FREQUENTLY ASKED QUESTIONS

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Coxib = COX-2-specific inhibitor; nsNSAID = non-specific non-steroidal anti-inflammatory drug

How should pain be assessed in an unconscious patient?

- Rely on behavioral and physiologic indicators

Behavioral indicators

- Facial expression
- Body movements
- Muscle tension
- Vocalization (extubated patients)/ compliance with ventilator (intubated patients)

Physiologic indicators

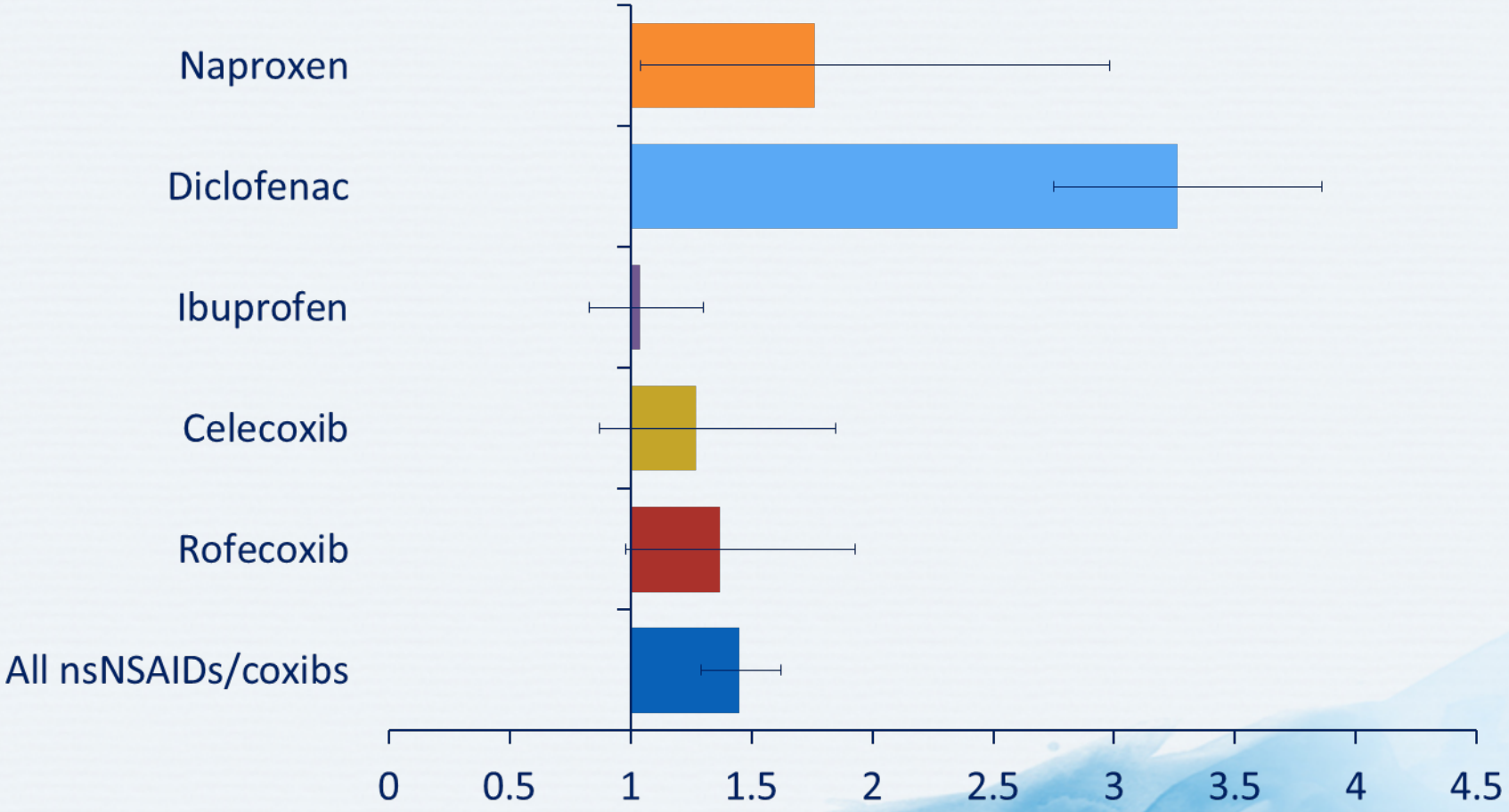
- Mean arterial pressure
- Heart rate
- Respiratory rate
- Transcutaneous oxygen saturation

