Cochrane Clinical Answers

Question:

What proportion of people with postoperative pain experience adverse events with single-dose oral analgesics?

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Answer

Compared with placebo in adults with at least moderate-intensity postoperative pain, people taking one of these analgesics at a single dose had greater rates of adverse events: aspirin 600/650 mg or 920/1000 mg, diflunisal 1000 mg, ibuprofen 200 mg plus caffeine 100 mg, dihydrocodeine 30 mg, paracetamol (any dose) + codeine 30 or 60 mg, and paracetamol 325 to 1000 mg plus oxycodone 5 to 10 mg. However, four analgesics led to lower rates of adverse events than placebo: ibuprofen 200 or 400 mg and ibuprofen 200 to 400 mg plus paracetamol 500 to 1000 mg, respectively. Trial authors typically reported serious adverse events as absent; such events were too few for statistical evaluation. Reviewers stated that trial results should be treated with caution, as the method used to collect adverse event data influences adverse event reporting rates; patient diaries yield significantly more adverse events when compared with other forms of assessment.

Comparisons

1. Non-steroidal anti-inflammatory drugs (NSAIDs) versus placebo

Expand All »

› **OUTCOME 1.1 At least one adverse event**

Narrative result

29/34 comparisons showed no statistically significant difference between NSAIDs and placebo. Five comparisons appear to show a benefit of an NSAID over placebo: aspirin 600/650 mg or 920/1000 mg; diflunisal 1000 mg; and ibuprofen 200 and 400 mg. Proportion of participants reporting an adverse event was 3% to 44% with NSAIDs versus 4% and 46% with placebo. For aspirin and diflunisal 1000 mg, adverse event rates were higher than placebo; number needed to treat for one extra adverse event was 7.5 (95% CI 4.8 to 17) for aspirin 1000 mg and 7.7 (4.8 to 20) for diflunisal 1000 mg.[1]

Quality of the evidence

The reviewers did not perform a GRADE assessment of the quality/certainty of the evidence. All included Cochrane Reviews used standardized methods. Reviewers stated that the results should be treated with caution as the method used to collect adverse event data influences adverse event reporting rates; patient diaries yield significantly more adverse events that other forms of assessment. See main text of the Cochrane Overview

Relative effect or mean difference

Relative risk (95% CI); * indicates statistically significant or near statistically significant result (table reproduced directly from the Cochrane Overview):

Absolute effect

Results were reported narratively and in Summary Table A in the results section.

Reference

Moore RA, Derry S, Aldington D, Wiffen PJ. Adverse events associated with single dose oral analgesics for acute postoperative pain in adults - an overview of Cochrane reviews. *Cochrane Database of Systematic Reviews* 2015, Issue 10. Art. No.: CD011407. DOI: 10.1002/14651858.CD011407.pub2. Search date May 2015

OUTCOME 1.2 At least one serious adverse event

Narrative result

Serious adverse events were typically reported as being absent, and there were too few of them for any statistical evaluation.[2]

Reference

Moore RA, Derry S, Aldington D, Wiffen PJ. Adverse events associated with single dose oral analgesics for acute postoperative pain in adults - an overview of Cochrane reviews. *Cochrane Database of Systematic Reviews* 2015, Issue 10. Art. No.: CD011407. DOI: 10.1002/14651858.CD011407.pub2. Search date May 2015

Population, Intervention, Comparator

Population

Adults with postoperative pain of at least moderate intensity. Reviewers stated that all included Cochrane Reviews had the same structure and organization, used the same criteria, used identical methods based on criteria established by extensive analysis and validation, and used individual participant data; the majority of studies in all Cochrane Reviews (typically > 80%) involved 3rd molar extraction

Intervention

NSAID: aspirin (600 to 1000 mg), celecoxib (200 to 400 mg), dexketoprofen (10 to 25 mg), diclofenac or diclofenac fast acting (25 to 100 mg), diflunisal (250 to 1000 mg), etodolac (50 to 400 mg), etoricoxib (120 to 240 mg), fenoprofen (200 mg), flurbiprofen (25 to 100 mg), ibuprofen (50 to 400 mg), ketoprofen (12.5 to 100 mg), lornoxicam (8 mg), lumiracoxib (400 mg), mefenamic acid (500 mg), naproxen (400 to 550 mg), or rofecoxib (50 to 500 mg; < 1% received 500 mg)

