Nathan Rawls, Pharm.D.

Clinical Pharmacy Specialist, Geriatrics
Veterans Affairs Medical Center
Professor, Department of Clinical Pharmacy
College of Pharmacy, University of Tennessee
Memphis, TN

Clinical Controversies in Geriatric Practice

Facts, Observations & Opinions

Disclosure Information

2014 Geriatric & Long-Term Care Conference
Nathan Rawls, Pharm.D.

I have no financial relationships to disclose
and
I will not discuss off label use and/or investigational use in my presentation

Presentation Topics

- Hypertension in the Elderly
- What did you say? (hearing loss)
- Statins in the Elderly: Risks vs Benefits
- Drug-induced movement disorders: What to worry about.
- Preventing Dementia?

Definitions of Aging

- Geriatric (1909) geras " old age" + iatric "of a physician"
- Senior Citizen- (1938) "usually retired, on a pension"
- Elderly-
- "old"
- "old as Methusala" (968 years old)
- "old as dirt" (pre-Adam)

Hypertension in the Elderly

When and how to treat?

Hypertension in the Elderly

- 60% of adults 60 to 69 years and 77% of those older than 80 years have hypertension.
  - Vasan et al, JAMA 2002
- Lifetime risk of developing hypertension in normotensive adults 55 to 65 years is 90%
  - Ostchega et al, J Am Geriatr Soc 2007

Why the elderly are at risk

- Arterial stiffness
- Salt sensitivity
  - Age related decrease in renal function
- Neurohormonal mechanisms
  - Age related decline in plasma renin activity

When to start treatment:

- Blood pressure readings taken after patient has been seated for 5 minutes, using correct sized culf, with arm supported and level with the heart.
- Patient should have abstained from caffeine, smoking and exercise half hour before checking.
- An elevated blood pressure as an average of two readings per visit on two or more clinic visits.

Acelajado MC, Oparil S. Hypertension in the Elderly, Clin Geriatr Med, 2009.

Lifestyle Modification

- Dietary sodium restriction
- Increased physical activity
- Weight reduction
- Limiting alcohol intake

2014 evident-based guideline for the management of high pressure in adults: Report from the panel members of the Eighth Joint National Committee (**JNC8**)

- Published in JAMA, February 5, 2014
- Evidence based report that answered three questions concerning treatment;
  - When to start?
  - What is the treatment goal?
  - Do drugs differ in outcomes?

JNC8 age related recommendations:

- Threshold for treatment;
  - 60 years and older – 150/90 mm Hg
  - Less than 60 years – 140/90 (diastolic goal should be less than 90 mm Hg)

JNC8 medication recommendations

Initial Therapy:

- Non-Black Population – thiazide diuretics, ACEI, ARB, Calcium channel blockers
- Black Population – thiazide diuretics, calcium channel blockers
- In chronic kidney disease (CKD) – initial or add-on with and ACEI or ARB

Challenges for blood pressure control in the Elderly

- Medication non-adherence
- Concomitant medications
  - Cold formulations, steroids, NSAIDs, estrogens, some herbals
- Orthostatic hypotension
  - Antihypertensives, alpha blockers, venlafaxine, SSRIs, antipsychotics.
- Dementia

What did you say?

(Age related hearing loss)

Presbycusis

- Age-related hearing loss
- Symmetrical (involving both ears) progressive loss that happens over a long period of time
- Initially affects high frequency hearing first
- World Health Organization (WHO) predicts by 2025 there will be 1.2 billion people over 69 years of age worldwide, and more than 500 million individuals with presbycusis.

Sprinzi and Riechelmann, Gerontology 2010

Epidemiology

Incidence increases with age:

11 % for persons 44-55 years of age

25% for persons 55-64 years of age

43% for persons 65-84 years of age

UpToDate, 2014

Risk Factors for hearing loss

- Exposure to loud noises
- Ototoxins (aminoglycosides, etc.)
- Infections
- Diseases (diabetes, vascular diseases, hypertension, etc.)

