The Effect of Dexlansoprazole MR on Nocturnal Heartburn and GERD-Related Sleep Disturbances in Patients with Symptomatic GERD: Randomized Trial

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BACKGROUND

- Among the 60 million adults reporting GERD symptoms, up to 89% report nocturnal symptoms which result in impairment in health-related quality of life and sleep quality.

OBJECTIVE

- This study's objective was to assess the efficacy and safety of dexlansoprazole 30 mg once daily compared with placebo for the relief of nocturnal heartburn and improvement of GERD-related sleep disturbances.

METHODS

- **Design**: randomized, placebo-controlled, double-blinded study
- **Duration:** 4 weeks
- **Inclusion Criteria**: age 18-66, ≥ 3 of 7 nights of nocturnal heartburn with a severity of moderate to very severe and its associated sleep disturbances, and normal esophageal mucosa upon screening endoscopy
- **Exclusion Criteria**: pregnancy or lactation; known hypersensitivity to PPIs, components of dexlansoprazole, or antacids; active ulcers or GI bleeding; conditions other than GERD that could be the primary cause of sleep disturbances; nightshift work or anticipated travel beyond three time zones; a history of alcohol abuse; use of PPIs 14 days before randomization; use of H2RAs or antacids during the screening period; chronic use of NSAIDs or COX-2 inhibitors within 30 days before randomization; use of sucralfate, misoprostol, corticosteroids, prokinetics, anticoagulants, antiseizure or psychotropic medications, bisphosphonates, or narcotics 14 days before screening; and use any drugs affecting the CNS that could mask perception of symptoms
- **Number of Patients Enrolled:** 305 patients underwent randomization; 152 were placed in the dexlansoprazole 30 mg group and 153 were placed in the placebo group
- **Drug Regimens:** patients self-administered the study drug (either dexlansoprazole or placebo) once daily by mouth, without regard to food intake
- **Primary Outcome Measure**: percentage of nights without heartburn over 4 weeks
- **Secondary Outcome Measures**: percentage of patients with relief of nocturnal heartburn (defined as 6 of 7 nights with no heartburn) over the last 7 days of treatment; percentage of patients with relief of GERD-related sleep disturbances (defined as 6 of 7 nights with no GERD-related sleep disturbances) over the last 7 days of treatment; mean severity of nocturnal heartburn during treatment; percentage of nights with GERD-related sleep disturbances; percentage of nights with each type of sleep disturbance; severity of GERD symptoms at week 4 as assessed by the investigator; percentage of heartburn-free days; change from baseline to week 4 in sleep quality assessed by PSQI score; change from baseline to week 4 in N-GSSIQ scores; and change from baseline to week 4 in WPAI scores
- **Power:** 95%, to detect a 21% treatment difference between dexlansoprazole and placebo for the primary efficacy endpoint of percentage of nights without heartburn
- **Data Handling Method:** intent-to-treat

RESULTS

- **Number of Patients Who Completed the Study:** 146 patients completed the study in the dexlansoprazole group and 147 patients completed the study in the placebo group
- **Findings and Statistical Results:** The primary efficacy end point of the percentage of nights free of heartburn was significantly greater in patients receiving dexlansoprazole than in those receiving placebo (median of 73.1 vs. 35.7%; $p < 0.001$).
    - Patients in the dexlansoprazole group, compared to placebo, also reported:
        - more relief of nocturnal heartburn or GERD-related sleep disturbances during the last 7 days of treatment (47.5 vs. 19.6% and 69.7 vs. 47.9%, respectively, $p< 0.001$ for both variables),
        - a greater percentage of 24-hour heartburn-free days (median 53.3 vs. 14.3%, $p < 0.001$),
        - and a lower percentage of nights with a sleep disturbance due to GERD (median of 11.1 vs. 36.8 %, $p < 0.001$).
- **Author's Conclusions:** The authors concluded that dexlansoprazole 30 mg daily was significantly better than placebo in improving symptoms of nocturnal heartburn in symptomatic GERD patients with frequent, moderate-to-very severe nocturnal heartburn leading to improved sleep quality, and decreased symptom severity and impact on morning activities.

STRENGTHS

- The study was double-blinded.
- Groups appeared equivalent at baseline.
- Statistical tests used were appropriate.

LIMITATIONS

- Authors were affiliated with Takeda, the makers of dexlansoprazole (Dexilant).
- The study did not report confidence intervals for data presented.
- Only median values were reported and no ranges were given for data presented.
- The inclusion and exclusion criteria limited extrapolation to the population.
- Only patients who had shown a previous response to acid-suppression therapy were randomized for treatment.
- Rescue medication use was not reported and could have affected study results.

CONCLUSION

- **My Conclusion:** Dexlansoprazole may have some benefit in the relief of nocturnal heartburn symptoms; however, further studies are needed.
- **Results Relating to Practice:** Dexlansoprazole is currently used for the treatment of GERD. Because of the limitations and lack of clinical significance shown, this study should not impact the prescribing of dexlansoprazole.
- **Future Research:** Further research is needed to see if benefits could be seen in patients who had not previously shown response to acid-suppression therapies. Studies are also needed to compare other PPIs against dexlansoprazole in the treatment of nocturnal GERD symptoms. Additional research should also involve trials with dexlansoprazole of longer than 4 weeks to see if symptoms continue to improve with further treatment.

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