Medication Therapy Management (MTM) Strategies for the Pharmacist-Geriatric Patient Interventions: Concepts to Cases

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Objectives: the participant should be able to-

- 1. State prospective and retrospective MTM methods for the pharmacist and learning resources to develop a strategy for offering this service for geriatric patients
- 2. Determine priorities for assessing the patients total drug regimen and disease as well as drug history

Objectives-cont'd

- 3. Detect the most common adverse drug reactions, drug changes and additions needed and compliance patterns that may lead to less than optimal use of medications
- 4. Differentiate the significance and severity of assessments made and ensure that the language of recommendations is appropriate

Objectives-

- 5.Formulate a concise and efficient written recommendation to the patient, their caregiver and/or primary care provider
- 6. Communicate and follow-up on their recommendations and document beneficial, as well as adverse outcomes of the acceptance and rejection of these recommendations

Retrospective and Prospective MTM Methods

- Retrospective methods- Usual drug regimen review (DRR) in LTCFs mandated since 1974; may be 30 or more days AFTER drug orders/changes and subsequent physical/lab findings noted and recommendations made by pharmacist
- Prospective- Point-of-filling Rx- OBRA 1990 requires patient education-mostly written PIs- ASCP Fleetwood Project found that prospective discovered more med problems and solved them more expediently than retrospective DRR.
- Medicare Part D-must be separate assessment process based on time spent and number of patient problems as of January 2006.

NEW SLIDE-CPT Codes per State Connection for Pharmacists vol.1, no.2 at www.pharmacistsconnection.com.

- AMA-CPT panel approved eff. 1 Jan 06 for MTMS new codes, payment rates determined by 3rd party payors:
- Code 0115T-for a first-encounter service performed face-to-face in up to 15 minutes
- Code 0116T-same pt. of up to 15 minutes for a subsequent or follow-up encounter
- Code+0117T-an add-on code which may be used to bill for additional increments of 15 minutes of time to either of preceeding codes.

NEW SLIDE-following elements are required to verify the service and dependent on the type and level of MTMS

- Review of the pertinent pt. medical Hx;
- Med profile (Rx, non-rx, Alternative Tx);
- Interventions and rec.s for optimizing medication therapy;
- Referrals, treatment compliance;
- Communications with other HCPs; and,
- Administrative functions (including pt. and family communications) relative to the pt. and/or follow-up care. Per ibid (State Connection for Pharmacists pub. By Fl. Soc. Cons.Pharm. At 850-212-6127, e-mail at info@flascp.com or www.flascp.com

Learning Resources

- 1. ASCP-www.ascp.com. two texts: the Consultant Pharmacist Handbook and Developing a Senior Care Pharmacy Practice: Your guide and Tools for Success.
- 2. A 40-hour geriatric pharmacy review course for the CGP exam and re-certification as a CGP may be found at www.geriatricpharmacyreview.com.
- 3. Cooper JW. Consultant Pharmacy and Long Term Care. Consultant Press, 1200 Colliers Creek Road, Watkinsville GA 30677-186, jcooper@ rx.uga.edu or Senior Health Consulting Alliance at www.shca-ga.org - a 20 hour CE course to compliment the ASCP resources in 1. includes lab tests and safe medication use in the older adult slides, as well as how to set up a clerkship
- 4. Cooper JW, Burfield AH. Geriatric Drug Therapy-A Clinicians' Guide- a 30 hour CE Course and practical guide to knowledge, assessment tools and interventions for most common medication needs and problems that occur in older adults. Available as above after 1 Oct 05
- 5. Cooper JW. Geriatric Case Management-a 50 hour CE course on advanced case management of complex cases of older adults. Available as of 1 Jan 06 from above.

Priorities for assessing the patients total drug regimen and disease as well as drug history

- Priority should be efficient written or on-line survey methods for patient or their caregiver to bring to the RPh at entry to care point or request for consultation
- Content should be both drug and disease state and conditions history
- Example is Cooper Drug & Disease State History form in handouts

MTM and Drug-Related Problems (DRPs)

- The most common DRP detected by the pharmacist is misutilization of drugs, both underuse of needed drugs and overuse of drugs with abuse potential.
- The intervention for this misuse may be to determine what the patient or their caregiver is actually doing with the drug(s) in question. In fact one-third of hospital admissions of older adult is related in 60% to underuse of needed drugs for the heart, HBP, diabetes mellitus and COPD! (Frisk PA, Cooper JW AJHP 1978)

MTMs and DRPs cont'd

- The same study found 40% of those DRP hospital admissions of older adults were due to preventable adverse drug reactions (ADRs) to drugs!
- A subsequent study of nursing home admissions found that one-half of these admission were due to DRPs of misuse and ADRs (Cooper JW Cons Pharm 1987)
- MTM Intervention strategies should therefore be directed toward improving compliance and minimizing ADRs!

Significance and Severity Terms

- Significance-"Suspected" eg diazepam use in any older adult due to falls, cognitive impairment, and dependence
- "Potential" any use of a BZ or propoxyphene or other inappropriate drugs per Beer's List (Fick, Cooper et al Arch Int Med 2003 8 Dec issue)
- "Possible"-something has happened to the patient, eg fall or disorientation after BZ started, which may be multifactorial due to patient conditions and diagnoses
- "Probable"-assignment of causation once other factors considered, eg. " patient fell 3X first week of lorazepam use with no Hx of falls"
- "Documented"- withdrawal of drug and change in patient condition- eg "patient has not fallen since lorazepam stopped, suggest escitalopram 5mg QAM for anxiety with suspected retarded lethargic depression if PCP agrees and depression scale indicates need"

Severity Terms

- Mild- most minor side effects of drugs, eg “mild” nausea, “mild” sedation, usually transient, not requiring drug changes, eg ASA 81mg with little water
- Moderate-more noticeable and requires change in therapy eg, ASA 81mg QD & risedronate 35mg q week with too little water, not sitting up and epigastric burning noted-ensure full glass water and sitting up1 hr after taking
- Severe- Life-threatening- patient took alendronate 70mg q week with too little water and had severe emesis X 3 weeks after dose; 4th week, acute abdomen with LES/gastric blockage, died 4 days later.

The most common Geriatric ADRs (Cooper JW, JAGS 1996 ;44:194-7, Sou Med J 1999)

- 1. Cardiovascular agents- diuretics, K-altering Tx, digoxin, antihypertensives, antianginals, antiarrhythmics
- 2. CNS-active agents- antipsychotics, anxiolytics, CNS stimulants, --->
- 2. Cont'd- antidepressants, anticonvulsants, antihistamines, narcotic analgesics & antidiarrheals, Antiparkinsons
- 3. NSAIDs
- 4. Endocrine- antidiabetics, thyroid

Most Common ADRs-cont'd

- 5. Antiinfectives
- 6. GI agents: H-2 blockers, antacids, laxatives, anticholinergics, antidiarrheals
- 7. Respiratory agents-theophylline, oral Beta agonists, expectorants, -->
- 7. Cont'd-antitussives, decongestants
- 8. Blood formation and coagulation agents-oral anticoagulants, hematinics

Epidemiology and patient factors

- Two-thirds of patients had TWO probable ADRs over the 4-year period
- One in 7 of those who had an ADR were hospitalized due to ADR-NSAIDs>Fall/Fx>Low FBS>dehydration
- Key factors- ADR sequence, PolyRx: 2 drugs/pt. active problems AND failure to recognize relative to absolute contraindications of renal impairment, prior GI problems. LABZs, antipsychotics, oral hypoglycemics

ADR factors/findings by drug class

- Diuretics-ave. Creatinine clearance 40ml/min and dehydration and falls secondary to incontinence
- K-altering therapy-renal impairment and no serum K+ when ACEI or KCl added
- Digoxin- renal impairment and not heeding wt. Loss and pulses
- Antihypertensives-failure to report/record BP<110-120/60-70mmHg or do orthostasis check

ADR factors/findings cont'd-CV and CNS actives

- Antianginals- nitrate-free interval, pulse w. beta and calcium channel blockers
- Antiarrhythmics-CAST study and not recognizing ADR
- CNS Active-predominantly polypharmacy!!!
- Antipsychotics-no AIMS, nor dosage tapering per OBRA + DDI with BZs
- Anxiolytics & hypnotics-use of LABZ vs. SABZ, multiple CNS-depressants, ADR sequence and failure to detect sleep cycle changes

ADR factors/findings, cont'd- CNS actives

- CNS stimulants- ADR sequence to BZs, wt. Loss, seizure Hx
- Antidepressants- TCAs: falls, CV Hx, anticholinergic effects; SSRIs-ADR sequence to BZs, wt. Loss; atypicals- falls w. trazadone, seizure/buproprion
- Anticonvulsants- recognition of ADR, low (SA) serum albumin/adjust level to ave. serum SA of 3.0
- Antihistamines- use of older H-1's with other CNS depressants & falls

Narcotics, antiparkinson, NSAIDs, muscle relaxants

- Narcotic analgesics- daily to weekly prn before peripheral agents (APAP/NAS) use and delirium/falls
- Antiparkinson agents- ADR sequence from metoclopramide and antipsychotics, anticholinergic effects and seligilene CNS
- NSAIDs- no H/Hs, failure to recognize GI Hx, accept alternative (APAP) recommendations, renal impairment and ASA concurrent DDI
- Muscle relaxants- polypharmacy and falls

ADR factors/findings-endocrine & antiinfectives

- Endocrine agents: antidiabetics-insulin + beta blockers, failure to adjust dose when FBG <100-120; chlorpropamide inappropriate in elderly-thyroid, whole product use and T3 storms, wt. Loss, ADR sequence, no TSH
- Oral glucocorticoids-inappropriate in osteoarthritis, GI Hx
- Antiinfectives- renal impairment, esp. with NTF, FQs, warfarin DDI,not recognizing pseudomembr.colitis, Tx aSx bacteriuria

GI and Respiratory Agents-

- GI agents- H2 blockers and renal impairment-confusion; antacids renal impairment and DDIs w. tets, FQs. Digoxin; laxatives-fecal impaction and dehydration, renal secondary to urine incontinence--> AND FALLS
- GI agents cont'd-anticholinergics-constipation, urinary retention in males; antidiarrheals-fecal impaction. Impaired renal function, not recognizing liquid KCl as common cause

Respiratory Agents-

- Theophylline- ADR sequence with caffeine and Trental to BZ or Ambien
- Oral beta agonists- ADR sequence to BZs, CV Hx and tachycardia, failure to try inhalation route
- Expectorants- SSKI and ETH&C : Hx iodine allergy and aspiration Hx
- Antitussives- other CNS depressants polyRx!
- Decongestants- Hx HBP, DM, MI, CVA or angina pectoris, ADR sequence to BZs

Blood formation and coagulation

- Oral anticoagulants- DDIs with ASA, NSAIDs, antiinfectives, no INRs, Hx GI PUD or diverticular problems
- Hematinics- masking NSAID or warfarin blood losses, XS H/H in COPD pts.
- Basic question is- do we know the history, drugs, patient factors and prescribers, as well as caregivers?

