Comparison 1: Single-dose oral analgesic (any dose) compared with placebo

Comparison 1a: Single-dose paracetamol compared with placebo

Source: Abalos E, Gyte GML, Sguassero Y. Paracetamol/acetaminophen (single administration) for perineal pain in the early postpartum period. Cochrane Database Syst Rev. 2021;(1):CD008407.

Certainty assessment							№ of patients		Effect		Certainty (GRADE)	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Paracetamol (single administration, any dose)	Placebo	Relative (95% CI)	Absolute (95% CI)		
Adequate pain relief as reported by the woman												
10	randomized trials	very serious [a]	serious [b]	not serious	not serious	none	422/700 (60.3%)	157/579 (27.1%)	**RR 2.14** (1.59 to 2.89)	**309 more per 1000** (from 160 more to 512 more)	⊕◯◯◯ VERY LOW	IMPORTANT
Adequate pain relief as reported by the woman – paracetamol 500–650 mg												
5	randomized trials	very serious [a]	serious [b]	not serious	not serious	none	146/275 (53.1%)	56/207 (27.1%)	**RR 1.86** (1.20 to 2.87)	**233 more per 1000** (from 54 more to 506 more)	⊕◯◯◯ VERY LOW	IMPORTANT
Adequate pain relief as reported by the woman – paracetamol 1000 mg												
6	randomized trials	serious [c]	serious [b]	not serious	not serious	none	276/425 (64.9%)	101/372 (27.2%)	**RR 2.42** (1.53 to 3.81)	**386 more per 1000** (from 144 more to 763 more)	⊕⊕◯◯ LOW	IMPORTANT
Additional pain relief												
8	randomized trials	serious [c]	serious [b]	not serious	not serious	none	65/620 (10.5%)	156/512 (30.5%)	**RR 0.34** (0.21 to 0.55)	**201 fewer per 1000** (from 241 fewer to 137 fewer)	⊕⊕◯◯ LOW	IMPORTANT
Additional pain relief – paracetamol 500–650 mg												
3	randomized trials	serious [c]	not serious	not serious	serious [d]	none	15/193 (7.8%)	33/124 (26.6%)	**RR 0.30** (0.17 to 0.53)	**186 fewer per 1000** (from 221 fewer to 125 fewer)	⊕⊕◯◯ LOW	IMPORTANT

Certainty assessment							№ of patients		Effect		Certainty (GRADE)	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Paracetamol (single administration, any dose)	Placebo	Relative (95% CI)	Absolute (95% CI)		
Additional pain relief – paracetamol 1000 mg												
6	randomized trials	serious [c]	serious [b]	not serious	not serious	none	50/427 (11.7%)	123/388 (31.7%)	**RR 0.36** (0.19 to 0.67)	**203 fewer per 1000** (from 257 fewer to 105 fewer)	⊕⊕◯◯ LOW	IMPORTANT
Maternal nausea – paracetamol 1000 mg												
1	randomized trials	not serious	not serious	not serious	very serious [d,e]	none	0/123 (0.0%)	2/109 (1.8%)	**RR 0.18** (0.01 to 3.66)	**15 fewer per 1000** (from 18 fewer to 49 more)	⊕⊕◯◯ LOW	IMPORTANT
Maternal sleepiness – paracetamol 1000 mg												
1	randomized trials	not serious	not serious	not serious	very serious [d,e]	none	3/123 (2.4%)	3/109 (2.8%)	**RR 0.89** (0.18 to 4.30)	**3 fewer per 1000** (from 23 fewer to 91 more)	⊕⊕◯◯ LOW	IMPORTANT
Maternal bowel movements (not pre-specified)												
1	randomized trials	serious [c]	not serious	not serious	very serious [d,e]	none	26/175 (14.9%)	13/88 (14.8%)	**RR 1.01** (0.54 to 1.86)	**1 more per 1000** (from 68 fewer to 127 more)	⊕◯◯◯ VERY LOW	IMPORTANT
Maternal bowel movements (not pre-specified) – paracetamol 500–650 mg												
1	randomized trials	serious [c]	not serious	not serious	very serious [d,e]	none	13/88 (14.8%)	6/44 (13.6%)	**RR 1.08** (0.44 to 2.66)	**11 more per 1000** (from 76 fewer to 226 more)	⊕◯◯◯ VERY LOW	IMPORTANT
Maternal bowel movements (not pre-specified) – paracetamol 1000 mg												
1	randomized trials	serious [c]	not serious	not serious	very serious [d,e]	none	13/87 (14.9%)	7/44 (15.9%)	**RR 0.94** (0.40 to 2.18)	**10 fewer per 1000** (from 95 fewer to 188 more)	⊕◯◯◯ VERY LOW	IMPORTANT
Maternal gastric discomfort (not pre-specified) – paracetamol 1000 mg												
1	randomized trials	serious [c]	not serious	not serious	very serious [d,e]	none	13/75 (17.3%)	11/75 (14.7%)	**RR 1.18** (0.57 to 2.47)	**26 more per 1000** (from 63 fewer to 216 more)	⊕◯◯◯ VERY LOW	IMPORTANT

