Comparison 3: Single-dose oral analgesic compared with a single dose of an alternative oral analgesic

Comparison 3a: Single-dose NSAID compared with single-dose paracetamol

Source: Wuytack F, Smith V, Cleary BJ. Oral non-steroidal anti-inflammatory drugs (single-dose) for perineal pain in the early postpartum period. Cochrane Database Syst Rev. 2021;(1):CD011352.

Certainty assessment							№ of patients		Effect		Certainty (GRADE)	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NSAID (single administration, any dose)	Paracetamol	Relative (95% CI)	Absolute (95% CI)		
Adequate pain relief (4 hours after administration)												
3	randomized trials	serious [d]	not serious	not serious	not serious	none	54/171 (31.6%)	35/171 (20.5%)	**RR 1.54** (1.07 to 2.22)	**111 more per 1000** (from 14 more to 250 more)	⊕⊕⊕◯ MODERATE	CRITICAL
Adequate pain relief (4 hours after administration) – ibuprofen 300–400 mg vs paracetamol 1000 mg												
1	randomized trials	not serious	not serious	not serious	very serious [a,b,c]	none	18/36 (50.0%)	11/37 (29.7%)	**RR 1.68** (0.93 to 3.04)	**202 more per 1000** (from 21 fewer to 606 more)	⊕⊕◯◯ LOW	CRITICAL
Adequate pain relief (4 hours after administration) – ibuprofen 300–400 mg vs paracetamol 500 mg												
1	randomized trials	not serious	not serious	not serious	very serious [a,b]	none	30/106 (28.3%)	21/104 (20.2%)	**RR 1.40** (0.86 to 2.28)	**81 more per 1000** (from 28 fewer to 258 more)	⊕⊕◯◯ LOW	CRITICAL
Adequate pain relief (4 hours after administration) – aceclofenac 100 mg vs paracetamol 650 mg												
1	randomized trials	serious [d]	not serious	not serious	very serious [a,b,c]	none	6/29 (20.7%)	3/30 (10.0%)	**RR 2.07** (0.57 to 7.50)	**107 more per 1000** (from 43 fewer to 650 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – aceclofenac 100 mg vs paracetamol 650 mg												
2	randomized trials	serious [d]	not serious	not serious	very serious [a,b,c]	none	18/49 (36.7%)	10/50 (20.0%)	**RR 1.82** (0.61 to 5.47)	**164 more per 1000** (from 78 fewer to 894 more)	⊕◯◯◯ VERY LOW	CRITICAL
Need for additional analgesia (4 hours after administration) – ibuprofen 300–400 mg vs paracetamol 1000 mg												
1	randomized trials	not serious	not serious	not serious	very serious [a,b,c]	none	8/36 (22.2%)	15/37 (40.5%)	**RR 0.55** (0.27 to 1.13)	**182 fewer per 1000** (from 296 fewer to 53 more)	⊕⊕◯◯ LOW	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty (GRADE)	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NSAID (single administration, any dose)	Paracetamol	Relative (95% CI)	Absolute (95% CI)		
Need for additional analgesia (6 hours after administration) – ibuprofen 300–400 mg vs paracetamol 1000 mg												
1	randomized trials	serious [d]	not serious	not serious	serious [b,c]	none	5/31 (16.1%)	16/28 (57.1%)	**RR 0.28** (0.12 to 0.67)	**411 fewer per 1000** (from 503 fewer to 189 fewer)	⊕⊕◯◯ LOW	CRITICAL
Maternal drug adverse effects (4 hours after administration) – ibuprofen 300–400 mg vs paracetamol 500 mg												
1	randomized trials	serious [d]	not serious	not serious	very serious [b,e]	none	0/106 (0.0%)	0/104 (0.0%)	not estimable	-	⊕◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (6 hours after administration)												
3	randomized trials	not serious	not serious	not serious	very serious [a,c]	none	6/150 (4.0%)	8/150 (5.3%)	**RR 0.74** (0.27 to 2.08)	**14 fewer per 1000** (from 39 fewer to 58 more)	⊕⊕◯◯ LOW	CRITICAL
Maternal drug adverse effects (6 hours after administration) – dipyrone 500 mg vs paracetamol 500 mg												
1	randomized trials	not serious	not serious	not serious	very serious [a,b,c]	none	5/101 (5.0%)	7/100 (7.0%)	**RR 0.71** (0.23 to 2.15)	**20 fewer per 1000** (from 54 fewer to 81 more)	⊕⊕◯◯ LOW	CRITICAL
Maternal drug adverse effects (6 hours after administration) – aceclofenac 100 mg vs paracetamol 650 mg												
2	randomized trials	serious [d]	not serious	not serious	very serious [a,b,c]	none	1/49 (2.0%)	1/50 (2.0%)	**RR 1.00** (0.07 to 14.90)	**0 fewer per 1000** (from 19 fewer to 278 more)	⊕◯◯◯ VERY LOW	-

