Exploring Clinical and Pharmacological Effects of Nalbuphine HCl ER Tablets in Hemodialysis Subjects with Pruritus

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Introduction

- Uremic pruritus is an itchy disorder associated with end-stage renal disease (ESRD) that can be severe and debilitating.
- Uremic pruritus is associated with significant deterioration in patients' quality of life, including depression and disruption of sleep.
- A 17% increase in mortality rate, attributed to sleep disturbances, is associated with moderate to severe pruritus in HD patients.
- The presence of moderate to severe pruritus correlates with a greater degree of sleep disruption and an increased risk of depression.

Objectives

- To assess the safety and pharmacokinetics (PK) of nalbuphine administered orally as nalbuphine HCl extended release (ER) tablets in hemodialysis (HD) patients with moderate to severe pruritus.
- To explore the clinical and pharmacological effects of nalbuphine on pruritus using a visual analog score (VAS).

Methods

- This study was designed to:
  - Assess the safety and pharmacokinetics (PK) of nalbuphine administered orally as nalbuphine HCl extended release (ER) tablets in hemodialysis (HD) patients with moderate to severe pruritus.
  - Explore the clinical and pharmacological effects of nalbuphine on pruritus using a visual analog score (VAS).

- Patients were randomized to two cohorts: Cohort 1 (HD) and Cohort 2 (healthy).
- The study was blinded to the patients and assessors.

Safety Assessments

- A 17% increase in mortality rate, attributed to sleep disturbances, is associated with moderate to severe pruritus in HD patients.
- The presence of moderate to severe pruritus correlates with a greater degree of sleep disruption and an increased risk of depression.

Pharmacokinetics

- Nalbuphine administered orally as nalbuphine HCl extended release (ER) tablets was safe and well tolerated up to the 240 mg BID dose tested in HD patients.
- The maximum tolerated dose was 240 mg BID.
- The study was blinded to the patients and assessors.

Results

- Nalbuphine exposure in HD patients on dialysis days and non-dialysis days was comparable.
- Nalbuphine administered as oral nalbuphine HCl ER tablets was safe and well tolerated up to the 240 mg BID dose tested in HD patients.
- The maximum tolerated dose was 240 mg BID.
- The study was blinded to the patients and assessors.

Conclusions

- Nalbuphine administered orally as nalbuphine HCl ER tablets was safe and well tolerated up to the 240 mg BID dose tested in HD patients.
- The maximum tolerated dose was 240 mg BID.
- The study was blinded to the patients and assessors.

References


Acknowledgements

Trevi Therapeutics, New Haven, CT; DaVita Clinical Research, Minneapolis, MN

Figure 1: Study Design: Open-Label, Single Slim, Multiple Escalating Doses

Table 1: Subject Demographics

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<td>Black or African American 11 (73.3)</td>
<td>White 4 (26.7)</td>
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<tr>
<td>HD</td>
<td>20</td>
<td>Male 12 (60.0)</td>
<td>Black or African American 11 (73.3)</td>
<td>White 4 (26.7)</td>
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Table 2: Preferred Terms and Grades

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Figure 2: Plasma Concentration of Nalbuphine Following a Single 30-mg and Repeat 180-mg Dose

Figure 3: Nalbuphine Exposure in Hemodialysis Patients on Dialysis Days and Non-Dialysis Days

Figure 4: Effect of Nalbuphine on VAS Score in Hemodialysis Patients

Figure 5: Difference in VAS Change from Baseline (A) or 30 mg BID (B) for All Patients and Patients With VAS ≥ 4.0 as a Function of Nalbuphine ER Dose