Strategies to Reduce ADRs in Elderly Patients

- 1. Avoid contraindicated drugs, e.g. NSAIDs, narcotic analgesics in non-terminal pain, LABZs, sleep meds &polyRx
- 2. Pay attention to Hx, especially renal, GI, CV contraindications, ADR sequence
- 3. Do prospective drug regimen review with each new Rx or OTC- d/c which?
- 4. Encourage patients and their caregivers to become active in drug use process

Strategies for ADR Reduction- POMR/SOAP

- 1. Do POMR for each patient- write a problem list of both active and status-post problems- NOTE: fewer than one half of actual problems are documented in pt. chart (Cooper JW, Consult Pharm 1987; 2:152-6)
- 2. Match meds, both RX and OTC with problems-recognize that both problems may not be treated nor meds rational and these are additional problems!!!
- 3. SOAP problems

Communicate Significant SOAP findings- ADRs

- 4. Communicate via significance (suspected, possible probable) and severity (mild, moderate, severe) hierarchies
- 5. With ADRs, apply Naranjo algorithm (Naranjo C. et al. Clin Pharmacol Ther 1981: 30:239-45)
- 6. Provide alternatives in therapeutic agents, e.g. APAP for NSAID, tapering schedule for BZs, conversion directions
- 7. Evaluate prescriber & patient acceptance of recommendations

Intervention Cost-Savings by Prevalence of Problems

- 1. NSAID Gastropathy hospital admissions-leading ADR: 5-year study routine H/Hs with NSAIDs-check lower eyelid/nailbeds color-reduced from 39 in 4 years (JAGS) to 3 in 5 years in recommendation acceptance group
- Even with 90% recommendation acceptance, the 10% rejection group had 9 hospitalizations; saving/year $115,489 for acceptance, but lost $40,166 with rejection. Aver. Cost /admission=$14,419 (Cooper JW, Consult Pharm 1997;792-6)

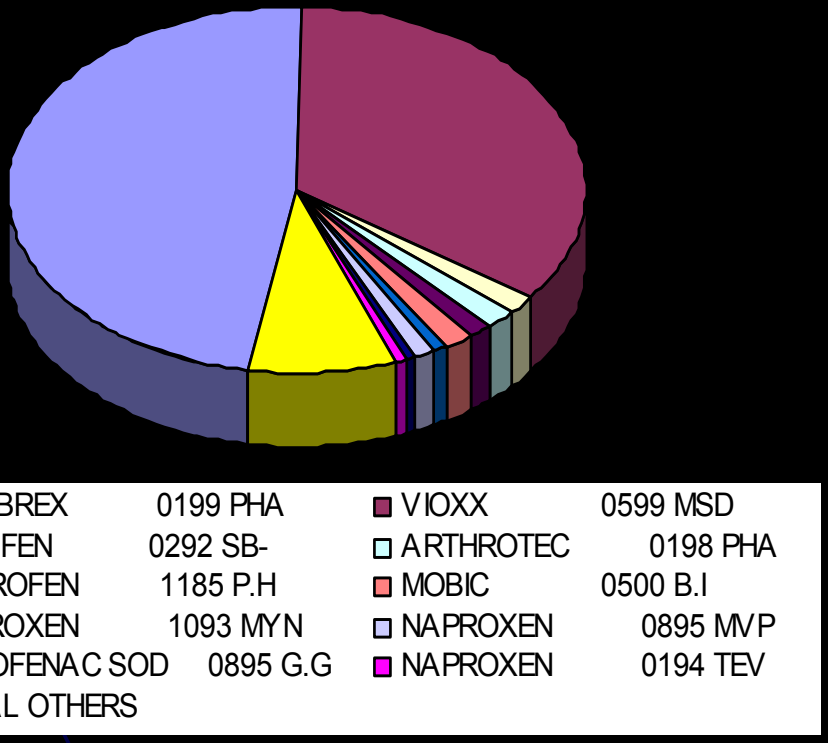
Cost-Savings: Falls and fractures

- 2. Second most common ADR admission: each fall costs $858. Drugs most commonly associated- BZs, antipsychotics, TCAs, narcotic analgesics, antihistamines;hospitalization=$12,000+
- Pyschoactive load reduction and buspirone conversion reduced falls from 0.4 to 0.06/pt/month for savings of $58,812/yr for acceptance and lost $99,211 with rejection of rec.s(Cooper Consult Pharm 1997; 12: 1294-1309 & JAMA 1997:278:1742-3)

Intervention in Diabetics and hospitalizations

- 3. With monthly assessment, both fewer episodes of hypo-/ hyperglycemia & DM-related hospitalizations were seen with accepted (3/26) vs. rejected (9/31) rec. groups (Cooper JW, Consult Pharm 1995;10:40-5)
- DM consultation is current area of reimbursement mandate by states
- Question remains- how did patients get less than adequate medication assessment?

Long Term Care Market: COX-2's and NSAID's



Source: IMS Health

NSAIDs and platelet-affecting drug uses

- Primary and secondary disease prevention , causation and symptomatic relief:
  - Prevention- MI, CVA, PVD, Multiinfarct dementia and perhaps Alzheimers (NEJM 2001;345:1515), familial adenomatous polyposis (FAP)
  - Treatment- OA/RA, pain

NSAID/Platelet affecting Agents Uses- Cont'd

- Causation/exacerbation of disease- GERD, Gastropathy, Nephropathy, HBP, CHF and Stroke
- Symptomatic relief-pain of OA, RA, trauma, cancer-related pain, especially in bones, antiemetic, radiation burn attenuation

Case Study-1

- GK is an 82 yobm with HBP and OA. He has a Hx of naproxen-associated gastritis and anemia. He c/o joint pains of 6-7 on a 10 scale. What do you recommend for his OA?
- A. COX-2 selective NSAID
- B. Acetaminophen (APAP) 2-3g/day
- C. B+Glucoseamine/chondroitin (G/C)
- D. A narcotic analgesic (NA)

NSAID Checkpoints

- High blood pressure (HBP)- assume that half or more of geriatric pts. have HBP, esp. if antihypertensive agents are in use-NSAIDs are the most common drug-induced cause of elevated BP in the elderly
- Congestive heart failure (CHF)-assume that one-third or more of elderly have CHF, and look for digoxin ACEI/ARBs, diuretics, Coreg and spironolactone- NSAIDs are the most common drug-induced cause of CHF in the elderly (Page J et al. Arch Int Med 2000160:777)

NSAID Checkpoints

- Renal Impairment- Assume that the average creatinine clearance of all elderly(~80yo) is 40ml/min or less (N=80-120ml/min) [Cooper JW, JGDT 1991;5(3):59072]This means that virtually all geriatric patients have moderate renal impairment or chronic renal insufficiency-check for incontinence of urine-at least three-fourths of NF residents have mild to severe type which leads to dehydration secondary to fluid deprivation by self or aides (U/A SpGr>1.015)

Renal Impairment and Urinary Incontinence

- The combination of both conditions increases the risk of NSAID-associated increases in fluid retention, blood pressure and CHF as well as stroke risk
- NSAIDs of all type are the most-common causes of reversible renal impairment
- the COX-2 inhibitors CAN NOT be used for longer periods of time due to increased risk of HBP and CHF –NEVER with HBP/CHF Meds

Case Study-2

- RT, a 83 yo 5'4" 167 lb wf has HX of HBP, OA. CHF, urinary incontinence and GERD.
- On 6/12/05 rounds she c/o OA pain. VS stable no edema. Meds are captopril 25mg BID, APAP 650mg QID and omeprazole 20mg HS. Weekend coverage orders celecoxib 200mg/day-On 7/10/05 rounds and drug regimen review she is noted to have gained 11 pounds, with 2-3+ pedal edema and BP is 174/96

Case Study- cont'd

- Calculated CrCl was 22 ml/min. What do you prefer to do?
- A. stop the celecoxib
- B. add furosemide 10-20mg qd to qod for 2-4 weeks, checking weight and BP daily- d/c if wt. back to pre-celecoxib and BP OK
- C. A, B and start APAP/G/C
- D. Increase captopril

NSAIDs and CHF in Elderly Pts.

- A matched case-control study of the relationship of NSAIDs and CHF hospitalization found:
  - Use of NSAIDs week before admission doubled risk of admission
  - Longer-half life NSAIDs were more likely than shorter-half life agents to cause exacerbation
  - One in 5 of CHF admissions were associated with NSAID usage (Page J, Henry D Arch Int Med 2000;160:777-784)

NSAID Use increases risk of CHF relapse

- Rotterdam study of 7,277 non-institutionalized ~70yo, 62% female pop. Found that use of any NSAID (not low dose ASA) after Dx of CHF increased RR of relapse by 9.9 (little OTC NSAID use in netherlands)
- Feenstra J et al. Arch Int Med 2002;163:265-70

Co-morbidities where Aspirin is indicated (with or without COX-2s)

- Angina pectoris (AP)-assume that those with a Hx of AP/ MI have silent angina and are in need of at least beta or calcium channel blocker and interval use of LA& SL nitroglycerin dosage forms
- Past MI- beta blocker (BB) plus aspirin even when BB contraindications are present
- CVA- non-atrial fibrillation-related, if a-fib and TIAs are present need warfarin to INR= 2-3, if ASA does NOT work->clopidogrel? NO!
- Diabetes mellitus- 2005 ADA Guidelines

Aspirin Dose and BP effects on Efficacy and Toxicity?

- Most studies suggest 50 to 325 mg per day, but----->Risk of GI bleeding goes up with dose, as does use with any NSAID, less so with COX-2 selective agents
- Risk of all major CV events (ie MI&CVA) with ASA is 0.59 at blood pressure systolic <130) and 1.08 at BP>145 in men. Stroke was 0.41 at <130 vs. 1.42 at >145 (Meade TW et al Br Med J 2000321:13-7)

Aspirin Effect on Platelet Aggregation and Total Cholesterol (T-C)

- ASA 325 mg daily may reduce the risk of MI in 75% of those with ischemic heart disease by 25-30%- M. Miller, UMd Med Ctr. study presented at AHA 15 Nov 00 meeting found that 60% of those with T-C 200 mg/dL or more still had platelet aggregation; 20% of those with T-C<180 mg/dL still had platelet aggregation
- AHA/ASA Jan 2000 CVA findings?

