

19. PARECOXIB SODIUM, AN INJECTABLE COX-2 SPECIFIC INHIBITOR, DOES NOT AFFECT ASPIRIN-MEDIATED PLATELET FUNCTION

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Introduction: Unlike conventional NSAIDs, COX-2 specific inhibitors effectively treat pain and inflammation without affecting platelet function. The objective of this study was to identify any potential pharmacodynamic interaction between the COX-2 specific inhibitor, parecoxib sodium, and aspirin by studying the effects of their co-administration on platelet function in healthy adults.

Methods: In this single-center, double-blind, placebo-controlled, parallel-group study 20 healthy adults were randomized to receive intravenous parecoxib sodium 40 mg BID or placebo BID for 3 days. A single dose of study medication on Day 4 was followed 2 hours later by a single dose of aspirin 325 mg. Platelet aggregation in response to arachidonate (AA), ADP or collagen; serum thromboxane B₂ (TxB₂) concentrations and Simplate II bleeding times were assessed at baseline and 2 hours following study drug administration on Day 1 and 2, 4, 8, and 22 hours following aspirin administration on Day 4.

Results: Platelet aggregation in response to AA, ADP, or collagen was not significantly altered from pre-dose values in either the parecoxib or placebo treatment groups at any post-medication time point prior to the administration of aspirin. Administration of aspirin 2 hours after the final dose of parecoxib or placebo on Day 4 lowered platelet aggregation in response to all 3 aggregants. Responses to the various aggregants at most time points were not significantly different in the parecoxib group when compared with placebo. Although the responses to ADP in the placebo group at 4 and 22 hours was significantly less than the parecoxib group, this was not clinically significant. There were no significant differences in serum TxB₂ concentrations between the placebo and parecoxib groups at any time point before or after the administration of aspirin. Simplate II bleeding times were not affected by parecoxib or placebo alone but were comparably prolonged after aspirin administration, with no significant differences between treatment groups. Few adverse events were recorded during the study and none were considered related to the medication or led to withdrawal from the study. Changes in vital signs and clinical laboratory values were minor.

Conclusions: Co-administration of parecoxib and aspirin does not increase or decrease the anti-platelet effect of aspirin. Additionally, parecoxib alone has no effect on platelet function either as a single dose or after several days' administration and is well tolerated.

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Mean Percent Platelet Aggregation after Co-administration of Aspirin with Placebo or Parecoxib Sodium on Day 4

	Placebo plus Aspirin (n=9)			Parecoxib plus Aspirin (n=10)		
	AA	ADP	Coll.	AA	ADP	Coll.
0 hr	71.89	62.56	70.0	79.5	61.90	72.30
2 hr	1.89	56.22	5.11	2.80	56.90	6.40
4 hr	2.44	50.44	4.56	1.80	62.00*	10.20
8 hr	2.22	41.00	5.00	3.90	45.50	8.40
22 hr	2.00	56.00	8.67	3.10	61.60*	15.60

* mean percent platelet aggregation is significantly higher than placebo ($p < 0.05$)