening?
Behaviors with Dementia: What can we do?

Alzheimer’s Association Tools: Undesirable behavior observed

**Connect:**
- Approach calmly and respectfully
- Be friendly first
- Use your knowledge of the person
- Join their reality
- Focus on feelings and emotions
- Validate their concerns
- Reassure and redirect

**Check for Physical Needs:**
- Pain
- Hunger
- Thirst
- Bathroom
- Cold/Hot
Behaviors with Dementia: What can we do?

Alzheimer's Association Tools: Undesirable behavior observed

Check for Emotional Needs: Fear
- Anxiety
- Frustration
- Boredom
- Overstimulation
- Loneliness

Reassess and plan for next time: What worked?
What didn't?

Behaviors with Dementia: What can we do?

Alzheimer’s Association Tools: Other helpful recommendations

- Respond without taking offense or arguing
- Logic and reasoning are not helpful
- Allow the person to make simple choices
- Consider doing the task at a different time/in a different way

Behaviors with Dementia: What can we do?

The Colorado Dementia Partnership

A Collaboration with:

Geriatric Doctors, The Colorado Society for Post-Acute and Long-Term Care Medicine, Geriatric Psychiatrist, Alzheimer’s Association, Colorado Health Care Association, and the Colorado Department of Health

Mission: To Enhance the Care of people with Dementia
Behaviors with Dementia: What can we do?

The Colorado Dementia Partnership

R Rule out acute illness, pain, or discomfort
E Engage the senses: sight, touch, smell, taste, and sound
S Soothe: Evaluate the environment of noise, climate and other stimulators
P Practice calm, adjust your body to be at their eye level
O Offer meaningful choices and things to do
N Never argue, confront, or tell the resident they are wrong
D Develop a plan for physical movement, exercise, and fresh air

Behaviors with Dementia: What can we do?

Caring for the Care Giver!

Thank you!
Questions?