Short Communication

L-Glutamine Therapy Reduces Hospitalization for Sickle Cell Anemia and Sickle β°-Thalassemia Patients at Six Months – A Phase II Randomized Trial

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Background: Increased oxidant stress plays an important role in the pathophysiology of sickle cell disease. Nicotinamide Adenine Dinucleotide (NAD) is an important anti-oxidant that protects hemoglobin as demonstrated in diseases such as methemoglobinemia. Early in-vitro studies have shown that L-glutamine, a precursor for NAD, reduced oxidant stress via improvement of NAD redox status in red blood cells.Oral administration of L-glutamine in early clinical studies supported in-vitro findings of improving NAD redox potential, therefore, a larger proof of concept clinical trial was designed and conducted. Methods: A Phase II randomized, double-blind, placebo-controlled, parallel-group, multicenter study was conducted to evaluate the safety and efficacy of L-glutamine therapy for patients 5 years or older diagnosed with sickle cell anemia or sickle β°-thalassemia. Eighty one patients were randomized (1:1 ratio) to oral L-glutamine at 0.3 g/kg or placebo twice daily for 48 weeks. The primary endpoint was the frequency of painful crises. Secondary endpoints included the frequency of hospitalization. Results: At Week 24 (6 months), the mean number of painful crises was 2.5 and 5.5 for L-glutamine and placebo groups respectively ($p = 0.060$). The mean number of hospitalizations was 0.8 and 1.3 for L-glutamine and placebo groups respectively ($p = 0.036$). Conclusion: At 6 months of therapy, L-glutamine treatment was efficacious in reducing the frequency of hospitalization (nearly 40% reduction) and there was a major trend for the decrease in frequency of painful crises (over 50% reduction) favoring the L-glutamine treatment arm. There was no difference in safety between groups. Based on these findings, a Phase III trial was conducted and results are now available.

Note: This work is partly presented at Webinar on Clinical Pharmacy, going to be held on May 31st, 2021 GMT+1.