Comparator

Placebo

2. NSAID plus non-opioid versus placebo Expand All »

› **OUTCOME 2.1 At least one adverse event**

Narrative result

There was a statistically significant difference between NSAID plus non-opioid and placebo for 3/4 comparisons. More people experienced an adverse event with ibuprofen 200 mg plus caffeine 100 mg (NNH 19, 8.9 to -220). However, fewer people experienced an adverse event with ibuprofen 200 mg plus paracetamol 500 mg (number needed to treat to prevent on adverse event [NNB] 5.4, 3.6 to 11) and for ibuprofen 400 mg plus paracetamol 1000 mg (NNB 5.1, 3.5 to 9.5). The RCTs in this Cochrane Review did have the highest adverse event rate with placebo of any Cochrane Review in the overview; proportion of participants reporting an adverse event was 11% to 30% with NSAID plus non-opioid versus 6% and 48% with placebo.[3]

Quality of the evidence

The reviewers did not perform a GRADE assessment of the quality/certainty of the evidence. All included Cochrane Reviews used standardized methods. Reviewers stated that the results should be treated with caution as the method used to collect adverse event data influences adverse event reporting rates; patient diaries yield significantly more adverse events that other forms of assessment. See main text of the Cochrane Overview

Relative effect or mean difference

Relative risk (95% CI); * indicates statistically significant or near statistically significant result (table reproduced directly from the Cochrane overview):

Absolute effect

Results were reported narratively and in Summary Table B in the results section.

Reference

Moore RA, Derry S, Aldington D, Wiffen PJ. Adverse events associated with single dose oral analgesics for acute postoperative pain in adults - an overview of Cochrane reviews. *Cochrane Database of Systematic Reviews* 2015, Issue 10. Art. No.: CD011407. DOI: 10.1002/14651858.CD011407.pub2. Search date May 2015

OUTCOME 2.2 At least one serious adverse event

Narrative result

Serious adverse events were typically reported as being absent, and there were too few of them for any statistical evaluation.[4]

Reference

Moore RA, Derry S, Aldington D, Wiffen PJ. Adverse events associated with single dose oral analgesics for acute postoperative pain in adults - an overview of Cochrane reviews. *Cochrane Database of Systematic Reviews* 2015, Issue 10. Art. No.: CD011407. DOI: 10.1002/14651858.CD011407.pub2. Search date May 2015

Population, Intervention, Comparator

Population

Adults with postoperative pain of at least moderate intensity. Reviewers stated that all included Cochrane Reviews had the same structure and organization, used the same criteria, used identical methods based on criteria established by extensive analysis and validation, and used individual participant data; the majority of studies in all Cochrane Reviews (typically > 80%) involved 3rd molar extraction

Intervention

NSAID (ibuprofen 100 to 400 mg) plus non-opioid (caffeine 100 mg or paracetamol 500 to 100 mg)

Comparator

Placebo

3. Paracetamol versus placebo Expand All »

OUTCOME 3.1 At least one adverse event

Narrative result

There were no statistically significant differences between paracetamol and placebo. Proportion of participants reporting an adverse event was 7% to 18% with paracetamol versus 6% to 16% with placebo.[5]

Quality of the evidence

The reviewers did not perform a GRADE assessment of the quality/certainty of the evidence. All included Cochrane Reviews used standardized methods. Reviewers stated that the results should be treated with caution as the method used to collect adverse event data influences adverse event reporting rates; patient diaries yield significantly more adverse events that other forms of assessment. See main text of the Cochrane Overview

Relative effect or mean difference

Relative risk (95% CI); none were statistically significant (table reproduced directly from the Cochrane overview):

Absolute effect

Results were reported narratively and in Summary Table C in the results section.

