

COX-2 INHIBITORS AND WORSENING HYPERTENSION

Background

The prevalence of hypertension (HTN) in the United States is increasing. Although many factors are thought to play a role, the use of certain medications including non-steroidal anti-inflammatory drugs (NSAIDs) has recently garnered attention in the clinical literature. Several studies have demonstrated an association between blood pressure destabilization and COX-2 selective or nonselective NSAID use, although conflicting data exist as to which group of agents has more pronounced hypertensive effects.

Comparison of COX-2 selective agents:

Brand	Generic	Dose	Cost*	Selectivity (for COX-2)**
Vioxx®†	Rofecoxib	12.5 mg po qd	\$86.27	80
		25 mg po qd	\$86.27	
		50 mg po qd	\$125.99	
Celebrex®	Celecoxib	100 mg po qd	\$52.67	9
		200 mg po qd	\$86.39	
Bextra®	Valdecoxib	10 mg po qd	\$91.47	18
		20 mg po qd	\$91.47	

*Cost based on 30 tablets per AWP from Red book (2003).

**Based upon 80% inhibitory concentration ratios in whole blood assays; ratios >1 indicate COX-2 selectivity.

†Vioxx® is the preferred agent for Idaho Medicaid.

Comparison of non-selective NSAID agents:

Brand	Generic	Dose	Cost*	Selectivity (for COX-2)
Lodine®	Etodolac	300 mg po tid	\$153.03	23
		400 mg po tid	\$161.79	
		500 mg po tid	\$162.81	
Lodine XL®	Etodolac	ER 400 mg po qd	\$49.47	23
		ER 500 mg po qd	\$51.70	
		ER 600 mg po qd	\$93.60	
Mobic®	Meloxicam	7.5 mg po qd	\$77.10	11
		15 mg po qd	\$89.58	
Voltaren®	Diclofenac	EC 25 mg po bid	\$28.00	4
		EC 50 mg po bid	\$54.39	
		EC 75 mg po bid	\$62.58	
		ER 100 mg po qd	\$84.43	
Motrin®	Ibuprofen	400 mg po tid	\$4.44	0.4
		600 mg po tid	\$5.16	
		800 mg po tid	\$9.59	
Naprosyn®	Naproxen	250mg po bid	\$46.60	0.3
		375mg po bid	\$63.84	
		500mg po bid	\$77.92	
Indocin®	Indomethacin	25 mg po tid	\$33.39	0.2
		50 mg po tid	\$56.49	
		ER 75 mg po qd	\$57.90	

*Cost of a 30 day supply based on AWP from Red book (2003); generic cost provided if available

Renal effects of NSAIDs

Although the COX-2 selective agents have safety advantages over non-selective NSAIDs in terms of reduced gastric ulcer risk and fewer GI bleeding complications, they do not afford superior protective benefits to the kidneys. Both forms of the COX enzyme are found renally and prostaglandins produced in the kidneys are responsible for renal blood flow regulation and sodium and water retention. The imbalance created in the kidneys by selectively inhibiting COX-2 may lead to cardiovascular effects that have yet to be fully characterized.

Recommendations

Both non-selective NSAID and COX-2 inhibitor use may be associated with significant cardiovascular effects. A precaution regarding the renal effects of COX-2 inhibitors is included in the product labeling of all three agents and current clinical data indicate that the inhibition of renal COX-2 by selective or non-selective agents may result in increased blood pressure. Cases of both new onset and worsening HTN have been documented. Although further research is indicated to fully determine the extent of cardiovascular risk in patients taking traditional NSAIDs or COX-2 inhibitors, prudence dictates judicious use of these agents in individuals at-risk for cardiovascular complications. **At this time, it is recommended that blood pressure be monitored following the initiation of chronic COX-2 inhibitor as well as non-selective NSAID therapy.**

References:

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4. Wright JM. The double-edged sword of COX-2 selective NSAIDs. *CMAJ.* 2002 Nov;167(10): 1131-37.
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6. Zhao SZ, Burke TA, Whelton A, von Allmen H, Henderson SC. Comparison of the baseline cardiovascular risk profile among hypertensive patients prescribed COX-2-specific inhibitors or nonspecific NSAIDs: data from real-life practice. *Am J Manage Care.* 2002 Oct; 8(15 Suppl):S393-400.