Cheatography

NSAID Pharmacology Cheat Sheet

by happyfeet2020 via cheatography.com/144934/cs/31540/

How Do NSAIDs Work?

NSAIDs have anti-inflammatory, antipyretic, analgesic and anti-platelet properties.

Goal is to inhibit the cox-mediated generation of pro-inflammatory eicosanoids and to limit extent of inflammation, pain and fever.

They do this by blocking the site in cyclooxygenase enzyme in which substrate arachidonic acid binds to

Most NSAIDs are metabolized in the liver by oxidation and conjugation to inactive metabolites which are typically excreted in urine

*patient sensitive to one NSAID may be sensitive to any other NSAID. Studies show that meloxicam can be a good option for NSAID intolerant patients

COX-1 Function

Contributes to homeostasis

Ongoing constitutive physiologic "house keeping", vascular homeostasis, maintenance of renal, myocardial and GI blood flow, platelet function, intestinal mucosal proliferation, antithrombogenesis

COX-1 Inhibition

Decreases mucosal defense

Increase GI acid, and decreases GI mucus

Decreases HCO2 secretion

Decreases mucosal blood flow

Special Consideration for NSAIDs

1. Both ibuprofen and naproxen may reduce the effects of furosemide (diuretic) and may reduct the effectiveness of several antihypertensive agents

2. Indomethacin is the NSAID most likely to cause nephrotoxicity

COX 2 Inhibitors

Due to sometimes severe GI adverse effects associated with long-term NSAID therapy, selective cox 2 inhibitors are used

Inhibition of the chemical mediators responsible for inflammation while maintaining the cytoprotective effects of the products of COX-1 activity

Meloxicam

Inhibition of COX-2 may generate some problems in wound healing, angiogenesis and the resolution of inflammation

Lower GI and renal problems

Cox 2 may induce hypertension, renal failure and cardiac failure

Naproxen has some cardioprotective properties

Contraindication for NSAIDs (cont)

Compromised Renal Function	NSAIDs reduce renal blood flow and therefore may further reduce renal function which may have an impact on the effects of concurrent meds and elimination of the NSAID and other meds and toxins
Compromised Liver Function	Most NSAIDs are metabolised in liver
Hypersensitivity	Happens more in asthmatics

COX 2 Function

Works at the site of pain and inflammation

Source of prostacyclin- platelet stability/dilate blood vessels

COX 2 Inhibition

Decrease pain and inflammation

Increases CV risk as it shifts the balance between platelet production TxA2 and PGI2, predisposing to platelet aggregation, thrombus formation and vasoconstriction

Salicylates

Salicylates (cont)

A single administration of aspirin decreases for several days the amount of thromboxane that can be generated, shifting the vascular TxA2-PGI2 balance toward PGI2 mediated vasodilation, platelet inhibition, and antithrombogenesis

Long term use of aspirin can lead to GI ulceration and hemorrhage, nephrotoxicity and hepatic injury

Two unique toxicities of aspirin: induced airway hyperactivity in asthmatics and reye's syndrome

NSAID Drug to Drug Interaction

Contraindication for NSAIDs	
Reye's Syndone	For patients under 18 years old
Pregnancy	

Includes Aspirin which acts in an irreversible manner by acetylating the active site serine residue in both COX-1 and COX-2

Daily low dose aspirin is used as an anti-thrombogenic agent for prophylaxis and post event management of MI and stroke

Aspirin is antithrombogenic because of its irreversible inhibition of COX, which prevents platelets from biosynthesizing TxA2

Within an hour of aspirin, the effects of COX-1 activity on newly formed platelets is irreversibly destroyed (acetylated) therefore TXA2 cannot be produced

Wendy's LAMP	mnemonic for remembering drug interactions
Warfarin	May increase risk of bleeding- Monitor PT and INR
Lithium	May increase lithium plasma levels and decrease its clearance renally- need to monitor
ACE Inhibitors	may decrease antihypertensiuve effects so need to monitor BP and CV function
	NSAIDs increase BP and decrease affects of diuretics, ACE inhibitors and ARB which all relax blood vessels as NSAIDs inhibit cox-2 in kidneys which decreases sodium excretion due to a decrease in prostaglandins
	NSAIDs may increase fluid retention and decrease blood flow to the kidneys as they block prostaglandins which dilate blood vessels and allow O2 to reach kidneys
Methotrexate	May lead to an increase in methotrexate toxicity- don't administer within 10 days of high dose methotrexate
Probenecid	May lead to reversal or uricosuric effects

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Non-Selective COX 1 and COX 2 Inhibition

GI irritation due to decreased protection of gastric mucosa.- N&V, GI ulcer, diarrhea

Skin reactions - mild rash, hives, photos-ensitivity

Inhibition of platelet function- increase risk of bleeding

Decreased renal blood flow- decreases GFR can cause renal ischemia- look out for pts w/ renal disease

CVD risk

Respiratory- bronchospasm- look out for asthmatic pts

Risk Factors for GI complications

Over 60 in age

history of peptic ulcer

use of anti coagulants or corticosteroids

History of pylori infection

High NSAID dose or use of two NSAIDs

Severe illness

Reducing GI risks

Misoprostol	Synthetic prostaglandin- Protects gastric mucosa from irritation
Protein Pump Inhibitors	Long lasting reduction of gastric acid production
	Drugs end in -"prazole"
H2 Receptor Antagonists	Blocks the action of histamine on parietal cells in the stomach decreasing the production of acid by these cells
	Drugs end in -"dine"
	Not enough evidence that these alone will work in reducing GI issues
COX-2 Inhibitor	Allow continued protective COX-1 function

Acetaminophen

Not an NSAID

Has analgesic and antipyretic effects similar to aspirin

anti-inflammatory effects are insignificant because of its weak inhibition of COX

May be a third functional COX isoform (COX-3)

MOA believed to involve the prostaglandin pathways within the CNS with little influence on peripheral prostaglandin synthesis

Adverse effect= hepatotoxicity as it is metabolized by hepatic cytochrome p450 enyzmes which produces a reactive molecule which is normally detoxified by conjugation with glutathione. An overdose of acetaminophen can overwhelm glutat-hione stores, leading to cellular and oxidative damage and in severe cases to acute hepatic necrosis

4000mg daily limit for adults. For those who are alcoholics or multiple medication patients and patients with liver disorders, even doses within the therapeutic range may be hepatotoxic

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