NSAID and Platelet-affecting Tx and Elderly GI Co-morbidities

- Post-mortem studies of the elderly have found significant hiatal hernia and esophageal scarring in over 60-75% suggesting GERD Hx-Up to one-half or more of the elderly have positive H.pylori tests and Hx of chronic NSAID usage-both of which predispose to gastritis and PUD; up to 75% have diverticulosis, predisposing to constipation and lower bowel bleeding

NSAID and Bisphosphonate Usage

- With an increasing awareness of the high prevalence of osteoporosis in older adults, alendronate and risedronate are more likely to be in use. Best to use weekly dose.
- Both Fosamax and Actonel are gastropathic- and worsen GERD, gastritis and PUD!
- Actonel may be less likely than Fosamax to cause GI upset, but both have same warning on sitting upright, full 8 oz.fluids and avoidance of concurrent drug administration

Alendronate and Naproxen are Synergistic in Causing Gastric Ulcers (Arch Int Med 2001;161:107-110)

- Since both NSAIDs and bisphosphonates can cause gastric ulcers-be careful how they are used together!
- A 10-day study of 18 women and 8 men age >30 yrs given 10mg/day of alendronate, 500mg naproxen sodium BID or both found with 1-4 week washout between crossovers found that 2 alendronate (8%), 3 naproxen (12%) and ten (38%) receiving both developed endoscopic evidence of ulcers!

Aspirin Use and Stroke Risk

- Concept-There is a dosing window for ASA and stroke risk-A 14-year, 79,319 female nurse study (ages 34 to 59) found that one to 6 ASA (325 to 1950mg/week) had a lower risk of ischemic stroke (85% of CVAs) than those who took no ASA; however hemorrhagic stroke risk tripled when more than 15 ASA 325 mg per week were consumed (Iso H et al. Stroke 1999;30:1764-71)

ASA, NSAIDs linked to Intracerebral Hemorrhage (ICH)

- Nosebleed may be a clue to increased risk of ICH, esp. in those taking high dose ASA or NSAIDs
- Epistaxis, defined as more than one nosebleed in prior 5 years was overall risk 4 to 15 times higher with high dose NSAIDs or ASA (<1225mg/week)- warn pts. If occurs call PCP! Stop ASA or NSAID?
- Saloheimo P et al. Stroke 2001;32:399-404

ASA Underuse in CV Disease

- A recent study found that only one-half of those with ischemic heart disease, MI or stroke were taking ASA (Rojas-Fernandez CH et al. Can J Cardiol 1999;15:291-6)
- The consultant pharmacist (CP) has been shown to increase the use of ASA prophylaxis in NF residents (Cooper JW, AGS/AFAR 2000)-Precautions on Hx are critical- one patient with s/p MI& CVA but no Hx of GERD or PUD died in 1st month of 81mg/day with a suspected GI bleed.

Recognizing NSAID and platelet-affecting adverse drug reactions (ADRs);

- Complying with HCFA regulations for ADRs- as of 1 July 1999, pharmacists must document suspected, potential or actual ADRs in monthly drug regimen review report-Probable ADRs may occur in 2/3 of residents over a 4-year period ; 1 of 7 of these are hospitalized-NSAID gastropathy is the most common cause of admission (Cooper JW, JAGS 1996;44:194-7 & Sou Med J 1999;92:485-90)

NSAID Gastropathy Interventions

- A 5-year follow-up study of NSAID gastropathy interventions by CPs found that by reducing use of longer-acting (piroxicam, naproxen) and use of lower doses of shorter-acting (ibuprofen) NSAIDs as well as therapeutic substitution of APAP 650-1000mg TID to QID that gastritis and GI bleeds hospitalizations could be reduced from 39 in prior 4 years to 3 in the subsequent 5 years, when RPh rec. accepted- (90% of the time) BUT----->

CP NSAID Intervention Recommendation Refusal

- When CP rec.s were refused in only 10% of cases, there were 9 NSAID-related hospitalizations from the NF in the 5-year period at an ave. cost of >$14,000
- Annualized cost saving/yr. With 90% acceptance were $115,489; with rejection $40,166/yr (Cooper JW Cons Pharm 1997;12:792-6)

Clinical Tools for NSAID ADRs-

- Naranjo Algorithm for ADR assessment and significance
- Fries NSAID Gastropathy Hospitalization or Death Risk Per Year Scale

COX-2 Selective Agents

- Celebrex 100 to 200mg daily, QD or BID-prefer QD ONLY
- Vioxx 12.5 to 25mg daily, QD-NOW OFF THE MARKET
- Bextra 10-20mg daily, QD-DITTO
- Mobic is claimed to be COX-2 selective but most regard as more non-selective

Celebrex vs. Vioxx- Arthritis and Hypertension in the Elderly

Objectives

- To compare in patients ≥65 y.o. on COX-2's, the incidence of clinically significant:
  - Renal events (edema)
  - Cardiovascular events (hypertension)
  - Other safety issues (UGI tolerability)

Study Design

- Double-blind, controlled, randomized, six-week trial
  - Celebrex 200 mg QD, Vioxx 25 mg QD
  - 860 OA patients (Whelton A, et al. American Journal of Therapeutics. March 2001).

Celebrex vs. Vioxx

6-Week OA/HTN Trial: Celebrex vs Vioxx

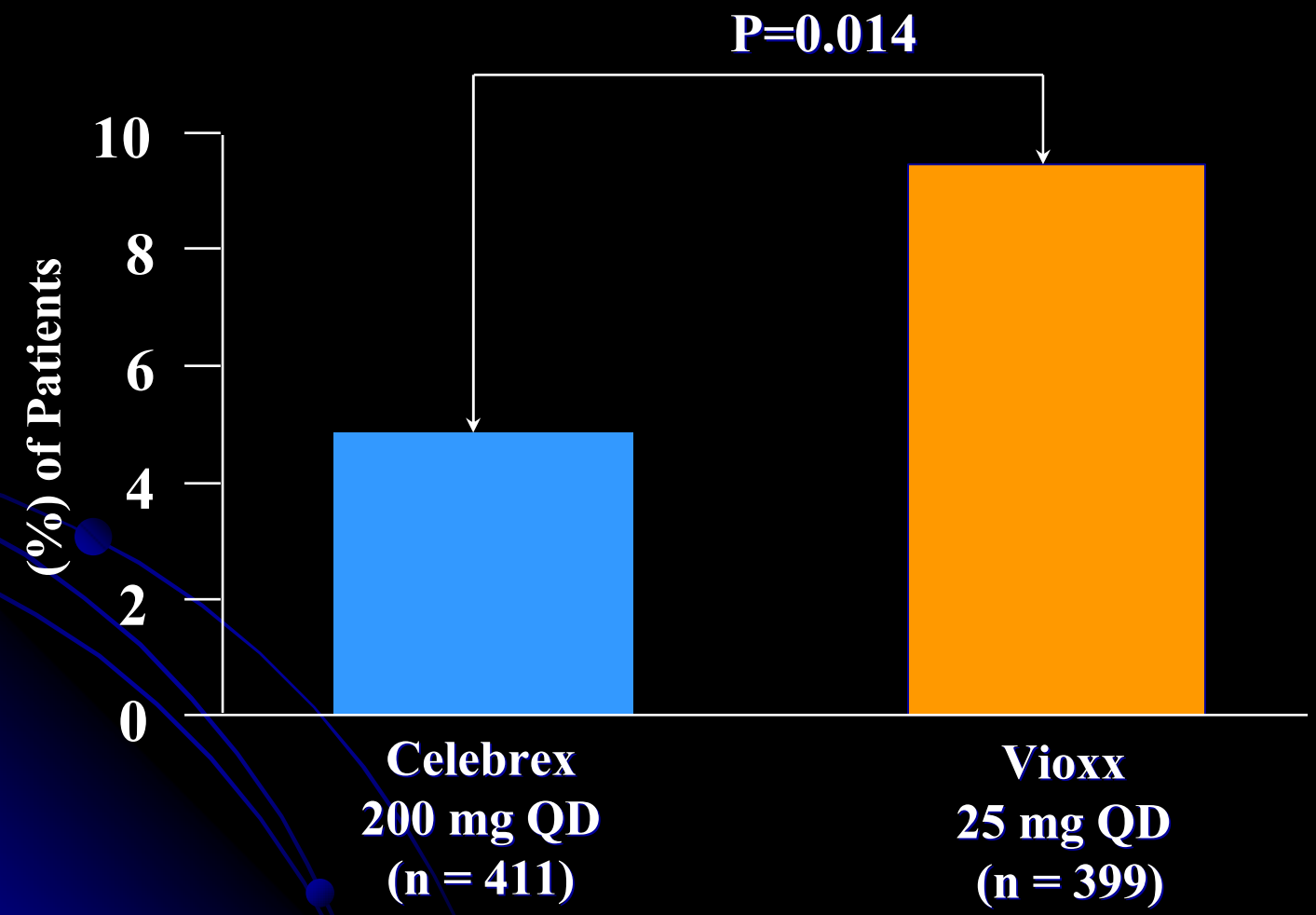
Baseline Demographics

	Celebrex 200 mg QD (n=411)	Vioxx 25 mg QD (n=399)
Mean age (yrs)	74.0	74.1
Age (%)		
65-74	54.5	53.4
75-79	28.2	25.8
≥ 80	17.3	20.8
Female (%)	66.5	66.4
Duration of HTN (mean yrs)	13.2	12.5
Duration of OA (mean yrs)	13.6	11.7
Mean treated blood pressure	138/76	137/76

Whelton A, et al. American Journal of Therapeutics. March 2001.

