Multiple sclerosis (MS) is a chronic demyelinating disorder in which 25-hydrovitamin D (25(OH)D) levels may play a role in disease activity and response to treatment. To determine the effects of 25(OH)D levels and treatment with interferon beta-1b on disease activity and response to treatment in multiple sclerosis (MS), we performed an analysis of the BENEFIT trial, a placebo-controlled, phase 3 trial of early interferon beta-1b treatment in patients with clinically isolated syndrome (CIS).

**Methods:** The BENEFIT trial was a double-blind, placebo-controlled, phase 3 trial that randomized 468 patients with CIS to interferon beta-1b or placebo over 2 years (early treatment) or placebo over 6 years (delayed treatment). Whole blood samples and contrast-enhanced magnetic resonance imaging (MRI) scans were obtained at baseline and after 6, 12, and 24 months in both treatment groups. The primary endpoint was gadolinium-enhanced (Gd+) lesion incidence rate on MRI. In a post hoc analysis, we performed gene expression analysis to determine the association of 25(OH)D and interferon beta-1b with Gd+ lesion count.

**Results:** Higher 25(OH)D levels (p=0.0001) and interferon beta-1b treatment (p<0.0001) were associated with lower Gd+ lesion count. Analysis of the association of 25(OH)D and interferon beta-1b with Gd+ lesion count revealed that 25(OH)D had a beneficial effect on Gd+ lesion count, similar to the beneficial effect of interferon beta-1b treatment. These genes represent the starting point for inferring the specific mechanism of action of 25(OH)D.

**Conclusions:** Our findings provide some evidence on a molecular level for the role of 25(OH)D in reducing disease activity in patients with MS.

25-hydrovitamin D and MS activity during therapy with interferon beta-1b

**ABSTRACT**

Background: Several studies suggest a beneficial effect of 25-hydrovitamin D (25(OH)D) on multiple sclerosis (MS) activity. We analyzed the BENEFIT trial to evaluate the impact of 25(OH)D on gene expression.

Objectives: We analyzed the relationship between 25(OH)D levels and interferon beta-1b treatment on gene expression to understand the mechanisms underlying the beneficial effect of 25(OH)D on MS.

Methods: The BENEFIT trial was a double-blind, placebo-controlled, phase 3 trial that randomized 468 patients with CIS to interferon beta-1b or placebo over 2 years (early treatment) or placebo over 6 years (delayed treatment). Whole blood samples and contrast-enhanced magnetic resonance imaging (MRI) scans were obtained at baseline and after 6, 12, and 24 months in both treatment groups. The primary endpoint was gadolinium-enhanced (Gd+) lesion incidence rate on MRI. In a post hoc analysis, we performed gene expression analysis to determine the association of 25(OH)D and interferon beta-1b with Gd+ lesion count.

Results: Higher 25(OH)D levels (p=0.0001) and interferon beta-1b treatment (p<0.0001) were associated with lower Gd+ lesion count. Analysis of the association of 25(OH)D and interferon beta-1b with Gd+ lesion count revealed that 25(OH)D had a beneficial effect on Gd+ lesion count, similar to the beneficial effect of interferon beta-1b treatment. These genes represent the starting point for inferring the specific mechanism of action of 25(OH)D.

Conclusions: Our findings provide some evidence on a molecular level for the role of 25(OH)D in reducing disease activity in patients with MS.