

NSAIDs

general

- NSAIDs have important clinical uses in critically ill patients, especially for treatment of pain. However, certain pharmacologic properties and their mechanism of action can cause serious side effects and can affect other medications used concomitantly.
- Common toxicities of NSAID therapy include gastrointestinal, cardiovascular, and renal side effects; mounting evidence suggests that COX-2 inhibitors are associated with an increased risk of cardiovascular adverse events
- Despite the common use of NSAIDs in clinical practice, serious acute overdose and adverse sequelae are reported infrequently.
- The mechanism of NSAID toxicity in overdose is related to both their acidic nature and their inhibition of PG production.

pharmacology

Generic name	Available dosages (mg)	Dose*		Pharmacokinetics	
		Common dosing intervals	Drug metabolism	Elimination half-life (h)	
Nonselective NSAIDs					
<i>Acetic acid^s group</i>					
Diclofenac ^s		25	tid	Oxidation	1-2
Ketorolac IM injection		30	qid	Conjugation	2.5-8.5
Indomethacin ^s		25	bid-tid	Oxidation, conjugation	4.5-6
<i>Oxicam group</i>					
Meloxicam ^s		7.5	qd	Oxidation	13-20
(Mobic)		15			
Piroxicam ^s		10	qd	Oxidation	30-86
(Feldene)		20			
<i>Propionic acid group</i>					
Ibuprofen ^s		400	tid-qid	Oxidation	2-2.5
Naproxen ^s		250	bid	Conjugation,	12-15
<i>Salicylate</i>					
Aspirin ^s		325	bid-qid	Hydrolysis, conjugation,	0.25-0.5
<i>Cyclooxygenase-2 agents</i>					
<i>Benzenesulfonamide group</i>					
Celecoxib ^s		100	qd-bid	Conjugation	11-16
<i>Furanone group</i>					
Rofecoxib		12.5	qd	Cytosolic enzymes	16-18

presentation of overdose

- Although patients with overdoses of aspirin and other NSAIDs may be asymptomatic depending on the amount ingested, common symptoms include nausea, vomiting, abdominal pain, tinnitus, hearing impairment, and CNS depression.
- With higher-dose aspirin ingestion, metabolic acidosis, renal failure, greater CNS changes (e.g., agitation, confusion, coma), and hyperventilation with respiratory alkalosis occur.
- The presence of acidemia permits more salicylic acid to cross the blood-brain barrier, with more severe CNS toxicity.

measurement of levels

- With salicylate overdose, the severity typically depends on the dose ingested and the salicylate concentration that correlates with the degree of acid-base disturbance.
- Measurement of salicylate levels is important in all cases of aspirin overdose to guide management. Serum salicylate levels should be measured 4 hours after ingestion and repeated in 2 to 4 hours to determine the peak concentration. If the acute ingestion was with an enteric-coated product, salicylate levels should be monitored for 12 hours, because of the delay in absorption and time to peak concentration.
- Generally, salicylate levels of 300 to 600 mg/L are associated with mild toxicity, 600 to 800 mg/L with moderate toxicity, and greater than 800 mg/L with severe toxicity. For other NSAIDs, plasma concentrations are not commonly measured and are less helpful, because the half-life of many of these agents is relatively short.

management

- convulsions or coma may necessitate airway protection
- patients may develop pulmonary oedema requiring breathing support
- appropriate hydration decreases risk of renal complications
- salicylate poisoning is classically associated with a raised anion gap acidosis in association with a respiratory alkalosis
- correction of acidosis is a priority of therapy as it aids in elimination & prevents CNS complications
- Although evidence is limited for the benefit of absorption therapy in aspirin overdose, activated charcoal is often administered within 1 hour after aspirin ingestion and repeated hourly for four doses until the salicylate levels peak.
- it is unlikely to be of benefit in other NSAIDs due to benign toxicity & rapid absorption
- Urine alkalinization increases salicylate elimination, especially in adult patients with salicylate levels of 600 to 800 mg/L and in the elderly.
- Because of the relatively neutral pK of salicylic acid, increasing the urine pH from 5 to 8 is associated with a 10- to 20-fold increase in renal salicylate clearance.
- In severe cases of aspirin overdose, hemodialysis is effective at removing salicylate and correcting acid-base imbalances and has been shown to reduce morbidity and mortality.
- Hemodialysis should be considered in patients with salicylate levels greater than 800 mg/L and in the elderly. Hemodialysis also should be considered in patients with metabolic acidosis refractory to treatment, severe and symptomatic CNS toxicity (e.g., coma, convulsions), acute pulmonary edema, or acute renal failure.
- self harm and suicide attempt

resuscitation

acid-base & electrolyte abnormalities

activated charcoal

urinary alkalinisation

haemodialysis

specific therapy

underlying causes