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Title **Paracetamol and Selective and Non-Selective non-Steroidal anti-Inflammatory Drugs (Nsaids) for the Reduction of Morphine-Related Side Effects after Major Surgery: A Systematic Review**

Agency **NETSCC, HTA, NIHR Evaluation and Trials Coordinating Centre**
Alpha House, University of Southampton Science Park, Southampton, SO16 7NS, United Kingdom;
Tel: +44 2380 595 586, Fax: +44 2380 595 639; hta@soton.ac.uk, www.hta.ac.uk

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Aim

To determine which class of non-opioid analgesics – paracetamol (acetaminophen), NSAIDs, or COX-2 inhibitors – is the most effective at reducing morphine consumption and associated adverse effects when used as part of multimodal analgesia following major surgery.

Conclusions and results

Compared to placebo, 24-hour morphine consumption decreased by 6.3 mg to 10.9 mg when paracetamol, NSAID, or COX-2 inhibitors were added to patient-controlled analgesia (PCA) morphine following surgery. Differences in effect between the 3 drug classes were small and unlikely to be of clinical significance. There does not appear to be a strong case to recommend routine addition of any of the 3 non-opioids to PCA morphine in the 24 hours immediately after surgery, or for favoring one drug class above the others.

Sixty relevant studies were identified. When paracetamol, NSAIDs, or COX-2 inhibitors were added to PCA morphine the reduction in morphine consumption was statistically significant: paracetamol (MD –6.34 mg; 95% CrI –9.02 to –3.65); NSAIDs (MD –10.18; 95% CrI –11.65 to –8.72); and COX-2 inhibitors (MD –10.92; 95% CrI –12.77 to –9.08). NSAIDs and COX-2 inhibitors were both significantly better than paracetamol, and there was no significant difference between NSAIDs and COX-2 inhibitors (MD –0.74; 95% CrI –3.03 to 1.56). There was a significant reduction in nausea and PONV with NSAIDs compared to placebo (OR 0.70; 95% CrI 0.53 to 0.88), but not for paracetamol or COX-2 inhibitors, nor for NSAIDs compared to paracetamol or COX-2 inhibitors.

Recommendations

See link www.hta.ac.uk/project/1853.asp.

Methods

See link www.hta.ac.uk/project/1853.asp.

Further research/reviews required

Given the overlap in the effects of the 3 analgesics, there does not appear to be a compelling case for a further trial. However, any future trials testing new analgesics in conjunction with postsurgical morphine should focus on morphine-related adverse effects, ensuring that the power calculation is based on key morphine-related adverse effects rather than on morphine consumption. Also, it would be valuable to explore whether taking baseline morphine consumption into account alters the results for morphine-related adverse effects.

Written by Dr Catriona McDaid, University of York, NETSCC, United Kingdom

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