Characteristics of elderly hearing loss

- Symmetric loss of high-frequency hearing followed by mid and low frequency loss.
- Presbycusis is sensorineural rather than conductive hearing loss.
- High frequency loss impacts consonant sounds so able to hear speech but not understand what is being said.
- May experience paradoxical hypersensitivity to loud sounds.
- Associated tinnitus and dizziness

Tinnitus

Tinnitus is a perception of sound in proximity to the head in the absence of an external source.

It can be perceived as being within one or both ears, within or around the head, or as an outside distant noise.

The sound is often a buzzing, ringing, or hissing, although it can also sound like other noises.

UpToDate 2014

Drugs that cause or worsen Tinnitus

(UpToDate, 2014)

- Aminoglycosides
- Chloroquine,hydroxychloroquine
- Benzodiazepines
- Calcium channel blockers
- Cisplatin
- Chlordiazepoxide
- COX-2 inhibitors
- Dapsone
- Doxazosin
- Fluroquinolone antibiotics
- Isotretinoin
- Lidocaine
- Loop diuretics
- Nitroprusside
- Prazosin
- Proton pump inhibitors
- Quinidine
- Salicylates
- Sertraline
- Tricyclic antidepressants
- Tolbutamide
- Valproic Acid

Tinnitus Treatment

- Treat associated factors
  - Depression, anxiety, drug toxicities
- Medications (limited benefit)
  - misoprostol, lidocaine, benzodiazepines. dexamethasone
- Behavioral therapies
  - Tinnitus retraining therapy (TRT)
  - Biofeedback & Stress reduction programs
  - Cognitive behavioral therapy
- Masking

Aids to Hearing

- Hearing aids
- Assistive listening devices (pocket talkers)
- Cochlear implants

Pharmacist counseling to hearing-impaired elderly

- Provide an environment with little background noise.
- Face the patient to allow for lip-reading cues.
- Speak slowly and use words that non-health professionals would understand.
- Make changes in topics obvious to allow time for comprehension.
- Be aware that persons with hearing loss may nod and appear to hear the conversation when they do not.
- Actively engage the individual in the conversation.

Statins in the Elderly

Risks vs Benefits

What about Statins?

- Do statins improve cognitive functioning in dementia?
- Do statins prevent the development of dementia?
- Do statins worsen cognitive functioning?
- What do the new ACC-AHA and AMDA guidelines say about the use in the elderly?

Potential Benefits of Statins

- Cholesterol reduction
- Antithrombotic activity
- Anti-inflammatory effect

Benefits of Statins in Dementia

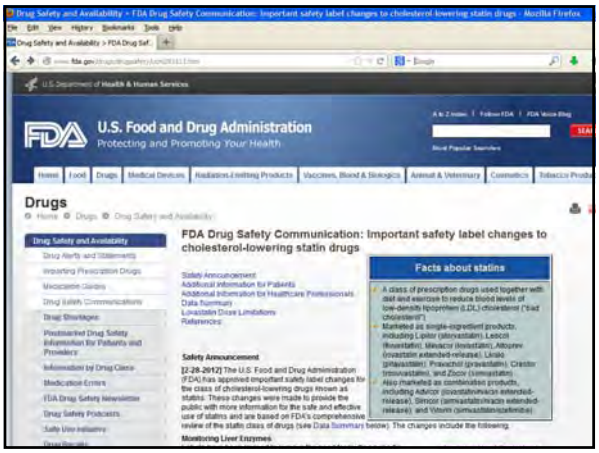
- Epidemiologic studies reporting lower risk of dementia with statin use.
  - Jick et.al. Lancet 2000, Wolozin et.al. Arch Neurol.2000
- Meta-analyses that indicated protective effects
  - Wong et.al. PharmDrugSaf 2013, Song et.al. Geriatr Gernotol Int 2013
- Reports limited by including inclusion of lower quality studies

"Statins and Cognition: A systematic review and meta-analysis of short- and long-term cognitive effects" Swiger et.al. Mayo Clin Proc Nov 2013

- Review of controlled trials or prospective cohort studies
- Studies of adults with no history of cognitive impairment.
- Supports the neurocognitive safety of statin therapy for short-term use.
- Results suggest a risk reduction for the incidence of dementia in long-term statin users.