CI: confidence interval; RR: risk ratio.
a. Most of the pooled effect provided by studies “B” or “C” but with a substantial proportion (i.e. > 50%) from studies “C”.
b. Severe, unexplained, heterogeneity ($I^2 \geq 60\%$ or $Chi^2 < 0.05$)
c. Most of the pooled effect provided by studies “B” or “C” but without a substantial proportion (i.e. < 50%) from studies “C”.
d. Small sample size and or few events.
e. Wide confidence interval crossing the line of no effect.

Comparison 1b: Single-dose aspirin compared with placebo

Source: Shepherd E, Grivell RM. Aspirin (single dose) for perineal pain in the early postpartum period. Cochrane Database Syst Rev. 2020;(7):CD012129.

Certainty assessment							№ of patients		Effect		Certainty (GRADE)	Importance
№ of studies	**Study design**	**Risk of bias**	Inconsistency	Indirectness	Imprecision	Other considerations	**Aspirin (single administration, any dose)**	**Placebo**	**Relative (95% CI)**	**Absolute (95% CI)**		
Adequate pain relief as reported by the woman												
13	randomized trials	serious [a]	not serious	serious [b]	not serious	none	258/550 (46.9%)	114/451 (25.3%)	**RR 2.03** (1.69 to 2.42)	**260 more per 1000** (from 174 more to 359 more)	⨁⨁◯◯ LOW	IMPORTANT
Adequate pain relief as reported by the woman – aspirin 300 mg												
1	randomized trials	very serious [c]	not serious	not serious	very serious [d,e]	none	8/40 (20.0%)	1/13 (7.7%)	**RR 2.60** (0.36 to 18.88)	**123 more per 1000** (from 49 fewer to 1000 more)	⨁◯◯◯ VERY LOW	IMPORTANT
Adequate pain relief as reported by the woman – aspirin 500–650 mg												
11	randomized trials	serious [a]	not serious	serious [b]	not serious	none	209/417 (50.1%)	101/383 (26.4%)	**RR 1.98** (1.64 to 2.39)	**258 more per 1000** (from 169 more to 367 more)	⨁⨁◯◯ LOW	IMPORTANT
Adequate pain relief as reported by the woman – aspirin 900 mg												
1	randomized trials	very serious [c]	not serious	serious [b]	very serious [d,e]	none	11/20 (55.0%)	6/20 (30.0%)	**RR 1.83** (0.84 to 3.99)	**249 more per 1000** (from 48 fewer to 897 more)	⨁◯◯◯ VERY LOW	IMPORTANT
Adequate pain relief as reported by the woman – aspirin 1200 mg												
3	randomized trials	very serious [c]	not serious	serious [b]	very serious [d,f]	none	30/73 (41.1%)	6/35 (17.1%)	**RR 2.75** (1.25 to 6.06)	**300 more per 1000** (from 43 more to 867 more)	⨁◯◯◯ VERY LOW	IMPORTANT