- Critical-Care Pain Observation Tool (CPOT) tool validated in conscious and unconscious critical care patients

Gélinas C *et al*. *Clin J Pain* 2007; 23(6):497-505.

What is the cardiovascular risk associated with the use of nsNSAIDs/coxibs in acute pain (i.e., for 7–10 days)?

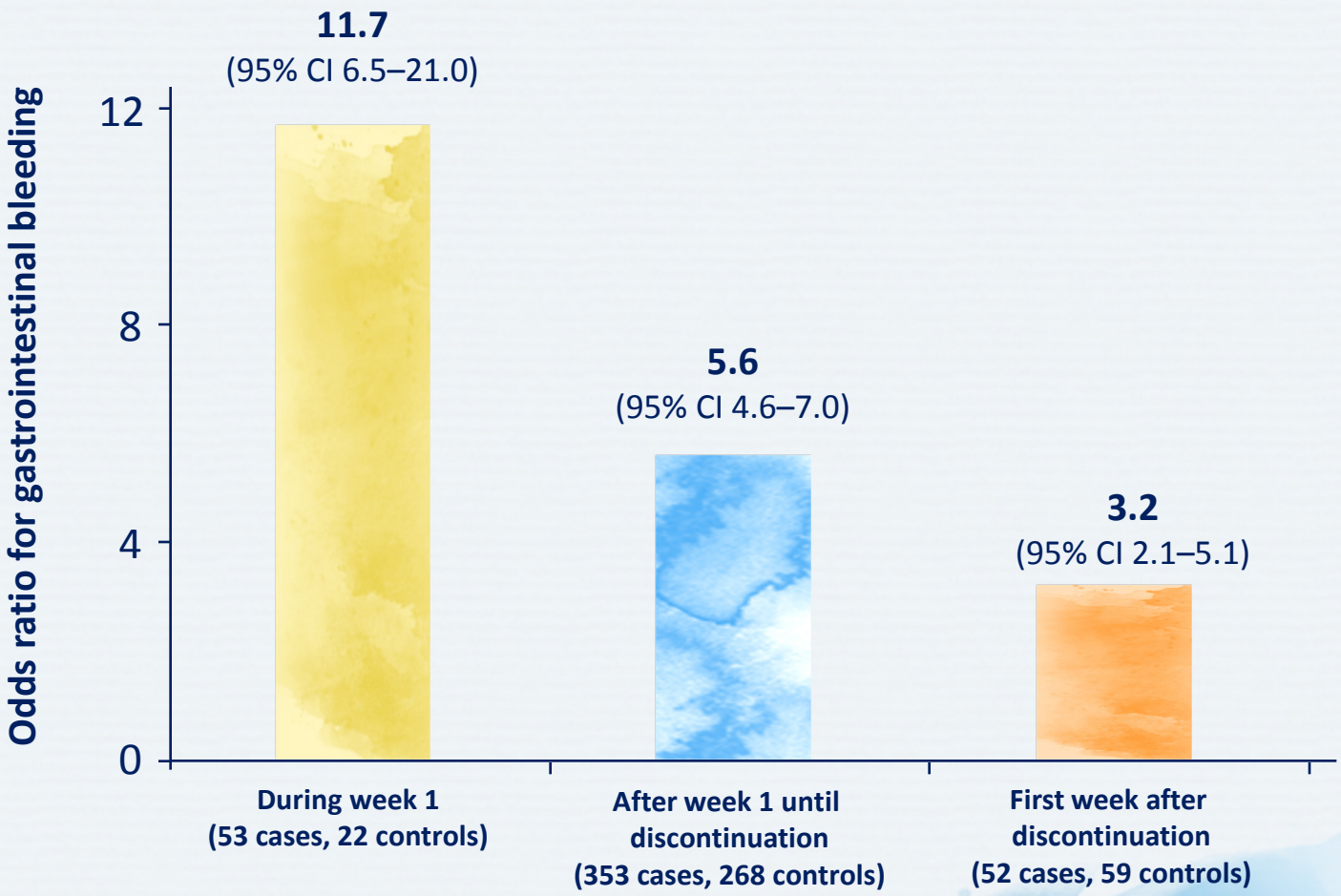
Risk of Death/Myocardial Infarction within First 7 Days of nsNSAID/Coxib Treatment in Patients with Previous Death/Myocardial Infarction