Cochrane review on 'Statins for the treatment of dementia' McGuinness, Int J Geriatr Psych, 2013

- Review of 3 studies (n = 748, ages 50-90)
- Diagnosis of probable or possible Alzheimer's disease with most taking a cholinesterase inhibitor.
- Change in Alzh Disease Assessment Scale – statins provided no beneficial effect
- MMSE – no significant benefit from statin use
- Conclusion: There is insufficient evidence to recommend statins for the treatment of dementia.



FDA labeling changes for statins warning of possible memory loss and confusion

- Released February 20, 1012 with a great deal of response from practitioners.
- Published review of literature stating no increased risk (Jukema et.al. J Am Coll Cardiol. 2012
- Review of studies indicating there is a concern of cognitive impairment with statins (Taylor et.al. Cochrane Database Syst Rev, 2013)

FDA Consumer Health Information January 2014

- "Cognitive (brain-related) impairment, such as memory loss, forgetfulness and confusion, has been reported by some statin users"
- "Reports about memory loss, forgetfulness and confusion span all statin products and all age groups."
- "In general the symptoms were not serious and were reversible within a few weeks after the patient stopped using the statin. Some people affected in this way had been taking the medicine for a day; others had been taking it for years."

Safety label changes by the FDA

- Rare post-marketing reports of cognitive impairment
- Memory loss, forgetfulness, amnesia, memory impairment, confusion
- Generally not serious
- Reversible
- Variable time to onset
- Variable time to symptom resolution

Guidelines for Statin Use

- American College of Cardiology/American Heart Association (ACC/AHA) released 2013
- AMDA- The Society for Post-Acute and Long-Term Care Medicine, Fall of 2013

ACC/AHA Guidelines

- Continue statin therapy for individuals >75 who are tolerating therapy
- Lack of data supporting high-intensity therapy for secondary prevention for individuals >75
- Lack of data supporting statin therapy initiation for primary prevention of ASCVD in persons >75

AMDA Statement

- "Don't routinely prescribe lipid-lowering medications in individuals with a limited life expectancy."
- No evidence that hyperlipidemia is an important risk factor in individuals >70 for:
  - all-cause mortality, coronary heart disease mortality, or hospitalization for myocardial infarction or unstable angina
- Highest mortality among the elderly with the lowest cholesterol

http://amda.com/tools/choosingwisely.cfm

Choosing Wisely

ConsumerReportsHealth -AMDA

April 2014

- Adults age 75 and older may not need statins
- For older adults there is no clear evidence that high cholesterol leads to heart disease or death.
- Older adults are more at risk of side effects from statins.
- Statins are indicated for older adults who have had a MI, CVA or TIA (for secondary prevention).

CVD Risk Calculator

National Heart, Lung, and Blood Institute

- From Framingham Heart Study
- Uses age, gender, total cholesterol, HDL cholesterol, smoking status and systolic blood pressure
- Predicts a person's chance of having a heart attack in the next ten years.
- Used in persons that do not have heart disease or diabetes.
- If generally healthy consider treating if risk score is 20% or greater
- Available at cvdrisk.nhlbi.nih.gov

Conclusions

- Guidelines provide direction for treatment in secondary prevention
  - moderately-dosed statin therapy in patients ≥ 75
- Lack of guidance in statin therapy in patients ≥ 75 for primary prevention
  - Clinical decision
  - Lack of data
- Assess patient's tolerability, potential drug interactions, comorbidities

Drug –Induced Movement Disorders

What to Worry About

Causes

- Neurological
  - Parkinson's disease
  - Essential tremor
  - Tourette's syndrome
- Non-neurological
  - Physical conditions (i.e. vision loss, ortho. Problems
  - Pain
- Psychogenic
- Drug-induced

Drug-induced Disorders

- Worsening of pre-existing movement disorders
- Dopamine antagonists in PD
  - Antipsychotics
  - metoclopramide
- Drug-induced chorea

Definitions

- Chorea – hyperkinetic, involuntary movements characterized by unpredictable contractions of limbs, face and trunk. From Latin "dance".
- Athetosis – slower, writhing movements, snake like.