Certainty assessment							№ of patients		Effect		Certainty (GRADE)	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Aspirin (single administration, any dose)	Placebo	Relative (95% CI)	Absolute (95% CI)		
Need for additional pain relief 4–8 hours after drug administration												
10	randomized trials	serious [a]	not serious	serious [b]	not serious	none	26/422 (6.2%)	86/322 (26.7%)	**RR 0.25** (0.17 to 0.37)	**200 fewer per 1000** (from 222 fewer to 168 fewer)	⊕⊕◯◯ LOW	IMPORTANT
Need for additional pain relief – aspirin 300 mg												
1	randomized trials	very serious [c]	not serious	not serious	serious [e]	none	2/40 (5.0%)	4/13 (30.8%)	**RR 0.16** (0.03 to 0.79)	**258 fewer per 1000** (from 298 fewer to 65 fewer)	⊕◯◯◯ VERY LOW	IMPORTANT
Need for additional pain relief – aspirin 500–650 mg												
9	randomized trials	very serious [c]	not serious	serious [b]	not serious	none	21/302 (7.0%)	73/267 (27.3%)	**RR 0.27** (0.17 to 0.41)	**200 fewer per 1000** (from 227 fewer to 161 fewer)	⊕◯◯◯ VERY LOW	IMPORTANT
Need for additional pain relief – aspirin 900 mg												
1	randomized trials	very serious [g]	not serious	serious [b]	very serious [d,e]	none	0/20 (0.0%)	3/20 (15.0%)	**RR 0.14** (0.01 to 2.60)	**129 fewer per 1000** (from 149 fewer to 240 more)	⊕◯◯◯ VERY LOW	IMPORTANT
Need for additional pain relief – aspirin 1200 mg												
2	randomized trials	very serious [c]	not serious	serious [b]	serious [e]	none	3/60 (5.0%)	6/22 (27.3%)	**RR 0.20** (0.06 to 0.70)	**218 fewer per 1000** (from 256 fewer to 82 fewer)	⊕◯◯◯ VERY LOW	IMPORTANT
Maternal adverse effects												
14	randomized trials	very serious [c]	not serious	serious [b]	very serious [d,h]	none	16/583 (2.7%)	13/484 (2.7%)	**RR 1.08** (0.57 to 2.06)	**2 more per 1000** (from 12 fewer to 28 more)	⊕◯◯◯ VERY LOW	IMPORTANT

Certainty assessment							№ of patients		Effect		Certainty (GRADE)	Importance
№ of studies	**Study design**	**Risk of bias**	Inconsistency	Indirectness	Imprecision	Other considerations	**Aspirin (single administration, any dose)**	**Placebo**	**Relative (95% CI)**	**Absolute (95% CI)**		
Maternal adverse effects – aspirin 300 mg												
1	randomized trials	very serious [g]	not serious	not serious	very serious [i]	none	0/40 (0.0%)	0/13 (0.0%)	not estimable		⨁◯◯◯ VERY LOW	IMPORTANT
Maternal adverse effects – aspirin 500–650 mg												
13	randomized trials	serious [a]	not serious	serious [b]	very serious [d,h]	none	11/463 (2.4%)	9/429 (2.1%)	**RR 1.13** (0.51 to 2.53)	**3 more per 1000** (from 10 fewer to 32 more)	⨁◯◯◯ VERY LOW	IMPORTANT
Maternal adverse effects – aspirin 900 mg												
1	randomized trials	very serious [g]	not serious	serious [b]	very serious [d,e]	none	5/20 (25.0%)	2/20 (10.0%)	**RR 2.50** (0.55 to 11.41)	**150 more per 1000** (from 45 fewer to 1000 more)	⨁◯◯◯ VERY LOW	IMPORTANT
Maternal adverse effects – aspirin 1200 mg												
2	randomized trials	very serious [g]	not serious	serious [b]	very serious [d,e]	none	0/60 (0.0%)	2/22 (9.1%)	**RR 0.10** (0.01 to 1.80)	**82 fewer per 1000** (from 90 fewer to 73 more)	⨁◯◯◯ VERY LOW	IMPORTANT

CI: confidence interval; RR: risk ratio.

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

b. Many studies excluded breastfeeding women – the evidence cannot be extrapolated to all women during the postpartum period.

c. Most of the pooled effect provided by studies “B” or “C” but with a substantial proportion (i.e. > 50%) from studies “C”.

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

e. Less than 300 women and few events.

f. Less than 300 women.

g. All of the pooled effect provided by study “C”.

h. Less than 30 events.

i. No events.