Coxib = COX-2-specific inhibitor; nsNSAID = non-specific non-steroidal anti-inflammatory drug

Schjerning Olsen AM *et al. Circulation* 2011; 123(20):2226-35.

What is the gastrointestinal risk associated with the use of nsNSAIDs/coxibs in acute pain (i.e., for 7–10 days)?



CI = confidence interval; coxib = COX-2-specific inhibitor; nsNSAID = non-specific non-steroidal anti-inflammatory drug

Lewis SC *et al*. *Br J Clin Pharmacol* 2002; 54(3):320-6.

Do nsNSAIDs/coxibs interfere with bone healing?

- Some animal and *in vitro* studies suggest nsNSAIDs may delay bone healing, though results are contradictory
- However, clinical experience and most *in vivo* studies do not substantiate this
- Balance of evidence suggests short-duration nsNSAID/coxib use is safe and effective for post-fracture pain control

Coxib = COX-2-specific inhibitor; nsNSAID = non-specific non-steroidal anti-inflammatory drug

Kurmis AP *et al*. *J Bone Joint Surg Am* 2012; 94(9):815-23; Pountos I *et al*. *ScientificWorldJournal* 2012; 2012:606404.

Does the peri-operative use of nsNSAIDs/coxibs increase the risk of bleeding?

- A meta-analysis of 36 studies suggests post-operative nsNSAID/coxib use had no effect on:
  - Bleeding that could be managed conservatively
  - Bleeding treated with reoperation
  - Readmission
- Similarly, there was no significant difference in rates of bleeding in studies that gave nsNSAIDs/coxibs at multiple times (e.g., both before and after surgery)

Coxib = COX-2-specific inhibitor; nsNSAID = non-specific non-steroidal anti-inflammatory drug

Riggin L *et al. Clin Otolaryngol* 2013; 38(2):115-29.

Can benzodiazepines be used to treat acute pain?

- No – benzodiazepines are not effective for the treatment of acute pain
- Little evidence of efficacy in acute pain
- Side effects include somnolence, fatigue and lightheadedness
  - 1 higher quality trial in acute low back pain found no difference between diazepam and placebo, while a lower quality trial found diazepam was superior

Chou R *et al. Ann Intern Med* 2007; 147(7):505-14.

What drug-drug interactions should clinicians consider when treating acute pain?

Interactions with nsNSAIDs/coxibs		
Drug	**Effect**	**Management**
Aminoglycoside antibiotics	Renal clearance inhibited	Monitor antibiotic concentration and adjust dose as necessary
Anticoagulants	Increased risk of bleeding	Monitor prothrombin time Avoid ASA use
Antihypertensive agents (with some NSAIDs)	Reduced antihypertensive effect Potential hyperkalemia with diuretics and ACE-Is	Monitor blood pressure, cardiac function and potassium concentration
Digoxin	Renal clearance inhibited	Monitor digoxin concentration and adjust dose as necessary

ACE-I = angiotensin-converting enzyme inhibitor; ASA = acetylsalicylic acid; coxib = COX-2-specific inhibitor; NSAID = non-steroidal anti-inflammatory drug; nsNSAID = non-specific NSAID

American Medical Association. *Table: Potential Drug Interactions with NSAID Analgesics.* Available at: http://www.ama-cmeonline.com/pain_mgmt/tables/table_nsaids_interactions.htm. Accessed: September 5, 2013.

