

# **The Use of NSAIDs in the Management of Persistent Pain in Older Persons**

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# Musculoskeletal conditions are highly prevalent

- Musculoskeletal disorders account for more than 50% of all chronic conditions in people over 50 years of age
- Musculoskeletal conditions are reported by 72% of persons aged 75 years and over

– SOURCE: National Center for Health Statistics, National Health Interview Survey, Adult Sample, 2005

# Musculoskeletal conditions are costly and debilitating

- Back disorders (including spinal stenosis) account for 81% of health care visits in persons aged 75 and over (in 2004)
- Among adults aged 65 and older, 22% report arthritis-attributable activity limitations

– SOURCE: National Center for Health Statistics, National Health Interview Survey, 2003-2005

# NSAIDs



- Daily Use: 17 million Americans
- Prescriptions: 60 million annually
- US annual expenditure: \$2 Billion

# A Detour into Herbal Medicine



# Salix babylonica:

- commonly known as the Weeping Willow
- native to China
- deciduous tree



Since ancient times preparations from *Salix*  
species have  
been used for the treatment of pain



24 g dried and powdered bark may contain up to  
1000 mg of salicin;



- crude plant material generally contains about 4% salicin
- Salicin exerts a dose-dependent analgesic effect
- Salicylic acid is a metabolite of salicin

# Why do we use NSAIDs?

- Pain
- Function
- *NOT* for structural modification



# Cyclooxygenase

- Converts arachadonic acid to prostaglandin  $H_2$
- $PGH_2$  is the precursor to prostaglandins and thromboxane

# Two Isoforms of Cyclooxygenase

## COX-1

- found in platelets, kidneys, and GI tract

## COX-2

- constitutively expressed in kidney and brain
- inducible at sites of inflammation

# Three Types of COX Inhibitors

- Aspirin
- nonselective NSAIDs
- “coxibs”



# ASA

- Irreversibly inhibits COX-1
- acetylates serine-529 residue
- inhibits thromboxane  $A_2$



# Conventional NSAIDs

- Inhibit both COX isoforms
- GI adverse events in 20%
- 107,000 hospitalized yearly
- 16,500 die yearly from NSAID-related ulcer complications

# Coxibs

- Selective for COX-2
- Effective anti-inflammatory agents
- Fewer clinical upper GI events

What are the class effects?



# Major Adverse Effects of NSAIDs as a Class

- HTN
- Renal Impairment
- Edema
- GI impairment
- Cardiovascular toxicity



# Key Recent Findings



# Tennessee Veteran's Administration study of noninstitutionalized Medicaid enrollees

- the risk for stroke is greatest in users of selective COX-2 inhibitors as compared to nonselective agents
  - *Stroke*. 2008 Apr 24 Nonaspirin NSAIDs, Cyclooxygenase 2 Inhibitors, and the Risk for Stroke. Roumie CL, Mitchel EF Jr, Kaltenbach L, Arbogast PG, Gideon P, Griffin MR

# NSAID-naïve users may benefit from testing for the presence of H. Pylori

- Eradication of H. Pylori does not guarantee prevention of future events
  - *Rheumatology* (Oxford). 2008 Use of NSAIDs and infection with Helicobacter pylori--what does the rheumatologist need to know? Kiltz U, Zochling J, Schmidt WE, Braun J.

# Concurrent use of low-dose ASA

- Combining traditional NSAIDs with low-dose aspirin therapy increases the risk of gastrointestinal bleeding beyond that of the traditional NSAID alone
  - McKellar, Madhok, Singh Update on the use of analgesics versus nonsteroidal antiinflammatory drugs in rheumatic disorders: risks and benefits *Curr opin rheumatol* 2008  
20:239-245

# The FDA Issued a Warning in 2006

- Ibuprofen *antagonizes* ASA effect on platelets by interfering with acetylation



# SPECIFIC RECOMMENDATIONS

- No differences in clinical efficacy among NSAIDs
- more data needed on safety of topical preparations of NSAIDs
- coxibs are associated with an increased risk for cardiovascular toxicity
- eradication of H. Pylori prior to initiating NSAID can reduce risk for future ulcer
- PPI + coxib reasonable for high risk individuals

# SPECIFIC RECOMMENDATIONS

- FDA recommends avoiding ibuprofen and low-dose ASA together
- More research needed to determine if low-dose ASA + other NSAIDs preserves cardioprotection of ASA alone
- monitor patient on any NSAID for edema, hypertension, and congestive heart failure



Helpful  
TIPS

# Clinical paradigm

- High GI/ low cardiovascular risk:
  - traditional NSAID + PPI, or
  - COX-2 inhibitor
    - consider co-administering low-dose ASA in older individuals
    - consider co-administering PPI because of age-associated risks



# Clinical paradigm



- High GI risk + high cardiovascular risk:
  - low dose-ASA together with
    - naproxen, or coxib
    - PPI

# IN CONCLUSION

- *Think twice* before prescribing NSAIDs in older individuals
- Know your drug-drug interactions
- Consider GI protective measures



Questions?