Celebrex vs. Vioxx - Incidence of Edema

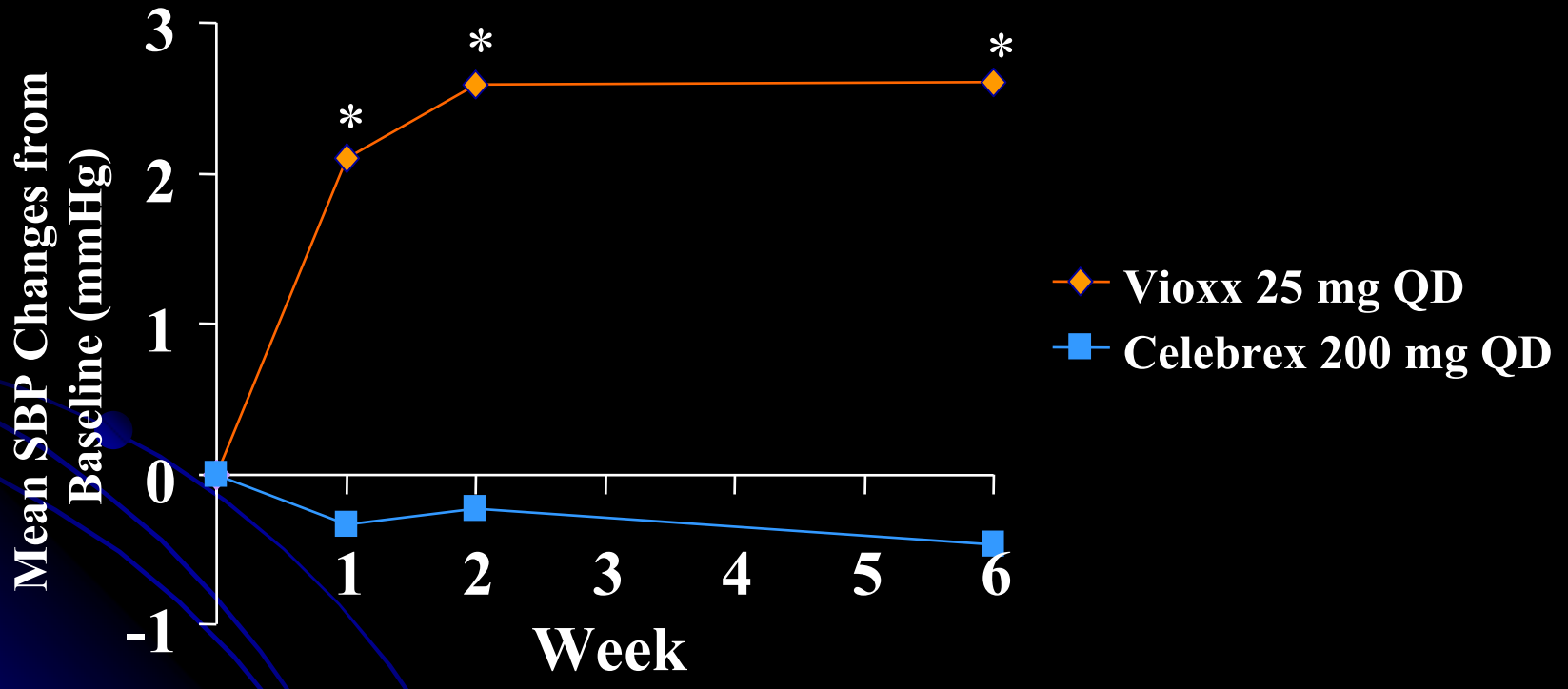
6-Week OA/HTN Trial: Celebrex vs Vioxx



Whelton A, et al. American Journal of Therapeutics. March 2001.

Celebrex - Systolic Blood Pressure Mean Change From Baseline (mmHg)

6-Week OA/HTN Trial: Celebrex vs VIoxx

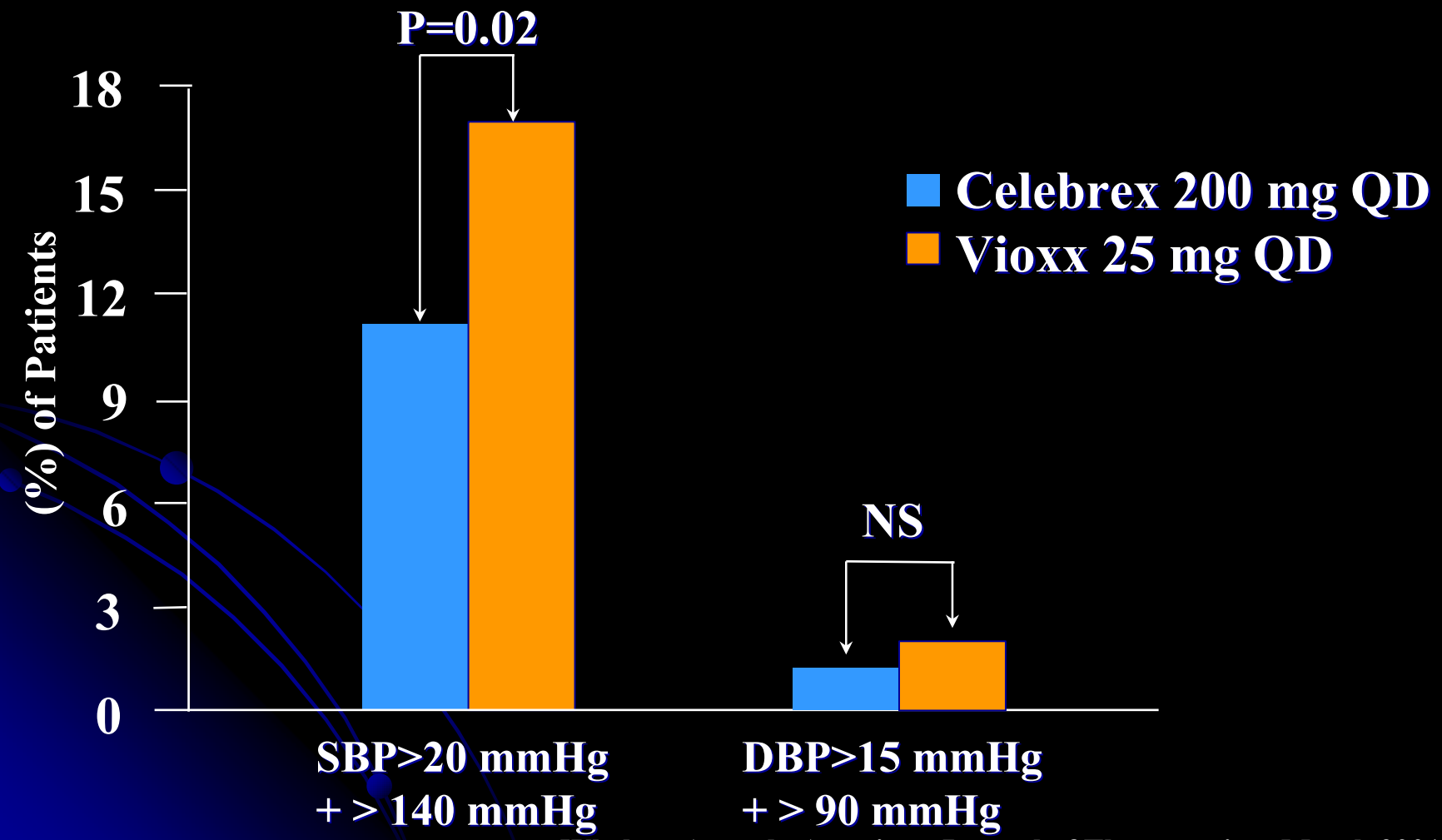


*P ≤ 0.01 vs. celecoxib at all time points (Fisher's Exact Test)

Whelton A, et al. American Journal of Therapeutics. March 2001.

Celebrex /Vioxx- Incidence of Clinically Important BP Elevation

6-Week OA/HTN Trial: Celebrex vs Vioxx



Whelton A, et al. American Journal of Therapeutics. March 2001.

NSAIDs and HBP, MI, CHF, CVA Prevention

- FDA to re-label ALL NSAIDs that they not be used for more than 10-14 days consecutively due to CV risk (2005)
- Even Celebrex may raise risk, if patient already has any CV problem or is on CV meds (diuretic, ACEI/ARB, beta or calcium channel blocker)
- Pts. Already taking should weight daily and report 3-5 lb. gain or any pedal edema to PCP and take BP, if >120/80 STOP NSAID!

Fries NSAID GI Hospitalization or Death Risk Scale (Fries JF Am J Med 1991;91:213-22)-NOTE: for NON-COX 2 Selectives

GI Event Score

Age (years) X 2=

Hx NSAID S/E add 50=

Disability Index (0-3) or ARA Class -1 X 10=

NSAID dose (% max) X 15

Current GC (or ASA?) use add 40=

Total Score=

Risk Per Year = (Score-100)/ 40

Case 3-NSAID Gastropathy Hospitalization or Death Risk

- Applying the Fries risk scale to an 80 yo with Hx of NSAID gastritis, disability index of 3, taking 2400mg ibuprofen/day (100% of max. dose) who also receives 5mg prednisone/day the risk is 80 X 2=160 + 50+20+15+40= 285-100/40=4.6 compared to 0 for non-NSAID users-This patient has an almost 5 times higher risk of hospitalization or death per year of NSAID use than non-NSAID users! The COX-2 selective agents have roughly half- the likelihood of gastropathy as older non-COX selective agents.

Naranjo Algorithm-Naranjo CA et al. Clin Pharmacol Ther 1981:30:239

ADR Events

	Yes	No
Appropriate temporal sequence	+2	-1
A known ADR	+1	0
Alternative explanation available	-1	+2
Objective evidence of ADR	+1	0
Approp.serum level or lab value	+1	0
Dechallenge improvement	+1	0
Rechallenge relapse	+2	-1*

*If rechallenge was not performed value assigned was 0

Scoring: doubtful=<1; possible=1-4; probable=5-8; definite=9=10

Case 4-Applying Naranjo Algorithm

- A 77 yobf starts NAPROXEN 220mgBID. Over the next month her H/H drops from 12/36 to 10/30 and she has black tarry stools and persistent heartburn. She states that she had prior admission to hospital from taking 6 to 15 ASA 325mg tablets per day. The temporal sequence is logical (+2); it is a known ADR (+1); there is no alternative explanation (e.g. concurrent alcohol, GC or ASA usage) (+2)--->

Case 4-Naranjo Ax cont'd

- …..there is objective evidence of an ADR (+1) and two lab tests to confirm ADR (+1), there is dechallenge improvement as her H/H stabilized and increased to 11/33 after naproxen stopped (+1) as well as no heartburn and the rechallenge (+2) after the ASA ADR gives a total = 2+1+2+1+1+1+2=10 or a DEFINITE ADR

APAP and Glucoseamine with Chondroitin (G/C)

- ACR, AMDA, AGS all recommend APAP as 1st step, 2-3g/day with NO ALCOHOL
- Glucoseamine and chondroitin are NSAID/APAP-sparing-start at 1500/1200mg/day x 30days, then 1000/800mg/day x 30 days, then 500/400 if less NSAID used-APAP/G/C preferred if Aggrenox, ASA or Plavix are needed for MI/CVA prophylaxis and/or Boniva, Fosamax or Actonel are needed to lower gastropathy risk.

