Opioid and Non-Opioid Analgesics in Acute Postsurgical Pain: A Randomized Placebo-Controlled Dose-Ranging Trial of Intravenous Tramadol, Ketoprofen, and Morphine

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Background

Effective postsurgical pain management is essential, yet opioid use is limited by adverse effects and the risk of addiction. This has increased interest in non-opioid alternatives. IV ketoprofen, an NSAID, reduces inflammation-mediated pain, while tramadol provides dual analgesic action via μ-opioid receptor activity and monoamine reuptake inhibition. However, direct comparisons of ketoprofen with tramadol and with strong μ-opioid receptor agonists remain limited. Using a validated model of impacted third molar extraction, this study evaluated the efficacy and safety of IV ketoprofen and tramadol versus morphine and placebo.

Objectives

To compare the analgesic efficacy and safety of IV ketoprofen and IV tramadol versus IV morphine and placebo for acute postsurgical dental pain.

Study Design

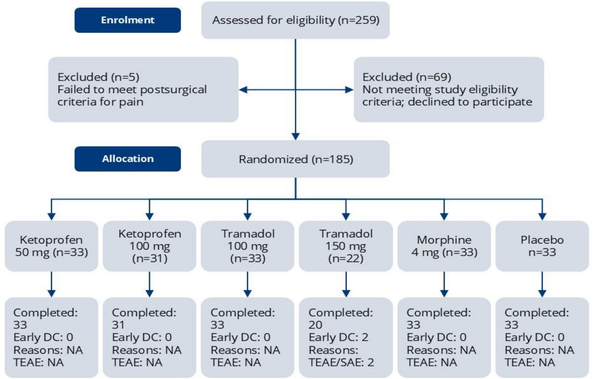

FIGURE 1: A CONSORT flow diagram of patient disposition from screening to study completion.

Results

Ketoprofen 50 mg and 100 mg, and tramadol 100 mg and 150 mg demonstrated significantly greater analgesic efficacy compared with morphine 4 mg and placebo across primary and secondary endpoints. Ketoprofen showed superior performance over tramadol, with faster onset and longer duration of pain relief. Morphine 4 mg did not demonstrate meaningful analgesia compared to placebo. Median time to meaningful pain relief was shortest with ketoprofen 100 mg, while placebo showed minimal effect. Adverse events were more frequent with tramadol and morphine. Two seizures occurred in the tramadol 150 mg group, leading to early discontinuation of that arm.

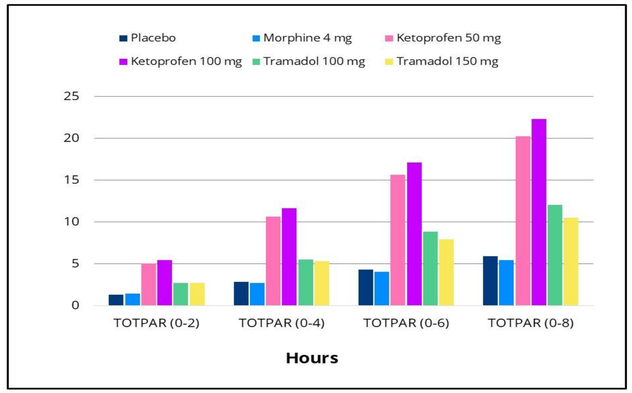

FIGURE 2: Total pain relief (TOTPAR) over 0 to 2, 0 to 4 (primary endpoint), 0 to 6, and 0-8 hour intervals

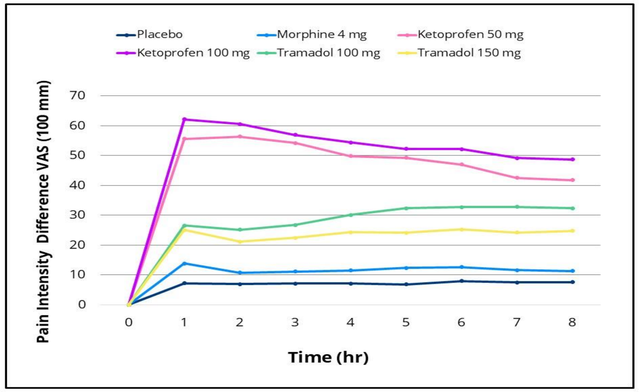

FIGURE 3: Pain intensity difference (VAS) over 0 to 8 hours post-dose

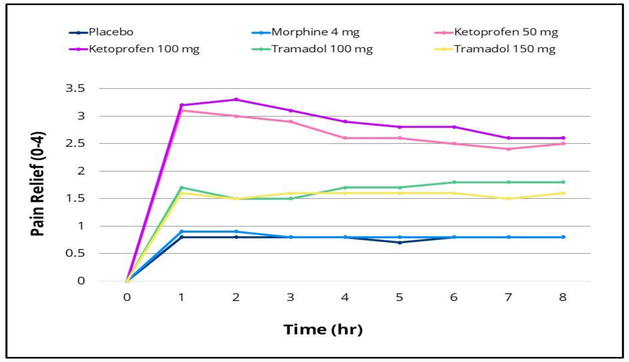

FIGURE 4: Pain relief (categorical scale) over 8 hours post-dose

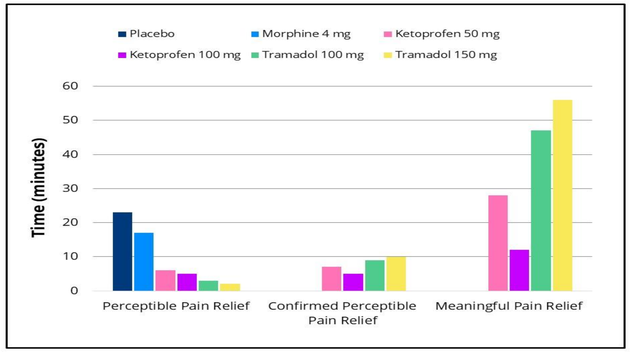

FIGURE 5: Time to perceptible and meaningful pain relief (Double Stopwatch)

Results

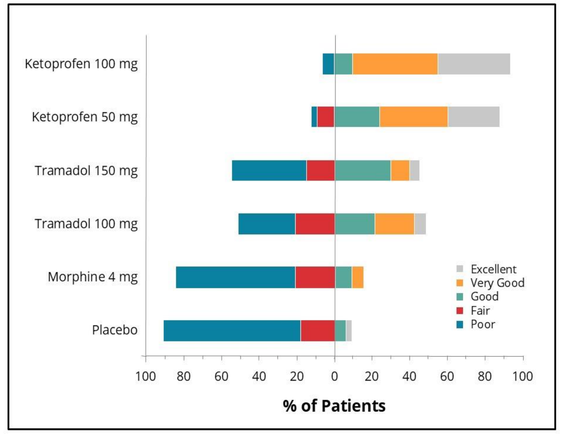

FIGURE 6: Global evaluation of study medication by subjects eight hours post-dose or immediately prior to rescue analgesia (ITT population) following a single IV dose of placebo, morphine 4 mg, tramadol 100 mg or 150 mg (terminated prematurely), or ketoprofen 50 mg or 100 mg.

Conclusion

IV ketoprofen 50 and 100 mg provided robust analgesia, superior to tramadol, morphine and placebo, and was well-tolerated. Tramadol showed modest efficacy, superior to morphine and placebo, and was associated with higher AEs, including 2 episodes of seizures at 150 mg. Morphine 4 mg was not superior to placebo. IV ketoprofen may be used alone or with strong opioids as part of multimodal analgesia.

References

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