Background

Monotherapy with first-line drugs for neuropathic pain often fails to provide sufficient pain relief or has unacceptable side effects because of the need for high doses.

Aim

The objective of this trial was to test whether the combination of imipramine and pregabalin in moderate doses would relieve pain more effectively than monotherapy with either of the drugs.

Methods

This was a randomized, double-blind, placebo-controlled, crossover, multicenter trial consisting of four 5-week treatment periods in patients with painful polyneuropathy. Treatment arms were imipramine 75 mg/d vs pregabalin 300 mg/d vs combination therapy vs placebo. Patients with polyneuropathy and symptoms for more than 6 months, age 20 to 85 years, pain intensity ≥4 on a 0- to 10-point numeric rating scale (NRS) and pain at least 4 days a week were included in the trial.

Results

A total of 262 patients were screened for participation, 73 patients were randomized, and 69 patients were included in the data analysis. Mean age of the 69 patients were 69 years (range 29-82 years), and 41 were male. The most frequent etiologies of polyneuropathy were diabetes (15), alcoholic (12) and idiopathic (28). The effect on average pain in comparison with placebo was: combination (-1.67 NRS points, $P < 0.001$), imipramine (-1.08 NRS points, $P < 0.001$), and pregabalin (-0.48 NRS points, $P = 0.03$). The combination therapy had significantly lower pain scores than both monotherapies: combination vs imipramine ($P = 0.009$), combination vs pregabalin ($P < 0.001$). During combination therapy, the dropout rate was higher and the patients reported a higher rate and severity of side effects.

Conclusion

Combination of moderate doses of the tricyclic antidepressant imipramine and pregabalin could be considered as an alternative to high-dosage monotherapy. However, the trial also emphasized that balance between efficacy and safety is an issue.

Publication of study results

Holbech JV, Bach FW, Finnerup NB, Brøsen K, Jensen TS, Sindrup SH. Imipramine and pregabalin combination for painful polyneuropathy: a randomized controlled trial. Pain 2015;156:958-966.