Addition of platelet-affecting agents to NSAIDs?

- How much does adding another NSAID or platelet affecting agents to traditional NSAIDs or COX-2 selective NSAIDs?- risk is greatly increased with traditional NSAIDs and intermediate between traditional and COX-2 selectives is best guestimate . ASA + Traditional NSAID~ doubles risk (little data)-On the other hand Celebrex and Mobic may not inhibit platelets-if given to someone who needs a platelet-affecting agent increase risk of heart/brain damage?

RPh Intervention in NSAID Gastropathy- Cooper JW, Wade WE Cons Pharm 2005

- When pharmacists intervene and recommend APAP instead of NSAIDs, there is a savings of as much as $2,000 per patient per month in drugs and hospitalization costs, when compared to NSAIDs without gastroprotection or with a PPI or misoprostol, AND 2 of 11 patients for whom the recommendations were refused died of GI bleeds!

CLASS and VIGOR Data, HBP, CHF GI Warnings and the FDA

- CLASS (celecoxib LT Arth Safety Study) of 8059 pts.found cumulative rate of ulcers was celecoxib 400mg/d(1.13%), ibuprofen 2400mg/d(3%), and higher rates of angina pectoris (4.1%) in celecoxib +ASA and 0.7% of those on Celebrex alone and more MIs in celecoxib group.
- ASA increased risk of GI ulcers 4-fold in all groups!

CLASS and VIGOR Cont'd

- VIGOR (Vioxx GI outcomes Res study) of 8,000 pts. found lower GI (2.1%) in rofecoxib 50mg/day than naproxen 1000mg/day (4.5%), BUT rofecoxib group had higher HBP and CHF-related adverse events-FDA refused to remove GI and CV warnings after review of VIGOR and CLASS trials. FDA Adv Comm Meeting Documents 7-8 Feb 2001. ww.fda.gov/orhms/dockets/ac/cder01.htm#arthritis)

MI Rate Comparison (Mukherjee D JAMA 2001;286:954 & Konstam MA Circ 2001:104:2280)

- Annualized rates of MIs in 4 studies, including CLASS and VIGOR comparing COX-2 selectives to healthy controls not taking low-dose ASA and concluded both increased MI risk. (Mukherjee)
- A second review of 23 studies found no evidence of excess CV events with rofecoxib compared to various NSAIDs or placebo. (Konstam)

Case 5-Professional Judgment

- A 73 yowf with a significant Hx 3 MIs, TIAs and one CVA, as well as Hx of OA and NSAID gastritis is started on Celebrex 200mg/day for OA pain. She was taking a ASA 325mg per day. What is your judgment on answering her question: " Do I still need to take my aspirin…."? What do you recommend as/to her attending clinician?

Case 5 What Would you recommend?

- A. change Celebrex to APAP 500mg q4h
- B. recommend glucoseamine/chondroitin
- C. check lower eyelid redness and Hb
- D. recommend a PPI with ASA and cut dose to 81mg/day and check LDL
- E. all of the above

NSAIDs and Anticoagulants (ACs)

- The risk of GI bleed is 13 times higher in those using traditional NSAIDs with oral anticoagulants (ShorrRI et al. Arch Int Med 1993;153:1665-70) Do heparin and LMWHs share this problem?- YES!!!!!!!!!
- Are NSAIDs safe with anticoagulants? NO!! Generally AVOID ALL NSAIDs with oral and injectable anticoagulants, unless cardiologist is following and assuring GI protection

Gastroprotection and NSAIDs

- With traditional NSAID usage, only PPIs and misoprostol have approval for prophylaxis- however side effects of cramps, diarrhea and uterine contractions may limit usage.
- H-2 antagonists, antacids and sucralfate are not reliable prophylaxis-higher doses of H-2s may have some effect on duodenal PUD with NSAIDs (Yeomans ND et al NEJM 1998;338:719-26)

Gastroprotection and NSAIDs

- Proton pump inhibitors (PPIs) are now approved for NSAID GERD or PUD prophylaxis BUT--> Prilosec and Aciphex 20mg, Prevacid 15-30mg, Nexium 10-20mg and Protonix 40mg may cut risk in half? (Yeomans ND ibid. and Hawkey CJ et al NEJM 1998;338:727-34)-Cost is $100-150/month for PPI vs. Cost of COX-2 selective, APAP, Glucoseamine/chondroitin, NA?

COX-2 Selective Vs. Older NSAIDs Gastropathy

- In 3 month trial comparing placebo, 100, 200 and 400mg celecoxib/day with naproxen 500mg BID, the respective rates of endoscopic ulcerations, were 4, 6, 4, 6 (NSS) and 26% which was SS ($p<0.001$) (Simon LS et al JAMA 1999;282:1921-8)
- A 6-month trial of placebo, 25 and 50mg rofecoxib/day and 2400mg ibuprofen/day found ulcers in 10, 10, 15 (NSS) and 46% respectively SS vs. rofecoxib (Laine L et al. Gastroent 1999;117:776-83)

Patients at risk for GI Bleeding Still receive NSAIDs

- Nearly three-fourths (73%) of older patients who have been hospitalized for GI bleeds still receive NSAIDs at some point after their discharge (Rotterdam study).
- 51% low-dose ASA;4% NSAID with oral anticoagulant (OA) but no antiulcer drug; 35% received NSAID with an antiulcer drug; 8% received NSAID with OA and an antiulcer drug . Visser LE et a;. Br J Clin Pharmacol 2002; 53:183-8

Key Points to Prevent Gastropathy and Nephropathy

- Review Hx-expect Hx GI and CV problems
- Over one-half of GI bleeds in the elderly are asymptomatic- why? NSAIDs are excellent analgesics and higher pain threshold in the elderly?
- Recommend APAP, COX-2 inhibitor, glucoseamine/chondroitin, and/or NA as alternatives to traditional NSAIDs or in those with CV Hx requiring antiplatelet Tx

H. pylori eradication, PUD and Chronic NSAID Use

- Latest evidence is that an HP eradication regimen may be needed to lower risk of PUD in all NSAID users, even low-dose ASA, those with Hx of GERD and/or PUD, concurrent use of oral cortisones or warfarin or use of more than one NSAID - Chan FKL Lancet 2002;359:9-13 & Huang J-Q, ibid, 14-22

Renal protection and NSAIDs

- Are the newer COX-2 selective agents any less likely to cause fluid retention, BP increases than the older NSAIDs in the elderly?- best curent evidence is NO! (Perazella MA et al Am J Kid Dis 2000;35:937)
- Is one COX-2 agent more likely to cause edema and BP increases? EULAR data suggests that 25mg rofecoxib is TWICE as likely to cause as 200mg celecoxib

Key Points to Prevent Renal and CV NSAID ADRs-

- Recommend weekly VS and weighing in all elderly who are started on an NSAID- a 5 pound or more wt. gain or consistent (X3) systolic >120 or diastolic > 80mmHg or 20mmHg increase in systolic or 10mmHg increase in diastolic suggests NSAID effect-patient most likely to have this problem are those on HBP, CHF or CRF meds, and/or urine incontinent

Renal effects of NSAIDs

- Are the COX-2 selective agents more likely to cause fluid retention and BP increases than traditional NSAIDs?
- Working hypothesis is YES- why? Since the COX-2 inhibitors are much less likely to cause GI problems, they are being used for longer periods in the elderly!

HBP and CHF due to Fluid Retention and NSAIDs

- A 5-year study of NSAIDs and wt. Gain before COX-2s were introduced found 4 suspected cases with traditional NSAIDs. A two-year subsequent study since COX-2s were introduced in the same long-term care facility found 11 suspected cases with almost exclusive use of COX-2 inhibitors and the same prevalence of OA between both periods (Cooper JW, unpublished data)

Pharmacoeconomic outcomes of NSAID intervention acceptance and rejection

- NSAID recommendation 90% acceptance has been shown to save over $100,000 per 100 bed facility per year when accepted and decrease hospitalizations by 92%
- NSAID recommendation 10% rejection has been shown to cost more than $40,000 per year in same facility and triple hosp. Rate! Cooper JW, Cons Pharm1997

NSAIDs Summary and Conclusions

- NSAIDs and platelet-affecting agents are clearly being used in a large percentage of the elderly; ASA may be underused?
- the COX-2 selective agents appear to be safer in terms of GI effects, but require low-dose ASA for CV primary or secondary protection in at-risk populations (Hx angina, MI, CHF, DM, TIA, CVA, PVD)
- COX-2 selectives + low-dose ASA =risk for GID bleed similar or greater than non-COX-2 selectives!

NSAIDs Summary and Conclusions

- Traditional NSAIDs and COX-2 selectives are both likely to cause renal, BP and cardiovascular problems in susceptible elderly
- Physicians, Nurses, NPs, PAs & Pharmacists can improve the use and safety of all of these agents!