CI: confidence interval; RR: risk ratio.
a. Wide confidence interval crossing the line of no effect.
b. Less than 300 participants.
c. Few events.
d. Most of the pooled effect provided by studies “B” or “C” but without a substantial proportion (i.e. < 50%) from studies “C”.
e. No events.

Comparison 3b: Single-dose NSAID (aspirin) compared with a single dose of another NSAID

Source: Wuytack F, Smith V, Cleary BJ. Oral non-steroidal anti-inflammatory drugs (single-dose) for perineal pain in the early postpartum period. Cochrane Database Syst Rev. 2021;(1):CD011352.

Certainty assessment							№ of patients		Effect		Certainty (GRADE)	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NSAID single dose	Alternative NSAID	Relative (95% CI)	Absolute (95% CI)		
Adequate pain relief (4 hours after administration)												
4	randomized trials	not serious	not serious	serious [a]	not serious	none	187/363 (51.5%)	200/368 (54.3%)	**RR 0.95** (0.83 to 1.09)	**27 fewer per 1000** (from 92 fewer to 49 more)	⊕⊕⊕◯ MODERATE	CRITICAL
Adequate pain relief (4 hours after administration) – aspirin 500–650 mg (A) vs diflunisal 125 mg (B)												
1	randomized trials	serious [b]	not serious	not serious	very serious [c,d,e]	none	17/32 (53.1%)	12/33 (36.4%)	**RR 1.46** (0.84 to 2.55)	**167 more per 1000** (from 58 fewer to 564 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (4 hours after administration) – aspirin 500–650 mg (A) vs diflunisal 250 mg (B)												
1	randomized trials	serious [b]	not serious	not serious	very serious [c,d,e]	none	17/32 (53.1%)	9/30 (30.0%)	**RR 1.77** (0.94 to 3.35)	**231 more per 1000** (from 18 fewer to 705 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (4 hours after administration) – aspirin 500–650 mg (A) vs diflunisal 500 mg (B)												
1	randomized trials	serious [b]	not serious	not serious	very serious [c,d,e]	none	17/32 (53.1%)	14/30 (46.7%)	**RR 1.14** (0.69 to 1.88)	**65 more per 1000** (from 145 fewer to 411 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (4 hours after administration) – aspirin 500–650 mg (A) vs ibuprofen 300–400 mg (B)												
1	randomized trials	serious [b]	not serious	serious [a]	very serious [c,d]	none	16/30 (53.3%)	21/30 (70.0%)	**RR 0.76** (0.51 to 1.15)	**168 fewer per 1000** (from 343 fewer to 105 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (4 hours after administration) – aspirin 500–650 mg (A) vs diclofenac 25 mg (B)												
1	randomized trials	not serious	not serious	serious [a]	very serious [c,d]	none	27/50 (54.0%)	32/52 (61.5%)	**RR 0.88** (0.63 to 1.23)	**74 fewer per 1000** (from 228 fewer to 142 more)	⊕◯◯◯ VERY LOW	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty (GRADE)	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NSAID single dose	Alternative NSAID	Relative (95% CI)	Absolute (95% CI)		
Adequate pain relief (4 hours after administration) – aspirin 500–650 mg (A) vs diclofenac 50 mg (B)												
1	randomized trials	not serious	not serious	serious [a]	very serious [c,d]	none	27/50 (54.0%)	34/50 (68.0%)	**RR 0.79** (0.58 to 1.09)	**143 fewer per 1000** (from 286 fewer to 61 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (4 hours after administration) – aspirin 500–650 mg (A) vs diclofenac 100 mg (B)												
1	randomized trials	not serious	not serious	serious [a]	very serious [c,d]	none	27/50 (54.0%)	37/51 (72.5%)	**RR 0.74** (0.55 to 1.01)	**189 fewer per 1000** (from 326 fewer to 7 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (4 hours after administration) – aspirin 500–650 mg (A) vs flurbiprofen 25 mg (B)												