Comparison 1c: Single-dose NSAID compared with placebo

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)	Placebo	Relative (95% CI)	Absolute (95% CI)		
Adequate pain relief (4 hours after administration)												
10	randomized trials	serious [a]	not serious	serious [b]	not serious	publication bias strongly suspected [c]	597/1105 (54.0%)	133/468 (28.4%)	**RR 1.91** (1.64 to 2.23)	**259 more per 1000** (from 182 more to 350 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (4 hours after administration) – ibuprofen 300–400 mg												
3	randomized trials	serious [a]	not serious	serious [b]	serious [d]	none	64/146 (43.8%)	16/94 (17.0%)	**RR 2.64** (1.62 to 4.30)	**279 more per 1000** (from 106 more to 562 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (4 hours after administration) – ibuprofen 800 mg												
1	randomized trials	serious [a]	not serious	not serious	very serious [d,e]	none	25/80 (31.3%)	7/41 (17.1%)	**RR 1.83** (0.87 to 3.87)	**142 more per 1000** (from 22 fewer to 490 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (4 hours after administration) – diclofenac 25 mg												
1	randomized trials	not serious	not serious	serious [b]	very serious [d,e]	none	32/52 (61.5%)	4/13 (30.8%)	**RR 2.00** (0.86 to 4.65)	**308 more per 1000** (from 43 fewer to 1000 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (4 hours after administration) – diclofenac 50 mg												
1	randomized trials	not serious	not serious	serious [b]	very serious [d,e]	none	34/50 (68.0%)	4/13 (30.8%)	**RR 2.21** (0.96 to 5.11)	**372 more per 1000** (from 12 fewer to 1000 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (4 hours after administration) – diclofenac 100 mg												
1	randomized trials	not serious	not serious	serious [b]	serious [d]	none	37/51 (72.5%)	4/13 (30.8%)	**RR 2.36** (1.03 to 5.42)	**418 more per 1000** (from 9 more to 1000 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)	Placebo	Relative (95% CI)	Absolute (95% CI)		
Adequate pain relief (4 hours after administration) – ketoprofen 25 mg												
1	randomized trials	very serious [f]	not serious	serious [b]	serious [d,g]	none	20/28 (71.4%)	3/14 (21.4%)	**RR 3.33** (1.19 to 9.34)	**499 more per 1000** (from 41 more to 1000 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (4 hours after administration) – diflunisal 125 mg												
1	randomized trials	serious [a]	not serious	not serious	very serious [d,e,g]	none	12/33 (36.4%)	1/8 (12.5%)	**RR 2.91** (0.44 to 19.22)	**239 more per 1000** (from 70 fewer to 1000 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (4 hours after administration) – meclofenamate sodium 100 mg												
3	randomized trials	serious [a]	not serious	not serious	serious [d]	none	110/173 (63.6%)	39/87 (44.8%)	**RR 1.42** (1.10 to 1.82)	**188 more per 1000** (from 45 more to 368 more)	⊕⊕◯◯ LOW	CRITICAL
Adequate pain relief (4 hours after administration) – meclofenamate sodium 200 mg												
3	randomized trials	serious [a]	not serious	not serious	serious [d]	none	112/175 (64.0%)	39/87 (44.8%)	**RR 1.42** (1.10 to 1.83)	**188 more per 1000** (from 45 more to 372 more)	⊕⊕◯◯ LOW	CRITICAL
Adequate pain relief (4 hours after administration) – ketoprofen 50 mg												
1	randomized trials	very serious [f]	not serious	serious [b]	very serious [d,g]	none	18/26 (69.2%)	3/14 (21.4%)	**RR 3.23** (1.15 to 9.10)	**478 more per 1000** (from 32 more to 1000 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (4 hours after administration) – diflunisal 250 mg												
1	randomized trials	serious [a]	not serious	not serious	very serious [d,e,g]	none	9/30 (30.0%)	1/8 (12.5%)	**RR 2.40** (0.35 to 16.26)	**175 more per 1000** (from 81 fewer to 1000 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (4 hours after administration) – diflunisal 500 mg												
1	randomized trials	serious [a]	not serious	not serious	very serious [d,e,g]	none	14/30 (46.7%)	1/8 (12.5%)	**RR 3.73** (0.57 to 24.29)	**341 more per 1000** (from 54 fewer to 1000 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 administration, any dose)	Placebo	Relative (95% CI)	Absolute (95% CI)		
Adequate pain relief (4 hours after administration) – flurbiprofen 25 mg												