Anemia Intervention

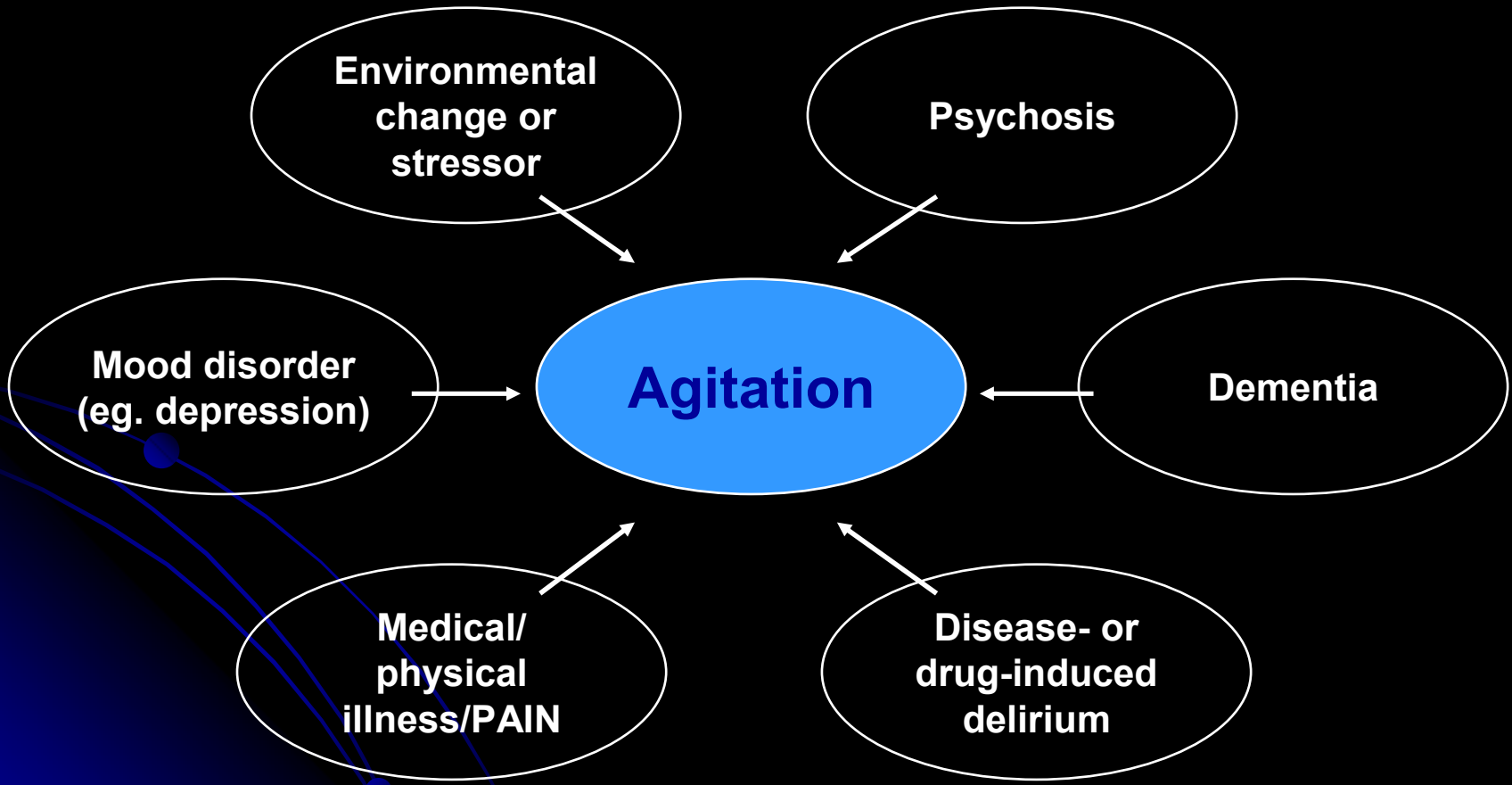
- Anemia is most commonly due to ASA, NSAIDs and underlying GERD/PUD-NEVER let anemia be treated simply by adding hematinics-always recommend occult blood from stools AND determination of the cause
- FeSO4 325mg not MORE than once daily; more often not absorbed and increases constipation
- Always ask for iron, folate and B12 supplement with epoetin (e) or (d) darbopoetin
- One Ga physician used $15,000 of e without hematinic, despite RPh asking for same with Hb6-7:after adding Fe/FA/B12 patient Hb increased to 11-11.6-RESULT Dr. had to refund $15K to Medicaid!

Blood Thinner Interventions

- Always intervene when you get an Rx for :
- Coumadin, Plavix, Aggrenox, Lovenox, Normiflo, Fragmin, Aristra or heparin and ensure that Hb is being done and GUT IS PROTECTED! Counsel patient on stool darkening and DO NOT LET IRON SALTS be used!

Fall Intervention in Geriatric Patients

Etiology of Agitation in Older Persons



Modified from Zayas EM, Grossberg GT. *J Clin Psychiatry*. 1996;57(suppl 7):46-51.

Dementia Differentiation

- Dementia- as Alzheimer's type 50-60%, Multi-Infarct 15-20% and rest mixed or reversible
- Depressive Syndromes- Depressive Sx in 30-40%, DSM IV major depression in 10-15%, dementia syndrome of depression (AKA pseudodementia) in 10-15% and grieving in all
- Delirium- X % drugs vs. infection

Dementia Associated Behaviors

- Agitation-graded from mild to severe and falling into one of three syndromes: physically nonaggressive behaviors, verbally agitated behaviors, and aggressive behaviors
- Another term-- disruptive behaviors
- Prevalence approaches 70-80% at some stage of dementia- usually by stage 6 on 1-7 scale of Reisberg .

Diseases Associated with Dementia or Depression

- Alzheimers, MID, Schizophrenia, Anxiety disorders, Parkinsonism
- Thyroid, Addisons and Cushings
- Anemias, AIDS, Lo Na and K
- Huntingtons, Picks, Creutzfeld-Jacob
- Cancer, Cardiovascular and Cerebrovascular disease

Drugs Associated with Cognitive Changes In Dementia

- Antipsyhotics, Anxiolytics except buspirone, tricyclics, barbiturates, meprobamate, older sedative/hypnotics, metoclopramide, esp. polypharmacy, many anticonvulsants, Sinemet, Eldepryl, theophylline/Trental, Permax, Requip, Mirapex

Drugs and Cognition

- Narcotic analgesics, muscle relaxants, NSAIDs, steroids of any type- gluco-, sex-, anabolic, and digoxin, beta blockers, sympatholytic HBP drugs, Anticholinergics- primary or side effect, e.g. antihistamines, drugs for stress/urge incontinence

Adverse Effects of Conventional Pharmacotherapy

- Patients who receive psychotropics for dementia-related agitation have 2 to 6 times greater risk of fall and injuries and twice the risk of hospitalization for all causes- falls, infections, dehydration, pressure ulcers than those with dementia who are not given psychotropics. Cooper J, Horner M, submitted

Chemical Restraints and OBRA

- Current regulations require that tapering attempts be made two to three times the first 6 to 12 months after admission to or having a antipsychotic or BZ started . (Buspar, trazodone and Depakote are exceptions) unless taper medically shown to cause pt. deterioration

OBRA Mandate

- Documentation of ADRs is also mandated-the most common ADR is psychotropic-related falls (Cooper JAGS 1996, JAMA 1997, SMJ 1999) AND Pressure ulcers (AKA bedsores, decubiti)-recent study found that 2/3 occurred within 2 weeks of a fall (Cooper JW BMJ 2000)

Nonpharmacologic Treatment of Agitation

- Staff education programs on ways to minimize patient agitation, aggression and disruptive behavior may cut by as much as 50%
- Aggressive behavior occurs most often during personal care-other recent findings are time spent in bed and noise levels may increase agitation and aggression

Nonpharmacologic Approaches to Disruptive Behavioral Symptoms (DBS)

- Reality Orientation, Channeling, multigenerational approaches
- Pet, Plant, Art, Music, Exercise, hand massage, therapeutic touch (forehead, shoulders), structured activities and dance therapy-Be careful how you mix the approaches!-e.g. hard rock with a c-w fan!

Difficult Behaviors in Dementia-8 Step Approach, Cooper JW, JGDT J Geriatr Drug Ther 1999; 12(3):5-28

- 1. Pinpoint nature of specific behavior and when it occurs;
- 2. Review physical and emotional stressors (e.g. staff interaction and empathy with resident)minimize time spent in bed!!
- 3. Check for co-existent affective or psychotic behaviors

Eight Steps, cont'd

- 4. Minimize medications that can worsen behavior (don't forget decaffeination!)-see prior list and taper many carefully to avoid withdrawal reactions-esp. with conventional psychotropics, e.g. haloperidol, lorazepam, amitriptyline

Eight-steps, cont'd

- 5. Reduce environmental stimulation (e.g. noises)
- 6. Simplify resident's tasks
- 7. Non-pharmacologic interventions(prior slide)
- 8. Drug therapy when appropriate with galantamine, memantine, risperidone, divalproex sodium, buspirone, trazodone
  (Cooper JW JGDT 1999;12(3):5-28)

Psychotropic ADRs within the Nursing Home

- In a 4-year study of ADRs, 65% of residents had 2 probable ADRs; psychotropics were second only to CV agents in terms of ADRs within the facility and 2nd to NSAIDs as the leading cause of ADR hospitalizations that occurred in 1 of 7 with an ADR (Cooper JW, JAGS 1996;44:194-7, Sou Med J 1999; 92:498-90)

Falls in Frail Elderly Taking Psychotropics

- Up to one-half or more of LTC residents fall each year; 85% of falls are drug-associated (Cooper JW)
- Fall rates appear to be directly proportional to the psychotropic ” load”; injuries occur in half of fallers, each fall costs $800+
- Falls are the leading cause of litigation against LTCFs (Nursing Homes 1995)

Falls in Frail Elderly Taking Psychotropics

- Reduction of psychotropic " load "and conversion to buspirone , risperidone or divalproex may cut the fall rate by as much as 75% over a 6-month period (Cooper JW Cons Pharm 1997;12:1294-1309 and JAMA 1997;278:1742)
- The main question is : what psychopharmacologic agents are the most effective and safest for AD-related agitation and aggression?

Psychotropics and Alzheimer's-related Agitation

- Recent 16-week study found that haloperidol (1.8 mg/d) or trazodone (200mg/d) were no better than behavioral management (BMT) or placebo for MMSE 12-15 and half of those receiving h or t got worse agitation and had more bradykinesia and parkinsonian gait. (L Teri et al Neurology 2000; 55:1271-1278)

Preferred Atypical Conventional and AP Dosages

- Risperidone is considered to be the treatment of choice for patients with dementia and psychosis
- Recommended starting and maintenance dosages are:

AP Dosages, initial; maintenance mg/day

- Risperidone (0.25-0.5; 0.5-2.0)
- Olanzapine (2.5; 5-10)-AVOID
- Quetiapine (25; 25-200)-AVOID
- Clozapine *(12.5; 12.5-100)-AVOID
- Haloperidol* (0.25-0.5; 0.5-4)-AVOID
- Thioridazine* (12.5; 25-100)-AVOID * second-line/reserved status due to hematologic and QTc interval effects) [ibid.]

