Efficacy and Safety of Nalbuphine Compared with Other Analgesics for Moderate to Severe Postoperative Pain: A Systematic Review and Network Meta-analysis

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Rong-Sheng Chen[1], He-Yu Chen[1], Ren-Jong Liang[1,2,3], Sung-Ling Tang[1], Hong-Jaan Wang[1] , Ping-Hsuan Hsieh[1]

1. College of Pharmacy, National Defense Medical University, Taipei, Taiwan
2. Clinical Pharmacy Department, Tri-Service General Hospital Keelung Branch, Keelung, Taiwan
3. Graduate Institute of Medical Sciences , College of Medicine, National Defense Medical University, Taipei, Taiwan

Background and Aims

- Postoperative pain is a common and challenging form of acute pain, especially at moderate to severe intensity[1]. Although opioids are effective, their adverse effects often limit clinical applicability.
- **Nalbuphine** has been proposed as a **safer alternative** with a ceiling effect on respiratory depression. Despite its favorable safety profile, it is less used than morphine, partly due to its limited comparative evidence against other postoperative analgesics[2, 3].
- **This study aims to comprehensively assess the efficacy and safety of nalbuphine with other analgesics for the management of moderate to severe postoperative pain**.

Methods

The systematic review and meta-analysis were performed following the guidelines outlined in the 2020 PRISMA statement.

- **Eligibility criteria** (i) patients: adults experiencing moderate or severe pain, (ii) intervention: analgesics, and (iii) outcomes: pain intensity measured by validated pain assessment tools such as Visual Analog Scale (VAS) or Numeric Rating Scale (NRS), and safety outcomes including adverse effects.
- **Search strategy and databases** Search filters were adapted to capture potentially relevant studies from OVID-Medline and PubMed until March 2025.
- **Quality assessment** Risk of bias assessed using **RoB 2.0** (RCTs) and **ROBINS-I** (observational studies).
- **Pain outcomes** were evaluated using **standardized mean differences** (SMDs) across **0–8, 8–24, and 24–48 hours postoperative intervals**, with **efficacy ranked by SUCRA values**.
- **Subgroup analyses** stratified by **types of surgical procedure**.
- **Sensitivity analyses** were conducted to assess the robustness of results.

Results

- **Study selection** A total of 379 records were initially identified through database searches. Following full-text review, **26 studies** met the inclusion criteria and were included in the final analysis.

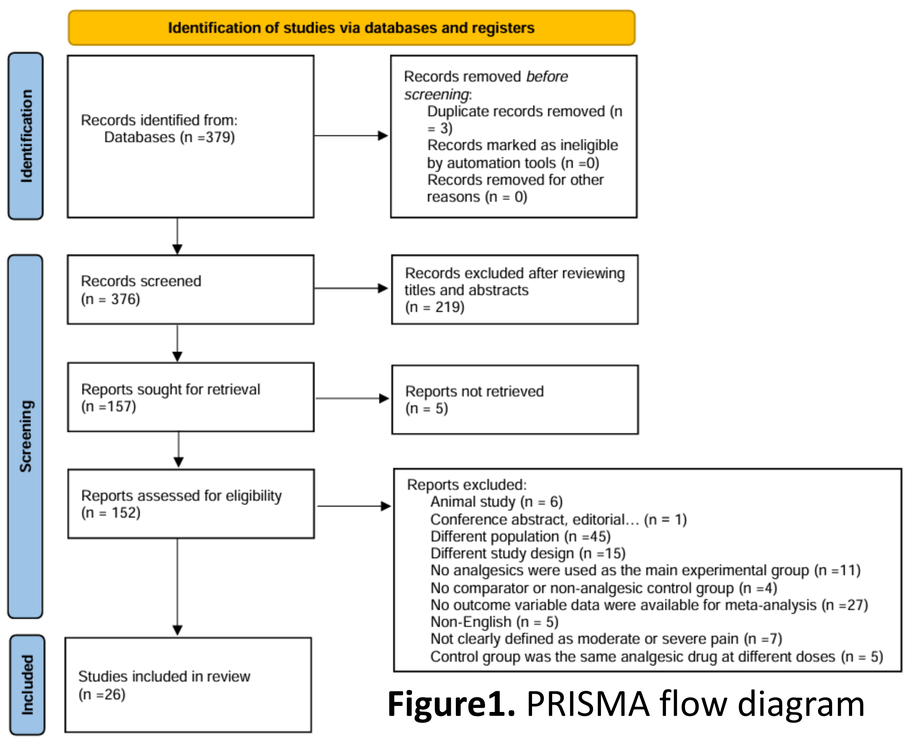

Figure1. PRISMA flow diagram

■ Study characteristics

- Among the 26 included studies (21 RCTs, 5 observational; 6,223 patients), **nalbuphine** was most commonly compared with **morphine** (4 studies, 340 patients), **sufentanil** (6 studies, 1,364 patients), and **placebo** (2 studies, 226 patients).
- Studies were categorized as **monotherapy** (14 studies, opioids only) or **combination therapy** (12 studies, opioids plus other analgesics).
- Pain outcomes were assessed using **VAS** in 18 studies, NRS in 2 studies, and VRS in 1 study.