1	randomized trials	not serious	not serious	serious [a]	very serious [c,d,e]	none	13/29 (44.8%)	11/32 (34.4%)	**RR 1.30** (0.70 to 2.44)	**103 more per 1000** (from 103 fewer to 495 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (4 hours after administration) – aspirin 500–650 mg (A) vs flurbiprofen 50 mg (B)												
1	randomized trials	not serious	not serious	serious [a]	very serious [c,d,e]	none	13/29 (44.8%)	15/29 (51.7%)	**RR 0.87** (0.51 to 1.48)	**67 fewer per 1000** (from 253 fewer to 248 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (4 hours after administration) – aspirin 500–650 mg (A) vs flurbiprofen 100 mg (B)												
1	randomized trials	not serious	not serious	serious [a]	very serious [c,d,e]	none	13/29 (44.8%)	15/31 (48.4%)	**RR 0.93** (0.54 to 1.60)	**34 fewer per 1000** (from 223 fewer to 290 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – aspirin 900 mg (A) vs ibuprofen 300–400 mg (B)												
1	randomized trials	not serious	not serious	serious [a]	very serious [c,d]	none	18/20 (90.0%)	17/20 (85.0%)	**RR 1.06** (0.84 to 1.34)	**51 more per 1000** (from 136 fewer to 289 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – aspirin 900 mg (A) vs ibuprofen 900 mg (B)												
1	randomized trials	not serious	not serious	serious [a]	very serious [c,d]	none	18/20 (90.0%)	17/20 (85.0%)	**RR 1.06** (0.84 to 1.34)	**51 more per 1000** (from 136 fewer to 289 more)	⊕◯◯◯ VERY LOW	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty (GRADE)	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NSAID single dose	Alternative NSAID	Relative (95% CI)	Absolute (95% CI)		
Adequate pain relief (6 hours after administration) – aspirin 500–650 mg (A) vs diflunisal 125 mg (B)												
1	randomized trials	serious [b]	not serious	not serious	very serious [c,d]	none	18/32 (56.3%)	13/33 (39.4%)	**RR 1.43** (0.85 to 2.41)	**169 more per 1000** (from 59 fewer to 555 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – aspirin 500–650 mg (A) vs diflunisal 250 mg (B)												
1	randomized trials	serious [b]	not serious	not serious	very serious [c,d,e]	none	18/32 (56.3%)	10/30 (33.3%)	**RR 1.69** (0.93 to 3.05)	**230 more per 1000** (from 23 fewer to 683 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – aspirin 500–650 mg (A) vs diflunisal 500 mg (B)												
1	randomized trials	serious [b]	not serious	not serious	very serious [c,d]	none	18/32 (56.3%)	16/30 (53.3%)	**RR 1.05** (0.67 to 1.66)	**27 more per 1000** (from 176 fewer to 352 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – aspirin 500–650 mg (A) vs etodolac 25 mg (B)												
1	randomized trials	serious [b]	not serious	serious [a]	very serious [c,d,e]	none	16/39 (41.0%)	11/40 (27.5%)	**RR 1.49** (0.80 to 2.80)	**135 more per 1000** (from 55 fewer to 495 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – aspirin 500–650 mg (A) vs etodolac 100 mg (B)												
1	randomized trials	serious [b]	not serious	serious [a]	very serious [c,d]	none	16/39 (41.0%)	15/40 (37.5%)	**RR 1.09** (0.63 to 1.89)	**34 more per 1000** (from 139 fewer to 334 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – aspirin 500–650 mg (A) vs flurbiprofen 25 mg (B)												
1	randomized trials	not serious	not serious	serious [a]	very serious [c,d,e]	none	14/29 (48.3%)	13/32 (40.6%)	**RR 1.19** (0.68 to 2.09)	**77 more per 1000** (from 130 fewer to 443 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – aspirin 500–650 mg (A) vs flurbiprofen 50 mg (B)												
