Comparison 3: An oral analgesic compared with an alternative oral analgesic from a different class

Comparison 3a: Paracetamol compared with NSAIDs

Source: Deussen AR, Ashwood P, Martis R, Stewart F, Grzeskowiak LE. Relief of pain due to uterine cramping/involution after birth. Cochrane Database Syst Rev. 2020;(10):CD004908.

Certainty assessment							№ of patients		Effect		Certainty (GRADE)	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Paracetamol	NSAID	Relative (95% CI)	Absolute (95% CI)		
Adequate pain relief as reported by the woman – paracetamol 650 mg vs aspirin 650 mg												
1	randomized trials	serious [a]	not serious	serious [b]	very serious [c,d]	none	15/22 (68.2%)	20/26 (76.9%)	**RR 0.89** (0.62 to 1.26)	**85 fewer per 1000** (from 292 fewer to 200 more)	⊕◯◯◯ VERY LOW	CRITICAL
Maternal adverse effects												
2	randomized trials	serious [a]	not serious	serious [b]	very serious [c,e]	none	12/58 (20.7%)	13/54 (24.1%)	**RR 0.89** (0.29 to 2.78)	**26 fewer per 1000** (from 171 fewer to 429 more)	⊕◯◯◯ VERY LOW	CRITICAL
Maternal adverse effects – paracetamol 650 mg vs aspirin 650 mg												
1	randomized trials	serious [a]	not serious	serious [b]	very serious [c,e]	none	10/22 (45.5%)	9/26 (34.6%)	**RR 1.31** (0.65 to 2.64)	**107 more per 1000** (from 121 fewer to 568 more)	⊕◯◯◯ VERY LOW	CRITICAL
Maternal adverse effects – paracetamol 1000 mg vs naproxen 500 mg												
1	randomized trials	serious [a]	not serious	serious [b]	very serious [c,e]	none	2/36 (5.6%)	4/28 (14.3%)	**RR 0.39** (0.08 to 1.97)	**87 fewer per 1000** (from 131 fewer to 139 more)	⊕◯◯◯ VERY LOW	CRITICAL

CI: confidence interval; RR: risk ratio.
a. The pooled effect provided by study "B".
b. Exclusion: breastfeeding women.
c. Wide confidence interval crossing the line of no effect.
d. Less than 300 women.
e. Less than 300 women and less than 30 events.

Comparison 3b: NSAIDs compared with opioids

Source: Deussen AR, Ashwood P, Martis R, Stewart F, Grzeskowiak LE. Relief of pain due to uterine cramping/involution after birth. Cochrane Database Syst Rev. 2020;(10):CD004908.