1	randomized trials	not serious	not serious	serious [b]	very serious [d,e,g]	none	11/32 (34.4%)	1/8 (12.5%)	**RR 2.75** (0.41 to 18.29)	**219 more per 1000** (from 74 fewer to 1000 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (4 hours after administration) – flurbiprofen 50 mg												
1	randomized trials	not serious	not serious	serious [b]	very serious [d,e,g]	none	15/29 (51.7%)	1/8 (12.5%)	**RR 4.14** (0.64 to 26.76)	**392 more per 1000** (from 45 fewer to 1000 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (4 hours after administration) – flurbiprofen 100 mg												
1	randomized trials	not serious	not serious	serious [b]	very serious [d,e,g]	none	15/31 (48.4%)	1/8 (12.5%)	**RR 3.87** (0.60 to 25.09)	**359 more per 1000** (from 50 fewer to 1000 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration)												
17	randomized trials	serious [a]	not serious	serious [b]	not serious	none	870/1455 (59.8%)	200/624 (32.1%)	**RR 1.92** (1.69 to 2.17)	**295 more per 1000** (from 221 more to 375 more)	⊕⊕◯◯ LOW	CRITICAL
Adequate pain relief (6 hours after administration) – ibuprofen 300–400 mg												
2	randomized trials	not serious	not serious	serious [b]	serious [d]	none	44/69 (63.8%)	16/55 (29.1%)	**RR 2.08** (1.30 to 3.32)	**314 more per 1000** (from 87 more to 675 more)	⊕⊕◯◯ LOW	CRITICAL
Adequate pain relief (6 hours after administration) – ibuprofen 900 mg												
1	randomized trials	not serious	not serious	serious [b]	very serious [d,e,g]	none	17/20 (85.0%)	2/7 (28.6%)	**RR 2.98** (0.91 to 9.74)	**566 more per 1000** (from 26 fewer to 1000 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – ketoprofen 25 mg												
1	randomized trials	very serious [f]	not serious	serious [b]	serious [d,g]	none	18/28 (64.3%)	3/14 (21.4%)	**RR 3.00** (1.06 to 8.49)	**429 more per 1000** (from 13 more to 1000 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 administration, any dose)	Placebo	Relative (95% CI)	Absolute (95% CI)		
Adequate pain relief (6 hours after administration) – ketoprofen 50 mg												
1	randomized trials	very serious [f]	not serious	serious [b]	serious [d,g]	none	17/26 (65.4%)	3/14 (21.4%)	**RR 3.05** (1.08 to 8.64)	**439 more per 1000** (from 17 more to 1000 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – meclofenamate sodium 100 mg												
3	randomized trials	serious [a]	not serious	not serious	serious [d]	none	103/173 (59.5%)	38/87 (43.7%)	**RR 1.36** (1.05 to 1.76)	**157 more per 1000** (from 22 more to 332 more)	⊕⊕◯◯ LOW	CRITICAL
Adequate pain relief (6 hours after administration) – meclofenamate sodium 200 mg												
3	randomized trials	serious [a]	not serious	not serious	serious [d]	none	105/175 (60.0%)	37/87 (42.5%)	**RR 1.40** (1.07 to 1.83)	**170 more per 1000** (from 30 more to 353 more)	⊕⊕◯◯ LOW	CRITICAL
Adequate pain relief (6 hours after administration) – diflunisal 125 mg												
1	randomized trials	serious [a]	not serious	not serious	very serious [d,e,g]	none	13/33 (39.4%)	1/8 (12.5%)	**RR 3.15** (0.48 to 20.69)	**269 more per 1000** (from 65 fewer to 1000 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – diflunisal 250 mg												
1	randomized trials	serious [a]	not serious	not serious	very serious [d,e,g]	none	10/30 (33.3%)	1/8 (12.5%)	**RR 2.67** (0.40 to 17.86)	**209 more per 1000** (from 75 fewer to 1000 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – diflunisal 500 mg												
1	randomized trials	serious [a]	not serious	not serious	very serious [d,e,g]	none	16/30 (53.3%)	1/8 (12.5%)	**RR 4.27** (0.66 to 27.51)	**409 more per 1000** (from 42 fewer to 1000 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – dipyrone 500 mg												
1	randomized trials	serious [a]	not serious	not serious	serious [d]	none	67/89 (75.3%)	15/44 (34.1%)	**RR 2.21** (1.44 to 3.39)	**413 more per 1000** (from 150 more to 815 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)	Placebo	Relative (95% CI)	Absolute (95% CI)		
Adequate pain relief (6 hours after administration) – aceclofenac 50 mg												
1	randomized trials	serious [a]	not serious	not serious	very serious [d,e,g]	none	14/18 (77.8%)	2/4 (50.0%)	**RR 1.56** (0.57 to 4.27)	**280 more per 1000** (from 215 fewer to 1000 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – aceclofenac 100 mg												
1	randomized trials	serious [a]	not serious	not serious	very serious [d,e,g]	none	20/24 (83.3%)	2/4 (50.0%)	**RR 1.67** (0.62 to 4.51)	**335 more per 1000** (from 190 fewer to 1000 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – aceclofenac 150 mg												
