Benfotiamine in Diabetic Polyneuropathy (BENDIP):

Results of a Randomised, Double Blind, Placebo-controlled Clinical Study

Stracke H, Gaus W, Achenbach U, Federlin K, Bretzel RC
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At a glance:

- 6 weeks treatment of patients with diabetic polyneuropathy (DPN) with 600 mg benfotiamine daily, resulted in an improvement of neuropathic symptoms as assessed by the Neuropathy Symptom Score (NSS).
- The best improvement among the individual parameters of the Total Symptom Score (TSS) was seen in the symptom “pain”.
- The number of patients with adverse events in the benfotiamine groups was comparable to placebo, demonstrating the good tolerability of daily doses of 300 mg and 600 mg benfotiamine, respectively.
- Due to its influence on the impaired glucose metabolism, benfotiamine could expand the treatment options for patients with DPN.

Introduction & Background

Polyneuropathy is found in about 30-50% of diabetic patients and it has been shown that a significant vitamin B1 deficiency exists in patients with diabetes.

In addition, experimental data show that benfotiamine inhibits several pathways of hyperglycemic damage through activation of transketolase (rate-limiting enzyme of the non-oxidative pentose phosphate pathway): the hexosamine pathway, activation of protein kinase C and activation of NFκB. Benfotiamine is also able to block the formation of Advanced Glycation Endproducts (AGEs), thereby preventing AGE-induced microvascular and macrovascular endothelial dysfunction.

Aim of this study was to verify the efficiency and safety of benfotiamine as monotherapy in the treatment of DPN.

Materials & Methods

This double blind, placebo-controlled, phase-III-study randomized 165 patients with DPN to one of three treatment groups: Benfotiamine 600 mg per day, benfotiamine 300 mg per day or placebo. The intention to treat (ITT) analysis included 47 subjects in the benfotiamine 600 mg group, 45 subjects in the 300 mg group and 41 subjects in the placebo group. The per protocol (PP) analysis included 43 individuals receiving benfotiamine 600 mg, 42 individuals receiving benfotiamine 300 mg and 39 with placebo treatment.

The NSS at 6 weeks was defined as the primary endpoint of this study. Secondary outcome parameters were the NDS (Neuropathy Disability Score), the TSS and the vibration perception threshold (tuning fork test).

Results

After 6 weeks of treatment, the improvement in NSS was greatest in the 600 mg benfotiamine group and smallest in the placebo group. This difference between groups was significant in the PP population (p = 0.033, see Figure 1) and was slightly above the significance level in the ITT population (p = 0.055).

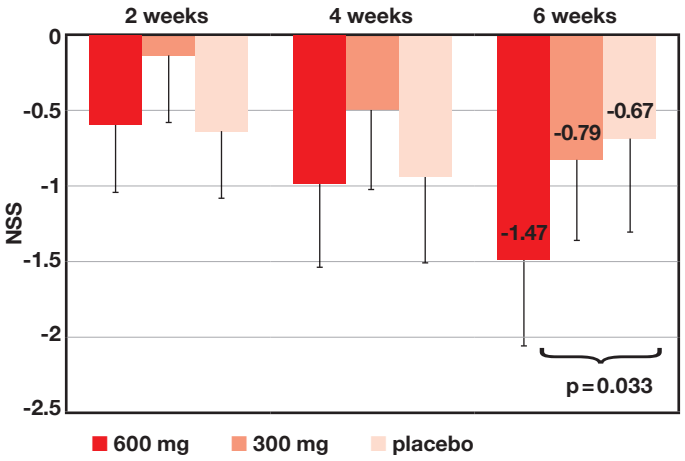

Figure 1 | Reduction of NSS under two different benfotiamine dosages (600 mg and 300 mg daily) and placebo. Each column represents mean of changes to baseline visit and its 95% confidence intervall.

Regarding TSS, the improvement from baseline after 6 weeks of treatment was greatest in the 600 mg group and smallest under placebo (yet the difference was not significant). The best improvement among the individual parameters of the TSS in the 600 mg benfotiamine group was shown in the symptom “pain”, followed by “numbness”, “burning” and “paresthesias”.

Regarding NDS, tuning fork test and HbA1c levels, there were no significant differences between the groups.

Overall, eight patients showed mild gastrointestinal disturbances or experienced skin or allergic reactions. The number of patients with adverse events in the benfotiamine groups was comparable to placebo, demonstrating the good tolerability of a daily dose of 300 mg or 600 mg benfotiamine.

Discussion & Conclusions

The study found greater efficacy of 600 mg/d benfotiamine compared to 300 mg/d in terms of improving the NSS over 6 weeks. The symptom “pain” seemed to be best influenced by benfotiamine.

As the treatment with benfotiamine is based on pathogenesis, it was expected to also improve the NDS or at least slow progression. A trend towards an improvement was found with both benfotiamine doses, but a high placebo effect caused the difference between groups to be nonsignificant. The treatment duration of 6 weeks may have been too short to demonstrate a slowing of progression.

Based on its effect on the impaired glucose metabolism, benfotiamine could enrich the treatment options for patients with DPN.

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