Certainty assessment							№ of patients		Effect		Certainty (GRADE)	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NSAID	Opioid	Relative (95% CI)	Absolute (95% CI)		
Adequate pain relief as reported by the woman												
5	randomized trials	serious [a]	not serious	serious [b]	not serious	none	266/395 (67.3%)	89/165 (53.9%)	**RR 1.33** (1.13 to 1.57)	**178 more per 1000** (from 70 more to 307 more)	⊕⊕◯◯ LOW	CRITICAL
Adequate pain relief as reported by the woman – aspirin 650 mg vs codeine 60 mg												
1	randomized trials	serious [a]	not serious	serious [b]	very serious [c,d]	none	12/17 (70.6%)	11/16 (68.8%)	**RR 1.03** (0.65 to 1.61)	**21 more per 1000** (from 241 fewer to 419 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief as reported by the woman – aspirin 650 mg vs codeine 120 mg												
1	randomized trials	serious [a]	not serious	not serious	very serious [c,d]	none	12/17 (70.6%)	10/16 (62.5%)	**RR 1.13** (0.69 to 1.84)	**81 more per 1000** (from 194 fewer to 525 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief as reported by the woman – fenoprofen 12.5 mg vs codeine 60 mg												
1	randomized trials	serious [a]	not serious	serious [b]	very serious [c,d]	none	12/27 (44.4%)	2/5 (40.0%)	**RR 1.11** (0.35 to 3.52)	**44 more per 1000** (from 260 fewer to 1000 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief as reported by the woman – fenoprofen 25 mg vs codeine 60 mg												
1	randomized trials	serious [a]	not serious	serious [b]	very serious [c,d]	none	15/27 (55.6%)	3/5 (60.0%)	**RR 0.93** (0.42 to 2.04)	**42 fewer per 1000** (from 348 fewer to 624 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief as reported by the woman – fenoprofen 50 mg vs codeine 60 mg												
2	randomized trials	serious [a]	not serious	serious [b]	very serious [c,e]	none	33/54 (61.1%)	6/12 (50.0%)	**RR 1.24** (0.68 to 2.27)	**120 more per 1000** (from 160 fewer to 635 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	Opioid	Relative (95% CI)	Absolute (95% CI)		
Adequate pain relief as reported by the woman – fenoprofen 100 mg vs codeine 60 mg												
2	randomized trials	serious [a]	not serious	serious [b]	very serious [c,e]	none	37/56 (66.1%)	6/13 (46.2%)	**RR 1.44** (0.77 to 2.66)	**203 more per 1000** (from 106 fewer to 766 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief as reported by the woman – fenoprofen 200 mg vs codeine 60 mg												
3	randomized trials	serious [a]	not serious	serious [b]	very serious [c,e]	none	42/68 (61.8%)	9/24 (37.5%)	**RR 1.42** (0.81 to 2.47)	**157 more per 1000** (from 71 fewer to 551 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief as reported by the woman – fenoprofen 300 mg vs codeine 60 mg												
1	randomized trials	serious [a]	not serious	serious [b]	very serious [c,d]	none	20/29 (69.0%)	3/8 (37.5%)	**RR 1.84** (0.73 to 4.65)	**315 more per 1000** (from 101 fewer to 1000 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief as reported by the woman – flurbiprofen 50 mg vs codeine 60 mg												
1	randomized trials	serious [a]	not serious	serious [b]	very serious [c,d]	none	13/15 (86.7%)	11/16 (68.8%)	**RR 1.26** (0.86 to 1.85)	**179 more per 1000** (from 96 fewer to 584 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief as reported by the woman – flurbiprofen 50 mg vs codeine 120 mg												
1	randomized trials	serious [a]	not serious	serious [b]	very serious [c,d]	none	13/15 (86.7%)	10/15 (66.7%)	**RR 1.30** (0.86 to 1.96)	**200 more per 1000** (from 93 fewer to 640 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief as reported by the woman – naproxen 300 mg vs codeine 60 mg												
1	randomized trials	serious [a]	not serious	serious [b]	very serious [c,e]	none	27/35 (77.1%)	9/17 (52.9%)	**RR 1.46** (0.90 to 2.36)	**244 more per 1000** (from 53 fewer to 720 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief as reported by the woman – naproxen 600 mg vs codeine 60 mg												
1	randomized trials	serious [a]	not serious	serious [b]	very serious [c,e]	none	30/35 (85.7%)	9/18 (50.0%)	**RR 1.71** (1.06 to 2.77)	**355 more per 1000** (from 30 more to 885 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	Opioid	Relative (95% CI)	Absolute (95% CI)		