1	randomized trials	not serious	not serious	serious [a]	very serious [c,d]	none	14/29 (48.3%)	18/29 (62.1%)	**RR 0.78** (0.49 to 1.25)	**137 fewer per 1000** (from 317 fewer to 155 more)	⊕◯◯◯ VERY LOW	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty (GRADE)	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NSAID single dose	Alternative NSAID	Relative (95% CI)	Absolute (95% CI)		
Adequate pain relief (6 hours after administration) – aspirin 500–650 mg (A) vs flurbiprofen 100 mg (B)												
1	randomized trials	not serious	not serious	serious [a]	very serious [c,d]	none	14/29 (48.3%)	19/31 (61.3%)	**RR 0.79** (0.49 to 1.26)	**129 fewer per 1000** (from 313 fewer to 159 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – aspirin 500–650 mg (A) vs dipyrone 500 mg (B)												
1	randomized trials	serious [b]	not serious	not serious	serious [d]	none	61/90 (67.8%)	67/89 (75.3%)	**RR 0.90** (0.75 to 1.08)	**75 fewer per 1000** (from 188 fewer to 60 more)	⊕⊕◯◯ LOW	CRITICAL
Need for additional analgesia (4 hours after administration) – aspirin 500–650 mg (A) vs ibuprofen 300–400 mg (B)												
1	randomized trials	serious [b]	not serious	serious [a]	very serious [c,d,e]	none	5/30 (16.7%)	0/30 (0.0%)	**RR 11.00** (0.64 to 190.53)	**0 fewer per 1000** (from 0 fewer to 0 fewer)	⊕◯◯◯ VERY LOW	CRITICAL
Need for additional analgesia (6 hours after administration) – aspirin 900 mg (A) vs ibuprofen 300–400 mg (B)												
1	randomized trials	not serious	not serious	serious [a]	very serious [c,d,e]	none	1/20 (5.0%)	0/20 (0.0%)	**RR 3.00** (0.13 to 69.52)	**0 fewer per 1000** (from 0 fewer to 0 fewer)	⊕◯◯◯ VERY LOW	CRITICAL
Need for additional analgesia (6 hours after administration) – aspirin 900 mg (A) vs ibuprofen 900 mg (B)												
1	randomized trials	not serious	not serious	serious [a]	very serious [d,f]	none	0/20 (0.0%)	0/20 (0.0%)	not estimable	-	⊕◯◯◯ VERY LOW	CRITICAL
Need for additional analgesia (6 hours after administration) – aspirin 500–650 mg (A) vs flurbiprofen 25 mg (B)												
1	randomized trials	not serious	not serious	serious [a]	very serious [c,d,e]	none	1/29 (3.4%)	1/32 (3.1%)	**RR 1.10** (0.07 to 16.85)	**3 more per 1000** (from 29 fewer to 495 more)	⊕◯◯◯ VERY LOW	CRITICAL
Need for additional analgesia (6 hours after administration) – aspirin 500–650 mg (A) vs flurbiprofen 50 mg (B)												
1	randomized trials	not serious	not serious	serious [a]	very serious [c,d,e]	none	1/29 (3.4%)	0/29 (0.0%)	**RR 3.00** (0.13 to 70.74)	**0 fewer per 1000** (from 0 fewer to 0 fewer)	⊕◯◯◯ VERY LOW	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty (GRADE)	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NSAID single dose	Alternative NSAID	Relative (95% CI)	Absolute (95% CI)		
Need for additional analgesia (6 hours after administration) – aspirin 500–650 mg (A) vs flurbiprofen 100 mg (B)												
1	randomized trials	not serious	not serious	serious [a]	very serious [c,d,e]	none	1/29 (3.4%)	0/31 (0.0%)	**RR 3.20** (0.14 to 75.55)	**0 fewer per 1000** (from 0 fewer to 0 fewer)	⊕◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (4 hours after administration) – aspirin 600 mg (A) vs diflunisal 125 mg (B)												
1	randomized trials	serious [b]	not serious	not serious	very serious [d,f]	none	0/32 (0.0%)	0/33 (0.0%)	not estimable	-	⊕◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (4 hours after administration) – aspirin 600 mg (A) vs diflunisal 250 mg (B)												
1	randomized trials	serious [b]	not serious	not serious	very serious [d,f]	none	0/32 (0.0%)	0/30 (0.0%)	not estimable	-	⊕◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (4 hours after administration) – aspirin 600 mg (A) vs diflunisal 500 mg (B)												