Drug-Drug Interactions with nsNSAIDs/Coxibs (cont'd)

Drug	Effect	Management
Lithium	Increased lithium concentration	Monitor lithium concentrations
Methotrexate	Increased methotrexate concentration	Monitor methotrexate concentration Avoid NSAIDs with high-dose methotrexate
Phenytoin (with ibuprofen)	Increased phenytoin levels	Monitor phenytoin concentration and adjust dose as necessary
Probenecid (with naproxen)	Reduced clearance of naproxen	Monitor for adverse effects

Coxib = COX-2-specific inhibitor; NSAID = non-steroidal anti-inflammatory drug; nsNSAID = non-specific NSAID

American Medical Association. *Table: Potential Drug Interactions with NSAID Analgesics.*
Available at: http://www.ama-cmeonline.com/pain_mgmt/tables/table_nsaids_interactions.htm. Accessed: September 5, 2013.

Drug-Drug Interactions with Opioids

Drug	Opioid(s)	Effect
Antibiotics Clarithromycin Erythromycin Rifampicin	 Fentanyl Methadone Morphine	 Reduced fentanyl clearance, respiratory depression Increased opioid metabolism (may induce withdrawal) Reduced analgesic effect, increase dose if needed
Antifungals (ketoconazole, itroconazole)	Fentanyl	Reduced fentanyl clearance and respiratory depression
Antihistamines	All	Increased sedation
Antiretrovirals Lopinavir Nelfinavir Ritonavir Zidovudine	 Methadone Fentanyl Fentanyl Methadone	 Increased opioid metabolism (may induce withdrawal) Reduced fentanyl clearance, respiratory depression Reduced fentanyl clearance, respiratory depression Zidovudine metabolism inhibited
Beta-blockers (metoprolol, propanolol)	Propoxyphene	Increased plasma levels of beta-blockers

American Medical Association. *Table: Important Opioid Drug Interactions.* Available at: http://www.ama-cmeonline.com/pain_mgmt/tables/table_opioid_interactions.htm. Accessed: September 5, 2013; Australian and New Zealand College of Anaesthetists and Faculty of Pain Medicine. Acute Pain Management: Scientific Evidence. 3rd ed. ANZCA & FPM; Melbourne, VIC: 2010; South African Society of Anaesthesiologists. *SAJAA* 2009; 15(6):1-120.

Drug-Drug Interactions with Opioids (cont'd)

Drug0	Opioid(s)	Effect
Butyrophenones	All	Increased sedation
Carbamazepine	Methadone Propoxyphene	Increased opioid metabolism (may induce withdrawal) Increased carbamazepine levels, potential toxicity
Cimetidine	Meperidine, morphine	Increased opioid effects
Desipramine	Methadone, morphine	Possible toxicity due to inhibition of desipramine metabolism
Doxepin	Propoxyphene	Possible toxicity due to increased doxepin levels
Erythromycin	Methadone	Increased opioid metabolism (may induce withdrawal)
MAOIs	Meperidine	Excitatory response (includes seizures, arrhythmia, hyperpyrexia)
Phenytoin	Methadone	Increased opioid metabolism (may induce withdrawal)
Quinidine	Codeine	Decreased analgesia
TCAs	All	Increased sedation

MAOI = monoamine oxidase inhibitor; TCA = tricyclic antidepressant

American Medical Association. *Table: Important Opioid Drug Interactions.* Available at: http://www.ama-cmeonline.com/pain_mgmt/tables/table_opioid_interactions.htm. Accessed: September 5, 2013.