Need for additional pain relief												
2	randomized trials	serious [a]	not serious	serious [b]	very serious [c,d]	none	2/134 (1.5%)	6/98 (6.1%)	**RR 0.37** (0.12 to 1.12)	**39 fewer per 1000** (from 54 fewer to 7 more)	⊕◯◯◯ VERY LOW	CRITICAL
Need for additional pain relief – aspirin 650 mg vs codeine 60 mg												
1	randomized trials	serious [a]	not serious	serious [b]	very serious [c,d]	none	1/17 (5.9%)	1/16 (6.3%)	**RR 0.94** (0.06 to 13.82)	**4 fewer per 1000** (from 59 fewer to 801 more)	⊕◯◯◯ VERY LOW	CRITICAL
Need for additional pain relief – aspirin 650 mg vs codeine 120 mg												
1	randomized trials	serious [a]	not serious	serious [b]	very serious [c,d]	none	1/17 (5.9%)	0/15 (0.0%)	**RR 2.67** (0.12 to 60.93)	**0 fewer per 1000** (from 0 fewer to 0 fewer)	⊕◯◯◯ VERY LOW	CRITICAL
Need for additional pain relief – flurbiprofen 50 mg vs codeine 60 mg												
1	randomized trials	serious [a]	not serious	serious [b]	very serious [f]	none	0/15 (0.0%)	0/16 (0.0%)	not estimable	-	⊕◯◯◯ VERY LOW	CRITICAL
Need for additional pain relief – flurbiprofen 50 mg vs codeine 120 mg												
1	randomized trials	serious [a]	not serious	serious [b]	very serious [c,d]	none	0/15 (0.0%)	1/16 (6.3%)	**RR 0.35** (0.02 to 8.08)	**41 fewer per 1000** (from 61 fewer to 443 more)	⊕◯◯◯ VERY LOW	CRITICAL
Need for additional pain relief – naproxen 300 mg vs codeine 60 mg												
1	randomized trials	serious [a]	not serious	serious [b]	very serious [c,d]	none	0/35 (0.0%)	2/17 (11.8%)	**RR 0.10** (0.01 to 1.98)	**106 fewer per 1000** (from 116 fewer to 115 more)	⊕◯◯◯ VERY LOW	CRITICAL
Need for additional pain relief – naproxen 600 mg vs codeine 60 mg												
1	randomized trials	serious [a]	not serious	serious [b]	very serious [c,d]	none	0/35 (0.0%)	2/18 (11.1%)	**RR 0.11** (0.01 to 2.09)	**99 fewer per 1000** (from 110 fewer to 121 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	Opioid	Relative (95% CI)	Absolute (95% CI)		
Maternal adverse effects												
3	randomized trials	serious [a]	not serious	serious [b]	serious [e]	none	38/146 (26.0%)	48/109 (44.0%)	**RR 0.62** (0.43 to 0.89)	**167 fewer per 1000** (from 251 fewer to 48 fewer)	⊕◯◯◯ VERY LOW	CRITICAL
Maternal adverse effects – aspirin 650 mg vs codeine 60 mg												
1	randomized trials	serious [a]	not serious	serious [b]	very serious [c,d]	none	4/17 (23.5%)	5/16 (31.3%)	**RR 0.75** (0.24 to 2.32)	**78 fewer per 1000** (from 238 fewer to 413 more)	⊕◯◯◯ VERY LOW	CRITICAL
Maternal adverse effects – aspirin 650 mg vs codeine 120 mg												
1	randomized trials	serious [a]	not serious	serious [b]	very serious [c,d]	none	4/17 (23.5%)	14/16 (87.5%)	**RR 0.27** (0.11 to 0.65)	**639 fewer per 1000** (from 779 fewer to 306 fewer)	⊕◯◯◯ VERY LOW	CRITICAL
Maternal adverse effects – fenoprofen 200 mg vs codeine 60 mg												
1	randomized trials	serious [a]	not serious	not serious	very serious [c,d]	none	6/12 (50.0%)	3/11 (27.3%)	**RR 1.83** (0.60 to 5.61)	**226 more per 1000** (from 109 fewer to 1000 more)	⊕◯◯◯ VERY LOW	CRITICAL
Maternal adverse effects – flurbiprofen 50 mg vs codeine 60 mg												
1	randomized trials	serious [a]	not serious	serious [b]	very serious [c,d]	none	3/15 (20.0%)	5/16 (31.3%)	**RR 0.64** (0.18 to 2.22)	**112 fewer per 1000** (from 256 fewer to 381 more)	⊕◯◯◯ VERY LOW	CRITICAL
Maternal adverse effects – flurbiprofen 50 mg vs codeine 120 mg												
1	randomized trials	serious [a]	not serious	serious [b]	very serious [c,d]	none	3/15 (20.0%)	13/15 (86.7%)	**RR 0.23** (0.08 to 0.65)	**667 fewer per 1000** (from 797 fewer to 303 fewer)	⊕◯◯◯ VERY LOW	CRITICAL
Maternal adverse effects – naproxen 300 mg vs codeine 60 mg												
1	randomized trials	serious [a]	not serious	serious [b]	very serious [c,d]	none	9/35 (25.7%)	4/17 (23.5%)	**RR 1.09** (0.39 to 3.05)	**21 more per 1000** (from 144 fewer to 482 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	Opioid	Relative (95% CI)	Absolute (95% CI)		
Maternal adverse effects – naproxen 600 mg vs codeine 60 mg												
1	randomized trials	serious [a]	not serious	serious [b]	very serious [c,d]	none	9/35 (25.7%)	4/18 (22.2%)	**RR 1.16** (0.41 to 3.25)	**36 more per 1000** (from 131 fewer to 500 more)	⊕◯◯◯ VERY LOW	CRITICAL