Antipsychotics (APs) and Falls

- Basic question is are the atypical APs or divalproex less likely to be associated with falls than the conventional low or high potency APs-Preliminary evidence suggests that in equipotent lower dosages, risperidone may be less likely to be associated with falls than olanzapine, ariprazole, quetiapine, thioridazine or haloperidol. This may equate to a net savings of at least $200/pt/month(Cooper JW, unpublished short-term data)

Conventional Psychotropic tapering, Buspirone Conversion, Agitation and Falls

- In a recent study of NF residents with AD who were agitated and treated with conventional psychotropics (CPs), CP tapering and buspirone conversion decreased the number of agitation AND fall episodes by 75% and improved cognition over a 6-month study period (Cooper JW, Cobb HH , Burfield AH , Cons Pharm, 2001;16:358-363; Cooper JW, Cons Pharm & JAMA 1997)

Conversion Protocol

- Start buspirone(B) 30mg/day along with conventional psychotropics; after 30 days begin taper at 10-25% of each q 2 weeks: Case- haloperidol (H) and lorazepam (L) 2mg aa daily. Taper H 1st at 1.5->1->0.5->d/c the L at same decrements q 2 wks; increase B to 45 to 60mg at 2 to 4 week intervals

Conventional AP Tapering

- If tapering of conventional APs introduces psychotic manifestations, risperidone at 0.25 to 0.5mg/day and stop the buspirone, as well as taper benzodiazepines to discontiunance; if agitation or aggressive behavior re-emerges start divalproex at 250-375 up to 625-825mg/day)

Tapering and Conversion Cost-Savings

- Each NF fall cost $855. The 24 of 27 sucessfully tapered and/or converted had reduced fall rate from 0.35 to 0.06 falls/month for savings of $249/pt/month and fewer (3.2 vs. 0.8) episodes of agitation/aggression/mo (AAM)
- The control group of 33 had 0.35 falls/month & 1.2 AAM(Cooper opt cit.)

Decreasing other Psychotropics and psychoactives

- Assess depression syndromes and treat low and slow- AVOID TCAs, Prozac, Wellbutrin in CVA or seizure Hx, prefer Lexapro, Zoloft, Effexor or Remeron- all increase falls; risperidone as preferred AP 0.25-1.5mg/day; Metoclopramide 40->10-15mg/day;Darvocets to APAP' minimize ;antihistamines except Claritin, Clarinex or Allegra; BPs to >120/70

Fall Risk Assessment Guidelines Cooper JW NH Pract 1994

- History of Falls: Ambulation Status CIRCLE: up-bed-walker-wheelchair
- One-two falls/month/quarter ___2
- More than two falls per /month or /qtr_____8
- FALL-RELATED-Fracture (date)_____5

Fall Risk- cont'd

- Postural Hypotension (orthostasis)_1
- Syncope/Dizziness___1
- Sensory Deficits: decreased hearing (1), vision (1), aphasia (1)
- Unsteady or shuffling gait___2
- Confusion/delirium/disorientation___2
- Agitation/increased anxiety___2

- SUB-TOTAL=_____

Fall Risk- meds

- Medications:cardiac (1), antihypertensives (1),diuretic(1),antipsychotic-or metoclopramide(2),hypnotics(2), antidepressant or antihistamine (H-1 or H-2 blockers) (2), anti-anxiety (2), NSAID (1) narcotic analgesic Mild (1); moderate (2), Anticonvulsant (1), muscle relaxants (1) SUB-TOTAL_____

Fall Risk- Dxs

- Diagnoses-Incontinence: Bowel (2) Bladder (2) Cardiac diseases: arrhythmia (1),CHF (1) Neurologic/Psychiatric diseases: Dementia (1) Parkinsonism (1) Seizures (1),Stroke (1), Musculoskeletal-Disease: arthritis(1),casts/splints/slings(1),prosthesis(1)

  SUB-TOTAL=_____

Fall Risk Score and Risk

- TOTAL SCORE_____
- Risk Ranges minimal: 0-3
- moderate: 4-7 high risk: 8 or more
- Average Risk for non-fallers <8-10
- Average Score from Fall studies for fallers~15 or more

Depression and Aggression in Dementia

- Recent study suggested that those with Cornell scale of 12 or > had greater aggression tendency and that treatment with antidepressants may lessen this aggression (Lyketsos CG, et al . Am J Psych 1999;156:66-71)

Psychotropics and falls Sleeper R et al. Pharmacotherapy 2000;308-17

- A 1966-1999 Medline search reviewed all psychotropic classes and found that all may be associated with falls, but most recently SSRIs
- Reviewed epidemiology, risk factors, prevention, and drug risks that were at least OR 2.0 or more per agent

Steps to Decrease Psychotropic Load

- Identify psychotropics and other psychoactive meds; Tx depressive syndromes
- Follow OBRA mandate to taper antipsychotics and benzodiazepines at least 2-3 times in first 6-12 months of admission to facility
- Document MMSE, BCRS/GDS before and after changes

Fall Assessment-Cooper JW, Horner R

# of psychotropics	# of patient months	# of patient falls	Pop. fall rate/month	Relative risk
0	727	44	0.06	
1	557	62	0.11	1.83
2	236	46	0.19	3.17
3	60	24	0.40	6.67
4	13	8	0.62	10.33

Subsequent Results

- In a 6,000 pt.month follow-up study in same population over 3 years, same doubling of rate per psychotropic agent was seen, AND
- Risk of injury from falls was 10X greater if faller was taking a psychotropic agent (Cooper JW, Herrin H, data in prep)

Case 6: antipsychotic agents

- A 77 yoaaf taking Zyprexa 5mg HS for dementia-associated agitation falls 3 times the first month on this med. Would you recommend:
- A. decrease Zyprexa dose to 2.5mg
- B. Change to Risperdal 0.5mg HS
- C. stop Zyprexa and evaluate
- D. Add lorazepam or Ambien for sleep
- HINT-change to B reduced to NO falls next month and improved ADLs

Case 7: falls with anxiolytic agents

- An 82 yocm taking diazepam 2mg TID (alone) fell twice first month in the NF would you recommend changing to:
- A. Chlorazepate 7.5mg TID
- B. Clonazepam 0.5mg
- C. Lorazepam 1mg TID
- D. Oxazepam 5 mg TID
- E. Paxil 10mg, Lexapro 5mg or Zoloft 25mg daily for 30 days, then taper diazepam at 10-25% q 2weeks

Case 8: falls with hypnotic agents

- A 74 yoaam is taking Ambien 5mg at 6-7 PM q HS, MRX1 and falling 2 to 3 times/week with excessive daytime sedation. What would you do:
- A. stop Ambien
- B. Sleep retrain (NO NAPS AFTER MEALS) and trazodone 25-50mg Hs up to 3X week
- C. evaluate for depression and suggest Remeron or Paxil
- D. all of the above

Case 9- falls with antidepressant (AD)

- An 89 yocm has amitriptyline 25mg HS started for depression, shingles and appetite and falls several time first week. You recommend:
- A. sleep retrain and depression assessment, ranitidine for shingles pain, MVM for appetite
- B. Switch to Lexapro, Remeron or Zoloft if still depressed via Cornell Scale
- C. Group activities as he gets AD effect
- D. all of the above

Inappropriate Drugs Research

- Liu GG and Christensen DB, JAPhA 2002;42:847-57 reviewed 11 studies and found that up to 40% of nursing home and 21% of community-dwelling elderly were receiving inappropriate drugs-predominantly propoxyphene, amitriptyline and LABZs-
- Risk factors were: polyRx, poor health status and female sex

Beer's Studies to date-

- Beers MH et al Explicit criteria for determining inappropriate medication use for nursing home residents, Arch Intern Med 1991;151:825-32.
- Beers MH. Explicit criteria for determining potentially inappropriate medication use by the elderly. An update ibid 1997; 157:1531-6.
- Fick DM, Cooper JW, Wade WE, Beers MH et al. Updating the Beers Criteria for Potentially Inappropriate Medication Use in Older Adults Arch Int Med 2003;163:2716-24.

Categories of Inappropriate Use in 2003 Study Fick et al.

- **Criteria for potentially inappropriate medication use in older adults:**
- **1. Considering diagnoses or conditions**
- **2. Independent of diagnoses or conditions**

Drugs and why?

- Propoxyphene (Darvon) and combination products (Darvon Cpd, Darvocet N, Wygesic AKA “Demoncet”)- Offers few analgesic advantages over acetaminophen, yet has the side effects of other narcotic drugs-to include 20-36 hrs. half life of norpropoxyphene metabolite and increased risk of delirium, confusion, falls, TdP due to QTc prolongation (Cooper JW Cons Pharm 1997)
- Alternative-Detox carefully at a dose/week if taking for more than 2 weeks at BID->QID-replace each dose with 500-650mg APAP. If opioid is needed consider tramadol 25-50mg/day or hydrocodone 2.5-5mg QID with APAP (codeine has many drug interactions preventing conversion to morphine)-Also Propoxyphene increases ADR events OR=2.34,ER visits and hospitalization costs 60-90% compared with APAP for pain in NH residents . Perri M, Cooper JW Ann Pharmacother 2005.

Case 10-Falls and Analgesics

- A 77 yowf started on Demoncet i TID for OA fell 3x the first week of Rx would you:
- A. d/c Darvocet/Demoncet
- B. Start APAP 500-650mg QID and consider Glucoseamine/chondroitin
- C. recommend full med evaluation
- D. all of the above

Pain Meds- cont'd

- Meperidine- (Demerol or "Demonal") May not be an effective analgesic and may have many disadvantages to other narcotic drugs- esp. normeperidine metabolite with t1/2 of 17-35 hrs and amphetamine-like side effects of CNS excitation to seizures (AHFS 2003). REMEMBER- meperidine was orginally a substitute for atropine!
- Alternatives-tramadol up to 100-110mg/day, fentanyl if on opioids X 2 weeks, oxycodone, morphine or hydromorphone

Case 11-Pain Intervention Cases and Costs

- MG a 77 yowf, 5'6" 220 lbs. GDS=2 , VAS=5-7, Given propoxyphene/APAP (DVN) QID for OA. Over 2 weeks became progressively more disoriented to time, place and person (GDS 2->6). Thioridazine and flurazepam added and admitted to NF 3 X for 3 to 4 months/admission over next year for falls and Fx-
- Cost?- **$60,000+**

MG Case Intervention

- Taper DVN weekly QID->TID->BID->QHS then d/c, replacing each DVN dose decrease with 650mg APAP
- Taper thioridazine then flurazepam 25% of dose q 2 weeks . VAS then 6-7, GDS=1-2 ;After DVN and psychotropic tapered and pt. Taking 500mg of APAP QID VAS=5-7, changed to celecoxib 400mg/day but HBP/CHF developed, then back to APAP 500mg QID +Ultracet ½ tab BID X one week then one tab BID. Added 70% sorbitol 30->60ml HS.

MG Case Outcome

- Over next three years, MG lived with daughter on this regimen at $7,200/yr
- MG kept GDS of 1-2 and VAS scores of 2-3 on this regimen
- MG resumed knitting and making pralines
- Cost savings? 1st-2nd year: $60,000-7,200= $52,000 saved

Does High OP Risk Predict Risk of Injury From a fall?

