Benefit-Risk of Postoperative, Parenteral, Non-Opioid Analgesics Using Multi-Criteria Decision Analysis (MCDA)

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INTRODUCTION

- Tools that compare and quantify the benefits and risks of medicines can help to inform and optimise treatment selection.
- For postoperative analgesia, this is an issue because multiple treatment options may have different modes of action and different efficacy and safety profiles.^{1,2}
- Multi-criteria decision analysis (MCDA) can quantify the benefits and risks of individual drugs, both overall and in comparison with each other.³⁻⁵
- Here, we used an MCDA model to compare the benefit-risk profiles of different parenteral analgesics in the acute postoperative setting.

METHODS

- An MCDA was constructed to determine and compare the benefit-risk profiles of 8 widely used parenteral, postoperative analgesics (acetaminophen, parecoxib, metamizol, nefopam, ketorolac, tramadol, morphine and diclofenac) and placebo.
- Publically available documents were examined to obtain efficacy and safety data for each analgesic and placebo.
- The benefit-risk profile of each analgesic and placebo was based on 3 favourable criteria (Benefits) and 14 unfavourable criteria (Risks) (Figure 1).

Figure 1. Effects tree for determining the comparative benefit-risk balance of analgesics and placebo

- Based on expert clinical opinion, 15 of the 17 criteria were scored from 0–100, with 100 awarded to the drug that scored best and 0 to the drug that scored worst; the remaining drugs were scored according to their standing with each other.
- The beneficial criteria of Duration of Action and Opioid Sparing were based on available clinical data.
- Data for morphine are based on a dose of 4 mg.
- Swing weights representing the added clinical value from worst to best were assessed as follows:
 - Benefits (Figure 2A).
 - Risks, eg, for the serious adverse effects (Figure 2B).
 - Highest-weighted Benefit against the highest-weighted Risk (Figure 2C).
- The weighting process creates a common unit of preference value across all the 0–100 scales.

Figure 2. Relative weighting of the data

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- The model was also conducted with a zero weighting placed on the criterion of Opioid Sparing to assess the benefit-risk profile of morphine when Opioid Sparing was not a consideration.
- Sensitivity analyses were conducted to assess the impact of varying the weighting of criteria on overall performance.
- Higher scores for the Risk criteria indicate less risk, ie, higher scores are better.
- No statistical comparisons were made between or among analgesics.

RESULTS

Comparison of the Benefit-Risk Profiles for the 8 Analgesics and Placebo

- Overall, Benefits had a relative weighting of 63.6% and Risks of 36.4%. These two weights are the result of normalising the assessed weights so that they sum to 100, preserving their original ratios.
- Of the Benefits, Pain Relief had the highest weighting (28.9%).
- Of the Risks, Gastrointestinal (GI) Effects had the greatest weighting (11.6%).
- Parecoxib was the most-preferred analgesic (total score = 93), followed by diclofenac (total score = 80) and ketorolac (total score = 75) (Figure 3).
- Morphine was the least-preferred option (total score = 57) mainly because it cannot have an opioid sparing effect.

Figure 3. Overall benefit-risk profiles and breakdown by individual benefit and safety criteria

Placing a Zero Weighting on Opioid Sparing Improves the Benefit-Risk Profile of Morphine

- When zero weighting was placed on the criterion of Opioid Sparing, parecoxib remained the most-preferred option (total score = 93).
- However, morphine became the third-most preferred analgesic (total score = 76), with similar score as metamizol (total score = 76) and ketorolac (total score = 74) (Figure 4).

Sensitivity Analysis for Overall Risk Effects

- Parecoxib remained the preferred option for a range of weights for the Risks.
- Only when the weight for Risk was increased to >75% did another analgesic, nefopam, become the most-preferred option.

Sensitivity Analysis for Pain Relief

- Parecoxib remained the preferred option no matter the cumulative weight for Pain Relief.
- For a range of cumulative weights from ~10%–100%, diclofenac was the second-most preferred option.

Figure 4. Benefit-Risk profiles when a weighting of zero was placed on the criterion of Opioid Sparing

Trade-off Between Benefits and Risk

- Comparison of the analgesics by the separate weighted values for Benefits and Risks, without regard for the trade-off weight between the Benefits and Risks, is shown in Figure 5.
- Parecoxib is close to the ideal (ie, scores of 100 for Benefit and Risk), with no analgesic showing greater benefits.
- Acetaminophen, metamizol and nefopam each have better values for Risk than parecoxib, but worse values for Benefit.

Figure 5. Weighted Benefit preference values vs weighted Risk preference values

CONCLUSIONS

- Of the 8 parenteral analgesics that were assessed in an MCDA model, parecoxib was the most-preferred option.
- High preference scores for Pain Relief, Opioid Sparing, Respiratory Depression and GI Effects drive the high overall score for parecoxib.
- Morphine was the least-preferred analgesic mainly due to its lack of opioid sparing effect. However, when the weighting of Opioid Sparing was placed at zero, morphine became the third-most preferred option.
- This highlights (i) how important Opioid Sparing is when assessing the benefit-risk profile of postoperative analgesics, and (ii) the effectiveness of morphine when Opioid Sparing is not a consideration.
- Under a number of sensitivity analyses where the weighting of criteria was varied, eg, for overall Risk and for Pain Relief, parecoxib remained the most-preferred option for the majority of situations.
- These results may help to inform clinicians and optimise treatment selection when considering analgesic options in the acute postoperative setting.

DISCLOSURES

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