Toxicity of gluten traces in patients on treatment for celiac disease. Results of a prospective, placebo-controlled, double-blind, randomized study.

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Background. Treatment of celiac disease (CD) is based on complete avoidance of gluten-containing products from the diet. However it is not known whether minimal amount of gluten are harmful for patients on long-term treatment. This is an important issue, as even a strict gluten-free diet (GFD) is usually contaminated by traces of gluten, e.g. in wheat starch and processed food.

Aim: to investigate the toxicity of the prolonged ingestion of gluten traces in treated CD patients.

Study-design, patients and methods: prospective, placebo-controlled, double-blind study. Patients were adults with biopsy-proven CD on treatment with the GFD for at least 2 years. Their daily gluten intake following strict GFD ranged between 0 and 3 mg. After baseline evaluation, patients continued their GFD and were assigned to ingest 0, 10 or 50 mg of daily gluten (incorporated in a capsule) for 90 days. The following evaluations were performed both at baseline and after the micro-challenge: clinical, serological (anti-transglutaminase and antigliadin antibodies), and small intestine histology (morphometry and immunohistochemistry).

Results. Thirty three of the 46 enrolled CD patients completed the microchallenge. Reasons for interruption were: abnormal histology at baseline (6), dropout (4), pregnancy (1), and development of symptoms (2, both challenged with 50 mg of gluten). In the 33 patients completing the study (placebo = 10; 10 mg gluten = 12; 50 mg gluten = 11) the clinical and serological evaluation showed no changes after challenge between treatment groups. At baseline, the mean villous height/crypt depth (vh/cd) (2.9 ± 0.6) and CD3+ intraepithelial lymphocyte (IEL) count (21 ± 6) detected in the enrolled CD patients were significantly different from 52 non-CD controls (2.3 ± 0.6 and 31 ± 12, respectively). The baseline and post-challenge vh/cd was 2.4 ± 0.2 vs 2.5 ± 0.1 (placebo), 2.2 ± 0.2 vs 2.5 ± 0.2 (10 mg group), and 2.5 ± 0.2 vs 2.2 ± 0.2 (50 mg group). The baseline and post-challenge IEL were 30 ± 4 vs 29 ± 5 (placebo), 31 ± 3 vs 31 ± 3 (10 mg group), and 32 ± 4 vs 36 ± 4 (50 mg group).

Conclusions. The protracted daily ingestion of 10 mg of gluten did not cause any measurable change while a dose of 50 mg was associated with minimal signs of relapse at the histological level and also caused symptomatic relapse in 15% of patients. This information is instrumental for establishing the threshold of tolerable gluten concentration in commercial gluten-free products.