1	randomized trials	serious [b]	not serious	not serious	very serious [d,f]	none	0/32 (0.0%)	0/30 (0.0%)	not estimable	-	⊕◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (4 hours after administration) – aspirin 600 mg (A) vs ibuprofen 400 mg (B)												
1	randomized trials	serious [b]	not serious	serious [b]	very serious [d,f]	none	0/30 (0.0%)	0/30 (0.0%)	not estimable	-	⊕◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (6 hours after administration) – aspirin 900 mg (A) vs ibuprofen 300–400 mg (B)												
1	randomized trials	not serious	not serious	serious [a]	very serious [c,d,e]	none	5/20 (25.0%)	3/20 (15.0%)	**RR 1.67** (0.46 to 6.06)	**100 more per 1000** (from 81 fewer to 759 more)	⊕◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (6 hours after administration) – aspirin 900 mg (A) vs ibuprofen 900 mg (B)												
1	randomized trials	not serious	not serious	serious [a]	very serious [c,d,e]	none	5/20 (25.0%)	3/20 (15.0%)	**RR 1.67** (0.46 to 6.06)	**100 more per 1000** (from 81 fewer to 759 more)	⊕◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (6 hours after administration) – aspirin 500–650 mg (A) vs dipyrone 500 mg (B)												
1	randomized trials	serious [b]	not serious	not serious	very serious [d,f]	none	0/89 (0.0%)	0/89 (0.0%)	not estimable	-	⊕◯◯◯ VERY LOW	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty (GRADE)	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NSAID single dose	Alternative NSAID	Relative (95% CI)	Absolute (95% CI)		
Maternal drug adverse effects (6 hours after administration) – aspirin 500–650 mg (A) vs flurbiprofen 25 mg (B)												
1	randomized trials	not serious	not serious	serious [a]	very serious [d,f]	none	0/29 (0.0%)	0/32 (0.0%)	not estimable	-	⊕◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (6 hours after administration) – aspirin 500–650 mg (A) vs flurbiprofen 50 mg (B)												
1	randomized trials	not serious	not serious	serious [b]	very serious [d,f]	none	0/29 (0.0%)	0/29 (0.0%)	not estimable	-	⊕◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (6 hours after administration) – aspirin 500–650 mg (A) vs flurbiprofen 100 mg (B)												
1	randomized trials	not serious	not serious	serious [a]	very serious [d,f]	none	0/29 (0.0%)	0/31 (0.0%)	not estimable	-	⊕◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (6 hours after administration) – aspirin 500–650 mg (A) vs diflunisal 125 mg (B)												
1	randomized trials	serious [b]	not serious	not serious	very serious [d,f]	none	0/32 (0.0%)	0/33 (0.0%)	not estimable	-	⊕◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (6 hours after administration) – aspirin 500–650 mg (A) vs diflunisal 250 mg (B)												
1	randomized trials	serious [b]	not serious	not serious	very serious [d,f]	none	0/32 (0.0%)	0/30 (0.0%)	not estimable	-	⊕◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (6 hours after administration) – aspirin 500–650 mg (A) vs diflunisal 500 mg (B)												
1	randomized trials	serious [b]	not serious	not serious	very serious [d,f]	none	0/32 (0.0%)	0/30 (0.0%)	not estimable	-	⊕◯◯◯ VERY LOW	CRITICAL

CI: confidence interval; RR: risk ratio.

a. Some studies included in this outcome excluded breastfeeding women – the evidence cannot be extrapolated to all women during the postpartum period.

b. Most of the pooled effect provided by studies “B” or “C” but without a substantial proportion (i.e. < 50%) from studies “C”.

c. Wide confidence interval crossing the line of no effect.

d. Less than 300 participants.

e. Few events.

f. No events.