CI: confidence interval; RR: risk ratio.
a. The pooled effect provided by studies "B".
b. Exclusion: breastfeeding women.
c. Wide confidence interval crossing the line of no effect.
d. Less than 300 women and less than 30 events.
e. Less than 300 women.
f. Less than 300 women and no events.

Comparison 3c: NSAIDs compared with herbal analgesia

Source: Deussen AR, Ashwood P, Martis R, Stewart F, Grzeskowiak LE. Relief of pain due to uterine cramping/involution after birth. Cochrane Database Syst Rev. 2020;(10):CD004908.

Certainty assessment							№ of patients		Effect		Certainty (GRADE)	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NSAID	Herbal analgesia	Relative (95% CI)	Absolute (95% CI)		
Adequate pain relief as reported by the woman												
4	randomized trials	serious [a]	not serious	not serious	not serious	none	87/197 (44.2%)	91/197 (46.2%)	**RR 0.96** (0.78 to 1.18)	**18 fewer per 1000** (from 102 fewer to 83 more)	⊕⊕⊕◯ MODERATE	CRITICAL
Adequate pain relief as reported by the woman – mefenamic acid 250 mg vs pimpinella anisum, apium graveolens and crocus sativus 500 mg												
1	randomized trials	serious [a]	not serious	not serious	very serious [b,c]	none	30/54 (55.6%)	31/54 (57.4%)	**RR 0.97** (0.69 to 1.35)	**17 fewer per 1000** (from 178 fewer to 201 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief as reported by the woman – mefenamic acid 250 mg vs melissa officinalis 395 mg												
1	randomized trials	very serious [d]	not serious	not serious	very serious [b,e]	none	11/55 (20.0%)	15/55 (27.3%)	**RR 0.73** (0.37 to 1.45)	**74 fewer per 1000** (from 172 fewer to 123 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief as reported by the woman – mefenamic acid 250 mg vs fennel 300 mg												
1	randomized trials	very serious [d]	not serious	not serious	very serious [b,c]	none	26/43 (60.5%)	26/43 (60.5%)	**RR 1.00** (0.71 to 1.41)	**0 fewer per 1000** (from 175 fewer to 248 more)	⊕◯◯◯ VERY LOW	CRITICAL
Adequate pain relief as reported by the woman – ibuprofen 400 mg vs fennel essence 20%												
1	randomized trials	serious [a]	not serious	not serious	very serious [b,c]	none	20/45 (44.4%)	19/45 (42.2%)	**RR 1.05** (0.66 to 1.69)	**21 more per 1000** (from 144 fewer to 291 more)	⊕◯◯◯ VERY LOW	CRITICAL
Need for additional pain relief – ibuprofen 400 mg vs fennel essence 20%												
1	randomized trials	serious [a]	not serious	not serious	very serious [b,e]	none	9/45 (20.0%)	9/45 (20.0%)	**RR 1.00** (0.44 to 2.29)	**0 fewer per 1000** (from 112 fewer to 258 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	Herbal analgesia	Relative (95% CI)	Absolute (95% CI)		
Pain however measured by the authors – VAS 0–10												
1	randomized trials	serious [a]	not serious	not serious	very serious [b,c]	none	54	54	-	MD **0.21 higher** (0.13 lower to 0.55 higher)	⊕◯◯◯ VERY LOW	CRITICAL
Maternal adverse effects – mefenamic acid 250 mg vs pimpinella anisum, apium graveolens and crocus sativus 500 mg												
1	randomized trials	serious [a]	not serious	not serious	very serious [b,e]	none	5/54 (9.3%)	1/54 (1.9%)	**RR 5.00** (0.60 to 41.39)	**74 more per 1000** (from 7 fewer to 748 more)	⊕◯◯◯ VERY LOW	CRITICAL

CI: confidence interval; MD: mean difference; RR: risk ratio.
a. Most of the pooled effect provided by studies “B”.
b. Wide confidence interval crossing the line of no effect.
c. Less than 300 women.
d. The pooled effect provided by study “C”.
e. Less than 300 women and less than 30 events.