

NSAIDs and Upper GI Bleed

Gonzalez ELM et al. Variability among NSAIDs in risk of upper GI bleeding. Arthritis & Rheumatism. 2010; 62(6): 1592-1601.

Stomach and platelets have much more COX-1 receptors than COX-2 receptors.

Systematic review of observational studies on NSAIDs and upper GI complications (bleeding, perforation) during 2000-2008. Nine studies were selected.

NSAID medication	Relative risk of complication* [95% CI]	
COX-1 Inhibitors	4.5	[3.82-5.31]
• Ibuprofen	2.69	[2.17-3.33]
• Diclofenac*	3.98	[3.36-4.72]
• Meloxicam*	4.15	[2.59-6.64]
• Indomethacin*	5.40	[4.16-7.00]
• Ketoprofen*	5.57	[3.94-7.87]
• Naproxen*	5.63	[3.83-8.28]
• Piroxicam	9.94	[5.99-16.50]
• Ketorolac	14.54	[5.87-36.04]
COX-2 Inhibitors	1.88	[0.96-3.71]
• Celecoxib	1.42	[0.85-2.37]
• Aceclofenac	1.44	[0.65-3.2]
• Rofecoxib	2.12	[1.59-2.84]

* = estimated Relative Risk

Independent risk factors for upper GI complication:

1. Longer drug half-life
 - Piroxicam has longest half-life of NSAIDs at 50 hours: RR = 9.94
2. Slow-release formulation
3. Dual inhibition of COX-1 and COX-2 isoenzymes (ketorolac, piroxicam, naproxen, ketoprofen, indomethacin)

Interestingly, RR is greatest when first starting medication (<30 days).