Reference

Moore RA, Derry S, Aldington D, Wiffen PJ. Adverse events associated with single dose oral analgesics for acute postoperative pain in adults - an overview of Cochrane reviews. *Cochrane Database of Systematic Reviews* 2015, Issue 10. Art. No.: CD011407. DOI: 10.1002/14651858.CD011407.pub2. Search date May 2015

OUTCOME 3.2 At least one serious adverse event

Narrative result

Serious adverse events were typically reported as being absent, and there were too few of them for any statistical evaluation.[6]

Reference

Moore RA, Derry S, Aldington D, Wiffen PJ. Adverse events associated with single dose oral analgesics for acute postoperative pain in adults - an overview of Cochrane reviews. *Cochrane Database of Systematic Reviews* 2015, Issue 10. Art. No.: CD011407. DOI: 10.1002/14651858.CD011407.pub2. Search date May 2015

Population, Intervention, Comparator

Population

Adults with postoperative pain of at least moderate intensity. Reviewers stated that all included Cochrane Reviews had the same structure and organization, used the same criteria, used identical methods based on criteria established by extensive analysis and validation, and used individual participant data; the majority of studies in all Cochrane Reviews (typically > 80%) involved 3rd molar extraction

Intervention

Paracetamol 500 to 1000 mg

Comparator

Placebo

4. Opioids versus placebo

Expand All »

OUTCOME 4.1 At least one adverse event

Narrative result

The incidence of adverse events was greater than placebo with: dihydrocodeine 30 mg (NNH 7.4, 95% CI 4.1 to 38; only 166 participants); paracetamol 600/650 mg plus codeine 60 mg (NNH 6.0, 95% CI 4.6 to 8.3); paracetamol plus codeine 30 mg or 60 mg (NNH 8.6, 95% CI 6.4 to 13); paracetamol 325 mg plus oxycodone 5 mg (NNH 4.5, 3.2 to 7.9); paracetamol 650 mg plus oxycodone 10 mg (NNH 3.5, 2.7 to 4.8); paracetamol 1000 mg plus oxycodone 10 mg (NNH 4.0, 2.8 to 7.3). Proportion of participants reporting an adverse event was 19% to 68% with opioids versus 6% to 43% with placebo.[7]

Quality of the evidence

The reviewers did not perform a GRADE assessment of the quality/certainty of the evidence. All included Cochrane Reviews used standardized methods. Reviewers stated that the results should be treated with caution as the method used to collect adverse event data influences adverse event reporting rates; patient diaries yield significantly more adverse events that other forms of assessment. See main text of the Cochrane Overview

Relative effect or mean difference

Relative risk (95% CI); * indicates statistically significant result (table reproduced directly from the Cochrane overview):

Absolute effect

Results were reported narratively and in Summary Table D in the results section.

Reference

Moore RA, Derry S, Aldington D, Wiffen PJ. Adverse events associated with single dose oral analgesics for acute postoperative pain in adults - an overview of Cochrane reviews. *Cochrane Database of Systematic Reviews* 2015, Issue 10. Art. No.: CD011407. DOI: 10.1002/14651858.CD011407.pub2. Search date May 2015

OUTCOME 4.2 At least one serious adverse event

Narrative result

Serious adverse events were typically reported as being absent, and there were too few of them for any statistical evaluation.[8]

Reference

Moore RA, Derry S, Aldington D, Wiffen PJ. Adverse events associated with single dose oral analgesics for acute postoperative pain in adults - an overview of Cochrane reviews. *Cochrane Database of Systematic Reviews* 2015, Issue 10. Art. No.: CD011407. DOI: 10.1002/14651858.CD011407.pub2. Search date May 2015

Population, Intervention, Comparator

Population

Adults with postoperative pain of at least moderate intensity. Reviewers stated that all included Cochrane Reviews had the same structure and organization, used the same criteria, used identical methods based on criteria established by extensive analysis and validation, and used individual participant data; the majority of studies in all Cochrane Reviews (typically > 80%) involved 3rd molar extraction

Intervention

Opioid: codeine (30 to 60 mg), dihydrocodeine (30 mg) or oxycodone (5 to 10 mg); both alone or with ibuprofen (100 to 400 mg) or paracetamol (325 to 1000 mg)

Comparator

Placebo

Additional Information

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