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Retarded Release Phosphatidylcholine in Steroid-Dependent Ulcerative Colitis

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Background: Phosphatidylcholine (PC) is a major component of the intestinal mucus–the key player in establishing a healthy mucus barrier function. One of the main pathogenetic hypotheses of ulcerative colitis (UC) holds an impaired mucus barrier function responsible for the development of the disease. The colonic mucus PC content is reduced by approximately 70% in UC patients irrespective of the inflammatory activity; we deduced that this critical reduction of phosphatidylcholine content in the colonic mucus impairs the mucosal barrier function and enables mucosal exposure to antigens and bacteria which induce inflammation and ulceration. Accordingly, we hypothesized that by supplementing phosphatidylcholine to the colonic mucus we could improve disease activity in ulcerative colitis.

Objective of the study: Long-term steroid treatment in chronic-active ulcerative colitis is generally discouraged. However, treatment alternatives in steroid-dependent courses are lacking when immunosuppressive agents fail. An insufficient level of phosphatidylcholine in colonic mucus is a possible pathogenetic factor in the development of ulcerative colitis. A first study with retarded release phosphatidylcholine in 60 non-steroid-treated patients with chronic-active ulcerative colitis suggested this treatment was safe and effective. The objective of the current trial was to evaluate whether retarded release phosphatidylcholine better

permits steroid withdrawal than placebo in adults with chronic-active, steroid-dependent ulcerative colitis.

Methods: This randomized, double-blind, placebo-controlled, phase IIA study over a 12-week period included 60 patients with steroid-dependent, chronic-active ulcerative colitis and moderate to severe disease activity. Subjects were recruited between 2003 and 2006 in the referral center for inflammatory bowel disease at the University Hospital of Heidelberg.

Study intervention was an orally applied granule of phosphatidylcholine with retarded release in the distal part of the small intestine. It was administered quarter-to-date with a total dose of 2g daily. This formula was developed to bypass absorption in the upper gastrointestinal tract.

Main outcome measure: Complete steroid withdrawal with a concomitant achievement of either a low clinical activity (CAI ≤ 3) or a clinical response (defined by a CAI improvement of $\geq$50%).

Results: The main outcome measure was achieved in 15 PC-treated patients (50%) and in 3 (10%) placebo patients (p=0.002). Twenty-four of the 30 PC-treated patients (80%) and 3 placebo patients (10%) could discontinue corticosteroids without experiencing disease exacerbation. All disease activity indices (clinical, endoscopic, histological activity and life quality) improved in the PC group during the course of the study. The follow-up rate was 97%.

Limitations of the trial: Small sample size and short study period

Conclusion: Phosphatidylcholine reduced the need for corticosteroids more than placebo did in patients with chronic steroid-refractory ulcerative colitis. Long-term, multicenter trials with a higher study population are needed to evaluate the sustainability of steroid withdrawal in these patients.