- Based on Cooper OP and fall Risk assessment method- there is a correlation between OP risk and injury from a fall (Cooper JW , submitted) if score is >50.
- Please see OP/Fall Risk assessment method for both risk and intervention method

Consultant Pharmacist Interventions in LTC OP AX and Tx (Cooper JW subm)

- A 5-yr. Intervention trial found-30% admissions with Hx Fx- adequate calcium intake via diet or drugs (86-93%)
- The citrate is better tolerated than the carbonate, gluconate salts-ensure 800 u Vitamin D daily
- The daily use of the bisphosphonate alendronate was d/cd in 17/23 within 3 months of start due to GI SEs. Weekly risedronate accepted in 14 of 16 recommended and other two on weekly alendronate

Reasons to Stop HRT/ERT or convert to Topical dosage forms and Recommend Other OP drugs

- 1. No evidence of nonvertebral benefit for OP
- 2. Strong evidence of PO increased risk of migraines, CV, DVT, CVA, diabetes and dementia risk with HRT/ERT
- 3. Convert to topical? Only PO HRT/ERT has been linked with evidence in 2.
- 4. Bisphosphonates simply better overall protection and increased BMD at all sites as well as decreased vertebral and non-vertebral Fx risk- Actonel is safest, Boniva is only vertebral and Fosamax may be most gastropathic!

Falls and Risk Management

- Falls are the number one and top four lawsuits against nursing facilities. The average out of court settlement is $27,000 (Fraser M, Nursing Homes Sep 1995)- Definition of “waste”?
- Each fall costs $800+ if not hospitalized, $12,000-22,000+ if hospitalized (Cooper JW, JAMA, Cons Pharm 1997 and subm 2005)

Successful OP Prevention Intervention

- Adequate calcium and vitamin D
- A bisphosphonate with least gastropathic NSAID or APAP for OA if no Hx of severe GERD nor erosive esophagitis nor Barretts Esophagus
- Adequate fluid, 6-8 oz. Water ONLY and must sit up for 30-60 minutes after each dose
- Move daily to weekly bisphosphonate- special caution if already taking H2RA or PPI for GERD/PUD or both caution if already taking either/both agents

Dementia Interventions

- A recent review by Osterweil D Ann LTC 2004;12(18-24) suggested that donepezil (Aricept), rivastigmine (Exelon) or galantamine (Razadyne ER) may be effective for behavioral symptoms in NH residents with dementia-
- memantine (Namenda) may benefit for this use, but some suggest Namenda before the drugs above to aide in titration and enable more to overcome GI side effecst

Which CI has best evidence to date?

- The Lancet 2004;363:2105-15 study of 39,000 UK patients for 5 years in a randomized double-blind controlled trial found that donepezil neither slows the onset, nor delays the need for NH placement- no word on behavioral modification in this study, but a recent meta analysis of all 4 CIs found all 4 to improve behavioral symptoms of Alzehimers dementia (Trinh NH et al JAMA;2003;289:210-6)
- The only head to head CI trial is between donepezil and galantamine (G Wilcock et al Drugs&Aging 2003;20(10):777)- the longest trial to date for 52 weeks found galantamine to produce significantly better responses in more patients on MMSE and ADAS-Cog/11 than donepezil

Changing Between Aricept, Reminyl->Razadyne and Exelon

- If Aricept is stopped and Razadyne is to be started- wait for at least one to two weeks to start another agent due to the 70-100 hour half-life of Aricept. Case reports of severe nausea and emesis have been reported when this interval is not applied-(Terry A, submitted) T1/2 Reminyl 7hrs; Exelon, 1.5hrs.If Razadyne IR or ER is started, a dose of 4mg BID or 8mgER daily for 4 weeks is recommended; if tolerated without GI upset, from nausea to diarrhea and wt. loss, bradycardia (p<50-60 BPM) increase toIR 8mg BID or ER 16mg daily- do not exceed 16mg/day if moderate renal impairment CrCl10-50ml/min. (Ave is 40 in most NF residents) Do NOT use if CrCl<9ml.min or Child-Pugh hepatic score is 7-9. Exelon starts at 1.5mg BID for 2 wks, then 3mg BID if tolerated at minimum 2 wk. Interval, then 4.5 and 6mg ibid.

Cholinesterase Inhibitors (CIs) and Drug Interactions

- Avoid anticholinergcs- some studies (JAGS May 2002) show that 28% of those on a CI were taking at least one anticholinergic.
- Avoid additive cholinergics- eg bethanecol or other Cis, even if topical (pilocarpine)
- Avoid NSAIDs- even low-dose ASA can increase risk of anemia to GI bleed. Cimetidine, paroxetine, erythromycin and ketoconazole can increase the area under the curve for Reminyl
- Enzyme inducers (e.g. carbamazepine, pb, DPH or rifampin can lower donepezil levels;
- NO Neuromuscular blocking agents-

Case 12- Antidementia Therapy

- A 76yof is taking galantamine and has the “four Ds” a. Darvocet b. Ditropan c. Dalmane and d. Donnatal added
- Which drugs by letter need to be stopped or e. all stopped for galantamine maximum benefit?
- When should memantine 5-10mg be tried if Razadyne ER is of benefit at 8mg/day but some nausea noted?

Sucessful Communications

- Case-12 The 4 “Ds” Intervention
- Patient- unable to comprehend NP=no problem
- HX- OA, GERD, mid-stage Dementia with some harmful behaviors with caregiver, antidepressant stopped 3 mos ago (Fluoxetine 20mg daily with increased agitation and wt. loss noted over 6 weeks trial), I=incontinence and severe constipation after 4 D’s started
- Caregiver or prescriber- RE: Mrs. ST-OA- Please consider stopping Darvocet and replace each dose with Tylenol XS one tablet 4 times a day and Glucoseamine 1500mg and chondroitin 1200mg/day with food; NP-taper Dalmane if taking for more than 1-2 weeks every night-go to QO nite X 2weeks, then q3rd nite ditto, then q4th night, and replace with Ambien 2.5mg HS no sooner than 10-11PM if NOT sleeping during day-if is sleeping during day NO SLEEPER at night if depressed Remeron 7.5mg QO nite; I-d/c Ditropan and try Oxytrol patch q3d; GERD- d/c Donnatal and try ranitidine 150mg BID or Omeprazole 20mg OTC q AM

Case 12 Communication Cont'd

- Prescriber additions Constipation-severe constipation noted, please start 70% sorbitol 30ml q HS with full glass water if still has impactions after 4 Ds stopped.
- Dementia-If Razadyne ER nausea is suspected but some cognition and ADL benefit seen, please add Namenda 5mg q AM to Razadyne 8mg/day for two weeks, before increasing Razadyne ER dose to 16mg/day, then after 4 weeks, increase Namenda to 10mg/day and do not push dose to 20mg/day due to decreased renal function. Please observe for improved orientation to time, place and person, socialization and recognition of loved ones and friends. Please add folic acid 1mg/day for possible added effect on cognition. Will repeat assessment per family or your request on next refill of Rxs. Thank you for the chance to offer these recommendations.
- Jim Cooper, RPh

Impact of Interventions on Geriatric Prescribing

- Impact of consultation on geriatric patient prescribing (Lipton HL, et al., Med Care 1992;30-646-58). 236 Hospitalized patients 65 yo or older with 3 or more meds, 88% had at least one-->
- Clinically-significant Rx problem and 22% had serious to life-threatening ADR problem due to meds; pharmacist consult intervention in-hosp., discharge &1 & 2 months afterward decreased problems vs. control group

In-hospital ADRs and Costs

- In hospital ADRs rank between 4th and 6th as leading causes of death in the USA- Lazarou J, et al. JAMA 1998;279:1200-5) 2.2 million hospitalized pts. Had serious ADRs and 106,000 died in 1994 via meta-analysis of 39 studies
- Two studies document high costs of ADRs within the hospital: Classen DC, et al. JAMA 1997;277:301-6 & Bates DW, et al. Ibid:307-11. In 1st, a 4-year study, ADRs occurred in 2.43/100 admissions AND-->

ADR costs cont'd-

- In 1st study, each ADR added 2+ days to LOS, >$2,200 in costs and doubling of death rate
- 2nd study (Bates) over 6 months, 247 ADRs were identified from 4,108 admssions
- Almost one-third of ADRs were deemed preventable.
- For preventable ADRs there was a 4.6 days increase in LOS & cost of $5,857; for all ADRs 2.2 days and $3244 increase in cost/ADR

Pharmacotherapy Recommendation Outcomes (Cooper JW J Nutr Health &Aging 1997;1:181-184)

- Are there pharmacoeconomic outcomes differences with recommendation acceptance vs. rejection of drug change recommendations? A two-year study found that even with a 90% acceptance rate that the $1094/pt. saved was negated by the $1101 lost with a 9.3% rejection rate

An Approach to Medication Therapy Management in the Geriatric Patient

- 1st rule in health care-"Do no harm"
- 2nd rule- "If its not broken do not try to fix it"
- 3rd rule-"if its broken offer several alternatives to fix it"
- Regulators may want to use the "inappropriate drug list" as a hammer and anvil for all HCPs
- Be sure you have a clinical problem before rec. change!

Summary and Conclusions

- In the year elderly become progressively to severely disabled a large proportion are hospitalized for a small number of diagnoses, most of which relate to drug use. (Ferruci L, et al JAMA 1997;277:728-34)
- ADRs are only 1/3 of drug-related admissions; other 2/3 are related to nonadherence to prescribed Tx (Cooper JW, et al. AJHP 1977; 34:738-42)
- How can health care practitioners improve drug use among older adults?

Assessment Questions

- 1. Agitation in cognitively-impaired older adults may be due to:
- A. depression
- B. pain
- C. drugs
- D. dementia and delirium
- E. All of the above

Ax Qs

- 2. True (a.) or false (b.)-The risk of falls and injury AND under-treatment of pain may be related to the use of inappropriate drugs in the older adult

Ax Qs

- 3. Which atypical antipsychotic has the lowest fall risk in equipotent doses?
- A. Abilify
- B. Risperdal
- C. Seroquel
- D. Zyprexa
- E. Geodon

Ax Qs

- 4. Which of the following is the best OP treatment for frail elderly, with adequate calcium and vitamin D, if they can swallow and drink adequate fluids?
- A. Actonel weekly
- B. Fosamax daily
- C. Forteo daily
- D. Miacalcin
- E. Oral hormone replacement therapy

Ax Qs

- 5. Which of the following is/are considered inappropriate in the older adult?
- A. Darvocet(AKA Demoncet)
- B. Demerol (AKA Demonal)
- C. Elavil (amitriptyline)
- D. Zyprexa (olanzapine)
- E. All of the above

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