1	randomized trials	serious [a]	not serious	not serious	very serious [d,e,g]	none	19/21 (90.5%)	2/4 (50.0%)	**RR 1.81** (0.67 to 4.87)	**405 more per 1000** (from 165 fewer to 1000 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – etodolac 25 mg												
1	randomized trials	serious [a]	not serious	serious [b]	very serious [d,e,g]	none	11/40 (27.5%)	4/13 (30.8%)	**RR 0.89** (0.34 to 2.33)	**34 fewer per 1000** (from 203 fewer to 409 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – etodolac 100 mg												
1	randomized trials	serious [a]	not serious	serious [b]	very serious [d,e,g]	none	15/40 (37.5%)	4/13 (30.8%)	**RR 1.22** (0.49 to 3.02)	**68 more per 1000** (from 157 fewer to 622 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – antrafenine 300 mg												
1	randomized trials	serious [a]	not serious	serious [b]	serious [d,g]	none	16/29 (55.2%)	3/29 (10.3%)	**RR 5.33** (1.74 to 16.36)	**448 more per 1000** (from 77 more to 1000 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – flurbiprofen 25 mg												
1	randomized trials	not serious	not serious	serious [b]	very serious [d,e,g]	none	13/32 (40.6%)	1/8 (12.5%)	**RR 3.25** (0.50 to 21.31)	**281 more per 1000** (from 63 fewer to 1000 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 administration, any dose)	Placebo	Relative (95% CI)	Absolute (95% CI)		
Adequate pain relief (6 hours after administration) – flurbiprofen 50 mg												
1	randomized trials	not serious	not serious	serious [b]	very serious [d,e,g]	none	18/29 (62.1%)	1/8 (12.5%)	**RR 4.97** (0.78 to 31.75)	**496 more per 1000** (from 27 fewer to 1000 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – flurbiprofen 100 mg												
1	randomized trials	not serious	not serious	serious [b]	very serious [d,e,g]	none	19/31 (61.3%)	1/8 (12.5%)	**RR 4.90** (0.77 to 31.33)	**488 more per 1000** (from 29 fewer to 1000 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – fenoprofen 12.5 mg												
1	randomized trials	very serious [f]	not serious	serious [b]	very serious [d,e,g]	none	10/24 (41.7%)	1/5 (20.0%)	**RR 2.08** (0.34 to 12.80)	**216 more per 1000** (from 132 fewer to 1000 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – fenoprofen 25 mg												
1	randomized trials	very serious [f]	not serious	serious [b]	very serious [d,e,g]	none	11/23 (47.8%)	1/5 (20.0%)	**RR 2.39** (0.39 to 14.53)	**278 more per 1000** (from 122 fewer to 1000 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – fenoprofen 50 mg												
2	randomized trials	very serious [f]	not serious	serious [b]	very serious [d,e]	none	28/50 (56.0%)	2/12 (16.7%)	**RR 3.38** (0.93 to 12.26)	**397 more per 1000** (from 12 fewer to 1000 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – fenoprofen 100 mg												
2	randomized trials	very serious [f]	not serious	serious [b]	serious [d]	none	33/50 (66.0%)	2/12 (16.7%)	**RR 3.95** (1.10 to 14.19)	**492 more per 1000** (from 17 more to 1000 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief (6 hours after administration) – fenoprofen 200 mg												
2	randomized trials	very serious [f]	not serious	serious [b]	serious [d]	none	32/49 (65.3%)	2/12 (16.7%)	**RR 3.95** (1.10 to 14.19)	**492 more per 1000** (from 17 more to 1000 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 administration, any dose)	Placebo	Relative (95% CI)	Absolute (95% CI)		
Adequate pain relief (6 hours after administration) – fenoprofen 300 mg												
1	randomized trials	very serious [f]	not serious	serious [b]	very serious [d,e,g]	none	19/27 (70.4%)	1/7 (14.3%)	**RR 4.93** (0.79 to 30.74)	**561 more per 1000** (from 30 fewer to 1000 more)	⊕◯◯◯ VERY LOW	CRITICAL
Need for additional analgesia (4 hours after administration)												
4	randomized trials	serious [a]	not serious	serious [b]	not serious	none	30/296 (10.1%)	58/190 (30.5%)	**RR 0.39** (0.26 to 0.58)	**186 fewer per 1000** (from 226 fewer to 128 fewer)	⊕⊕◯◯ LOW	CRITICAL
Need for additional analgesia (4 hours after administration) – ibuprofen 300–400 mg												
3	randomized trials	not serious	not serious	serious [b]	serious [d]	none	12/146 (8.2%)	32/94 (34.0%)	**RR 0.32** (0.18 to 0.56)	**231 fewer per 1000** (from 279 fewer to 150 fewer)	⊕⊕◯◯ LOW	CRITICAL