Drugs that can cause chorea

Suchowersky et.al. UpToDate 2014

- Dopaminergics
  - Dopamine agonists
  - COMT inhibitors
  - Levodopa
- Dopamine blockers
  - Antipsychotics
  - Amantadine
- Dopamine depletors
  - Reserpine
  - Tetrabenazine
- Ca channel blockers
  - Verapamil
  - Flunarizine
- Anticonvulsants
  - Carbamazepin
  - Gabapentin
  - Lamotrigine
  - Phenytoin
  - Valproic Acid
- CNS stimulants
  - Amphetamines, cocaine
  - Cyproheptadine, Ritalin

Other Drugs

Suchowersky et.al. UpToDate 2014

- Antihistamines (H_1 and H_2 blockers)
- Benzodiazepines
- Baclofen
- Cimetidine
- Digoxin
- Estrogens & oral contraceptives
- Glucocorticoids
- Lithium
- Opioids
- SSRIs
- Tricyclic antidepressants

Tardive Dyskinesia

- "late onset" dyskinesia- oral facial movements, athetosis, chorea, tics and grimacing
- Related to prolonged treatment with typical antipsychotics and to lesser extent atypicals.
- At least one month of exposure to offending agent
- Geriatric population five times more to develop.

Mental Health Clin N Am, 2012

Preventing Dementia?

Memory Decline and Aging

- In 2011 Baby Boomers (born 1946-64) began entering the 65 years-plus bracket to become "Golden Boomers".
- Life expectancy in 1840 was 45 years with a yearly increase of approximately 3 months per year with life expectancy now of 80 years.*
- 65 year olds today can expect to live 16 to 20 years more (add 3 to 6 years more for women).*
- There is a concern that we will outlive our brains

* Kinsella et.al. US Census Bureau population reports, 2009

Age Associated Memory Decline

- "Normal" aging
  - Processing speed declines with difficulty in spontaneous recall of facts, names or events but other functions intact.
- Mild Cognitive Impairment (MCI)
  - Memory loss greater than above without functional impairment (approx. 10% of persons over 65 years)
- Dementia
  - Memory loss with other cognitive and functional impairments (Alzheimers, Lewy Body, Vascular, etc.)

From: Merrill DA, Small GW, Prevention in Psychiatry: Effects of healthy lifestyle on cognition. Psych Clin N Am. 2011.

Increased Risk of Dementia

- Smoking
- Depression
- Diabetes
- Genetics (APOE4)

What might impact dementia?

- Cigarette smoking (don't)
- Drinking *
  - light to moderate alcohol consumption has been associated with decreased risk.
- Aerobic exercise#

* Anstey et.al. Alcohol consumption as a risk factor for dementia and cognitive decline, Am J Geriatr Psychiatry 2009.

*Orgogozo et.al. Wine consumption and dementia in the elderly. Rev Neurol (Paris) 1997.

Williams et.al. Preventing Alzheimer's Disease & cognitive decline. AHQA pub. 10-E005, AHRQ,2010.

Other Factors

Merrill DA, Small GW, Prevention in Psychiatry: Effects of healthy lifestyle on cognition. Psych Clin N Am. 2011

- Obesity – no consistent results but:
  - midlife obesity associated with increased risk
  - late life obesity may decrease relative risk of dementia
- Head Trauma
  - associated with increased risk
  - h/o loss of consciousness greater than one hour had double risk of Alzheimer disease.
- Toxin exposure
  - Pesticides
  - Less consistent – solvents
  - Absent – lead, aluminium

Summary

- Treat medical illnesses (diabetes, hypertension, hyperlipidemia).
- STOP Smoking!
- Exercise more often
- May continue 1-2 alcoholic drinks /day <u>but</u> don't start for dementia protection!
- Protect your head.

From "A Treatise on Insanity"

For, in diseases of the mind, **as well as in all other ailments,** it is an art of no little importance to administer medicines properly: but, it is an art of much greater and more difficult acquisition to know when to suspend or altogether to omit them.

Philippe Pinel (1745-1826)