EFFICACY AND SAFETY OF LOW-DOSE THALIDOMIDE COMBINED WITH MESALAZINE IN THE TREATMENT OF REFRACTORY ULCERATIVE COLITIS IN ADULTS

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Background To evaluate the efficacy and safety of low-dose thalidomide combined with mesalazine in the treatment of refractory adult ulcerative colitis (UC).

Methods The refractory adult UC patients treated with low-dose thalidomide combined mesalazine from Jan. 2018 to May. 2020 were included. Their clinical records such as the clinical characteristics, course of treatment, efficacy and adverse reactions were reviewed.

Results Among the 14 patients with refractory UC in adults, 9 males, 5 females, 14 total colon involvement, 14 chronic relapse type, the average duration were 7.47 years, and the average age was 45-years old, while all patients had previously received adequate amounts of hormone-induced remission. 14 active UC patients were treated with low dose thalidomide (25-50 mg/d p.o) combined with mesalazine on the premise that sufficient mesalazine (≥4 g/d p.o) was ineffective for 2 weeks. After treatment, the median onset time was 3.5 weeks and the clinical remission rates within 8 weeks and mucosal healing rate by endoscopy was 78.6% (11/14) and 62.5% (5/8) respectively. Among the 3 patients with ineffective treatment, 1 patient was handled by infliximab injection and 2 by surgery. 3 patients had ADRs, all of which were nerve damage, and were taken off medication, and 1 patient had disease recurrence and was reclassified to infliximab treatment.

Conclusions Low-dose thalidomide combined with mesalazine is effective in the treatment of refractory adult UC, which can be used to induce remission and promote mucosal healing, with few and can be tolerated by most patients. However, in clinical application, it is necessary to select the right group and closely monitor ADRs during treatment.

META-ANALYSIS ON THE EFFECT OF PROBIOTICS ON NEURODEGENERATIVE DISORDERS IN HUMANS CLINICAL TRIALS

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Background Probiotics have been shown to improve neurocognitive behaviour in animal models via the gut-brain-axis. This meta-analysis aims to evaluate the evidence in human studies on the potential of probiotics as a treatment for age-related neurodegeneration such as Mild Cognitive Impairment (MCI) and Alzheimer’s Disease (AD).

Methods A PRISMA meta-analysis was conducted by screening through MEDLINE, Embase, Scopus, Web of Science and Cochrane library for human studies using equivalent combinations of ‘probiotics’, ‘age-related neurodegeneration’, ‘MCI’ and ‘AD’. Studies with Mini-mental State Examination (MMSE), a test for cognitive function with comparable quantitative outcome were meta-analysed using RStudio. The analysis for overall effect (95% CI) and heterogeneity (I²) was performed by Forest Plots and subgroup analysis. We further assessed whether the results varied with age, gender, BMI, dosage and sample size with weighted meta-regression. Probiotic amelioration of neurodegeneration was also evaluated through biomarker analysis.

Results 9 human studies were identified, where 5 studies had quantitative results. Meta-analysis demonstrates that there is a
0.9 mark (0.1 to 1.9) improvement in MMSE scores in human RCTs, though the results are quite heterogeneous ($I^2 = 94\%$) (figure 1). Subgroup analysis of MCI and AD models were divergent with a difference of -0.1 (-0.3 to 0.2) versus a 1.7 (0.9 to 2.5) difference in MMSE score between the two groups. Studies also report improvement in other cognitive tests, such as CERAD and RBANS. Meta-regression revealed that the improvement in MMSE scores is age-dependent ($p < 0.005$) in humans. Biomarker analysis suggests that probiotic supplementation upregulates anti-oxidative ($\#$ MDA) and anti-inflammatory ($\#$ hs-CRP) pathways. Studies also show an improvement in non-neurological symptoms such as in insulin sensitivity ($\#$ HOMA-IR, $\#$ QUICKI), and lipid profiles ($\#$ TG, VLDL). However, an intervention study reported an increase in kynurenine:tryptophan ratio post probiotic supplementation, suggesting an activation of inflammatory pathways.

**Conclusions** Human study evidence generally shows an association between probiotic supplementation and improved neurocognitive function, although confounded by age and severity of neurodegeneration. Caution should be applied in the use of probiotics as an intervention for cognitive decline.

**Background** Prebiotics, as non-digestible substances that stimulate the growth and activity of beneficial bacteria, is hypothesized to improve neurocognitive function through the Gut-