Need for additional analgesia (4 hours after administration) – ibuprofen 800 mg												
1	randomized trials	serious [a]	not serious	not serious	very serious [d,e,g]	none	7/80 (8.8%)	7/41 (17.1%)	**RR 0.51** (0.19 to 1.36)	**84 fewer per 1000** (from 138 fewer to 61 more)	⊕◯◯◯ VERY LOW	CRITICAL
Need for additional analgesia (6 hours after administration)												
10	randomized trials	serious [a]	not serious	serious [b]	not serious	publication bias strongly suspected [c]	81/628 (12.9%)	168/384 (43.8%)	**RR 0.32** (0.26 to 0.40)	**298 fewer per 1000** (from 324 fewer to 263 fewer)	⊕◯◯◯ VERY LOW	CRITICAL
Need for additional analgesia (6 hours after administration) – ibuprofen 300–400 mg												
3	randomized trials	not serious	not serious	serious [b]	serious [d]	none	16/100 (16.0%)	46/86 (53.5%)	**RR 0.33** (0.20 to 0.54)	**358 fewer per 1000** (from 428 fewer to 246 fewer)	⊕⊕◯◯ LOW	CRITICAL
Need for additional analgesia (6 hours after administration) – ibuprofen 900 mg												
1	randomized trials	not serious	not serious	serious [b]	very serious [d,e,g]	none	0/20 (0.0%)	1/7 (14.3%)	**RR 0.13** (0.01 to 2.81)	**124 fewer per 1000** (from 141 fewer to 259 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 administration, any dose)	Placebo	Relative (95% CI)	Absolute (95% CI)		
Need for additional analgesia (6 hours after administration) – meclofenamate sodium 100 mg												
3	randomized trials	serious [a]	not serious	not serious	serious [d]	none	23/173 (13.3%)	37/126 (29.4%)	**RR 0.34** (0.21 to 0.53)	**194 fewer per 1000** (from 232 fewer to 138 fewer)	⨁⨁◯◯ LOW	CRITICAL
Need for additional analgesia (6 hours after administration) – meclofenamate sodium 200 mg												
2	randomized trials	serious [a]	not serious	not serious	serious [d]	none	24/95 (25.3%)	26/47 (55.3%)	**RR 0.45** (0.29 to 0.70)	**304 fewer per 1000** (from 393 fewer to 166 fewer)	⨁⨁◯◯ LOW	CRITICAL
Need for additional analgesia (6 hours after administration) – antrafenine 300 mg												
1	randomized trials	serious [a]	not serious	serious [b]	serious [d,g]	none	5/29 (17.2%)	16/29 (55.2%)	**RR 0.31** (0.13 to 0.74)	**381 fewer per 1000** (from 480 fewer to 143 fewer)	⨁◯◯◯ VERY LOW	CRITICAL
Need for additional analgesia (6 hours after administration) – flurbiprofen 25 mg												
1	randomized trials	not serious	not serious	serious [b]	serious [d,g]	none	1/32 (3.1%)	4/8 (50.0%)	**RR 0.06** (0.01 to 0.49)	**470 fewer per 1000** (from 495 fewer to 255 fewer)	⨁⨁◯◯ LOW	CRITICAL
Need for additional analgesia (6 hours after administration) – flurbiprofen 50 mg												
1	randomized trials	not serious	not serious	serious [b]	serious [d,g]	none	0/29 (0.0%)	4/8 (50.0%)	**RR 0.03** (0.00 to 0.56)	**485 fewer per 1000** (from 220 fewer to --)	⨁⨁◯◯ LOW	CRITICAL
Need for additional analgesia (6 hours after administration) – flurbiprofen 100 mg												
1	randomized trials	not serious	not serious	serious [b]	serious [d,g]	none	0/31 (0.0%)	4/8 (50.0%)	**RR 0.03** (0.00 to 0.53)	**485 fewer per 1000** (from 235 fewer to --)	⨁⨁◯◯ LOW	CRITICAL
Maternal drug adverse effects (4 hours after administration)												
1	randomized trials	not serious	not serious	serious [b]	very serious [d,h]	none	0/60 (0.0%)	0/30 (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 administration, any dose)	Placebo	Relative (95% CI)	Absolute (95% CI)		
Maternal drug adverse effects (4 hours after administration) – aspirin 500–650 mg												
1	randomized trials	not serious	not serious	serious [b]	very serious [d,h]	none	0/30 (0.0%)	0/15 (0.0%)	not estimable	-	⨁◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (4 hours after administration) – ibuprofen 300–400 mg												
1	randomized trials	not serious	not serious	serious [b]	very serious [d,h]	none	0/30 (0.0%)	0/15 (0.0%)	not estimable	-	⨁◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (6 hours after administration)												
13	randomized trials	not serious	not serious	serious [b]	serious [e]	none	24/897 (2.7%)	11/491 (2.2%)	**RR 1.38** (0.71 to 2.70)	**9 more per 1000** (from 6 fewer to 38 more)	⨁⨁◯◯ LOW	CRITICAL
Maternal drug adverse effects (6 hours after administration) – ibuprofen 300–400 mg												