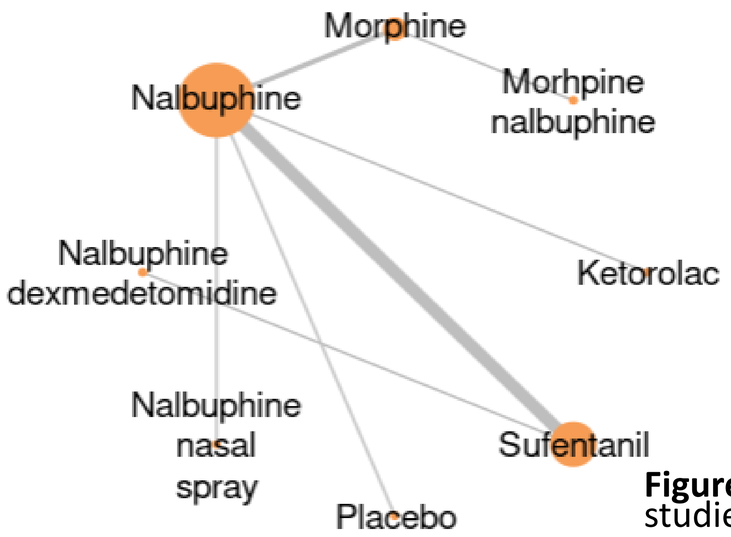

Figure 2. Network plot of all studies for the 0-8 hours period.

■ Efficacy

- In the **0–8 hours** period (n = 12), **nalbuphine** showed **moderate** efficacy, ranked **below morphine** but **above sufentanil**.
- Similar efficacy trends observed in 8–24 and 24–48 hours intervals.

■ Subgroup analysis

- **Greater efficacy in gynecological and abdominal surgeries.**
- Lower efficacy in **orthopedic procedures**.

■ Sensitivity analysis

- Imputed SDs were tested at 10%, 20%, and 30% of the mean pain scores; **SUCRA rankings remained stable**, confirming robustness of results.
- An **RCT-only subgroup analysis** (n = 21) for the 0–8h interval showed **similar rankings to the main analysis**, confirming the robustness of the findings.

■ Safety

- Compared to morphine, nalbuphine showed significantly lower rates of nausea (RR = 0.44), vomiting (RR = 0.43), and pruritus (RR = 0.07).

■ Quality assessment

- RCT: Among the 21 included RCTs, 18 studies had low risk of bias across all domains. The remaining 3 had moderate risk of bias.
- Observational studies: Among the 5 included observational studies, 4 had low risk of bias across all domains. The remaining 1 had moderate risk of bias.

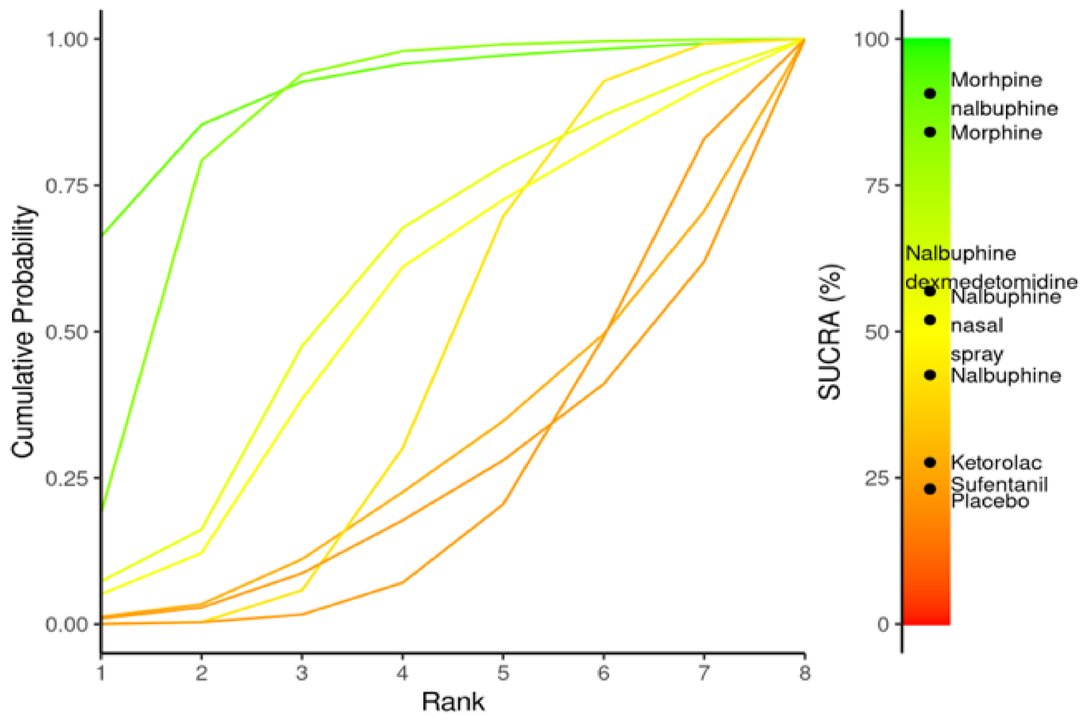

Figure 3. The Surface Under the Cumulative Ranking Curve (SUCRA) For the 0–8 hours period.

Conclusion

- ■ **Moderate analgesic efficacy demonstrated across postoperative intervals.**
- ■ **Favorable safety profile**, especially in visceral pain surgeries.
- ■ Though less potent than morphine, nalbuphine offers:
- **Reduced opioid-related adverse effects**
- **A valuable clinical alternative** in appropriate patient populations.

Reference

- Small C, Laycock HJ. Acute postoperative pain management. Journal of British Surgery, 2020. 107(2): p. e70-e80.
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Correspondent to: Rong-Sheng Chen. Email: johnson891104@gmail.com