
Design: Randomized clinical trial

Population/sample size/setting:
- 70 patients (34 men, 36 women, mean age 53) treated for post-herpetic neuralgia at a university dermatology department in India
- Eligibility based on at least 8 weeks of PHN pain after healing of rash, with pain intensity at least 40 on a scale from 0-100 at screening, average pain score at least 4 on Likert scale during the baseline week
- Exclusion criteria were prior treatment with nortriptyline or gabapentin, surgical treatment for PHN, immunocompromised state, medical comorbidity (hepatic, renal, hematologic), severe pain not related to PHN, illicit drug or alcohol use in past year, or any unstable medical or psychological condition
- Muscle relaxants, anticonvulsants, topical analgesics, and antiviral agents were discontinued at least 1 week prior to screening

Main outcome measures:
- Randomized to either nortriptyline (n=36) or gabapentin (n=34)
- Study had a 1 week run-in period and an 8 week treatment period for a total of 9 weeks, with the primary outcome being the difference in pain between baseline and the end of the study period
- Adverse effects were taken from a checklist given at baseline and for every 2 weeks until the end of the study; for each adverse effect, the patient was asked whether it was tolerable or intolerable
- Starting dose of nortriptyline was 25 mg bid; for gabapentin, starting dose was 300 mg tid; to preserve blinding, the nortriptyline group received a blank capsule for the second daily dose (thus, identical appearing capsules were taken tid)
- Dose escalation was done at 2 weeks and again at 4 weeks, depending on how well the drugs were tolerated; for nortriptyline, the escalation was 25 mg bid and for gabapentin 300 mg tid; the final daily dose of gabapentin was 2700 mg
- Average pain scores were reduced at the end of the study in both groups, and by an approximately equal amount: by 47.6% in the nortriptyline group and by 42.8% in the gabapentin group
- The proportion of patients with a 50% pain reduction was 25% in the nortriptyline group and 21% in the gabapentin group; no group difference was observed for this or for secondary outcomes such as sleep improvement
- Adverse effects were recorded less often in the gabapentin group than in the nortriptyline group, one of whom dropped out due to severe urinary retention; 50% of the nortriptyline group reported dry mouth, which did not occur in any patient in the gabapentin group
- Although there were similar improvements in the two treatment groups, one third of patients did not show any improvement or worsened.

Authors’ conclusions:
- After 8 weeks of treatment, nortriptyline and gabapentin show similar levels of pain relief.
- There were more dose-limiting side effects with nortriptyline than with gabapentin.
- Gabapentin can be recommended for PHN as an alternative to nortriptyline, because of its more favorable safety profile.

Comments:
- The adverse effects were reported from a checklist given to the patients at baseline, but this checklist may have omitted some important side effects of gabapentin while including those associated with nortriptyline.
- In other gabapentin trials, there have been reports of headache, confusion, and diarrhea, which were not on the list in Table 3; presumably, dizziness, another common side effect of gabapentin, is recorded in Table 3 as “giddiness.”
- Attrition was low in both groups (2 with nortriptyline and 4 with gabapentin), suggesting that there were few withdrawals due to adverse effects.
- The actual safety and tolerability profiles of nortriptyline and gabapentin may be more similar than the authors imply.

Assessment: Adequate for evidence that nortriptyline and gabapentin are equally effective in pain relief of PHN and are equally acceptable alternatives for treatment; inadequate for evidence that the safety profile of gabapentin is superior.