3	randomized trials	not serious	not serious	serious [b]	very serious [d,e,g]	none	5/100 (5.0%)	3/86 (3.5%)	**RR 1.01** (0.27 to 3.85)	**0 fewer per 1000** (from 25 fewer to 99 more)	⨁◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (6 hours after administration) – ibuprofen 900 mg												
1	randomized trials	not serious	not serious	serious [b]	very serious [d,e,g]	none	3/20 (15.0%)	1/7 (14.3%)	**RR 1.05** (0.13 to 8.52)	**7 more per 1000** (from 124 fewer to 1000 more)	⨁◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (6 hours after administration) – ketoprofen 25 mg												
1	randomized trials	very serious [f]	not serious	serious [b]	very serious [d,h]	none	0/28 (0.0%)	0/14 (0.0%)	not estimable	-	⨁◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (6 hours after administration) – ketoprofen 50 mg												
1	randomized trials	very serious [f]	not serious	serious [b]	very serious [d,h]	none	0/26 (0.0%)	0/14 (0.0%)	not estimable	-	⨁◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (6 hours after administration) – aceclofenac 50 mg												
1	randomized trials	serious [a]	not serious	not serious	very serious [d,e,g]	none	1/18 (5.6%)	0/4 (0.0%)	**RR 0.79** (0.04 to 16.59)	**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 administration, any dose)	Placebo	Relative (95% CI)	Absolute (95% CI)		
Maternal drug adverse effects (6 hours after administration) – aceclofenac 100 mg												
1	randomized trials	serious [a]	not serious	not serious	very serious [d,h]	none	0/24 (0.0%)	0/4 (0.0%)	not estimable	-	⨁◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (6 hours after administration) – aceclofenac 150 mg												
1	randomized trials	serious [a]	not serious	not serious	very serious [d,h]	none	0/21 (0.0%)	0/4 (0.0%)	not estimable	-	⨁◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (6 hours after administration) – diflunisal 125 mg												
1	randomized trials	serious [a]	not serious	not serious	very serious [d,h]	none	0/33 (0.0%)	0/8 (0.0%)	not estimable	-	⨁◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (6 hours after administration) – diflunisal 250 mg												
1	randomized trials	serious [a]	not serious	not serious	very serious [d,h]	none	0/30 (0.0%)	0/8 (0.0%)	not estimable	-	⨁◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (6 hours after administration) – diflunisal 500 mg												
1	randomized trials	serious [a]	not serious	not serious	very serious [d,h]	none	0/30 (0.0%)	0/8 (0.0%)	not estimable	-	⨁◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (6 hours after administration) – dipyrone 500 mg												
2	randomized trials	not serious	not serious	not serious	very serious [e,g]	none	5/190 (2.6%)	2/145 (1.4%)	**RR 2.48** (0.49 to 12.46)	**20 more per 1000** (from 7 fewer to 158 more)	⨁⨁◯◯ LOW	CRITICAL
Maternal drug adverse effects (6 hours after administration) – antrafenine 300 mg												
1	randomized trials	serious [a]	not serious	serious [b]	very serious [d,h]	none	0/29 (0.0%)	0/29 (0.0%)	not estimable	-	⨁◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (6 hours after administration) – flurbiprofen 25 mg												
1	randomized trials	not serious	not serious	serious [b]	very serious [d,h]	none	0/32 (0.0%)	0/8 (0.0%)	not estimable	-	⨁◯◯◯ VERY LOW	CRITICAL
Maternal drug adverse effects (6 hours after administration) – flurbiprofen 50 mg												
1	randomized trials	not serious	not serious	serious [b]	very serious [d,h]	none	0/29 (0.0%)	0/8 (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 administration, any dose)	Placebo	Relative (95% CI)	Absolute (95% CI)		
Maternal drug adverse effects (6 hours after administration) – flurbiprofen 100 mg												
1	randomized trials	not serious	not serious	serious [b]	very serious [d,h]	none	0/31 (0.0%)	0/8 (0.0%)	not estimable	-	⨁◯◯◯ VERY LOW	CRITICAL

CI: confidence interval; RR: risk ratio.
a. Most of the pooled effect provided by studies “B” or “C” but without a substantial proportion (i.e. < 50%) from studies “C”.
b. Many studies excluded breastfeeding women – the evidence cannot be extrapolated to all women during the postpartum period.
c. Evident asymmetry in funnel plot with at least 10 studies.
d. Less than 300 participants.
e. Wide confidence interval crossing the line of no effect.
f. Most of the pooled effect provided by studies “B” or “C” but with a substantial proportion (i.e. > 50%) from studies “C”.
g. Few events.
h. No events.