



MEDICAL RESEARCH

Open Access

The remember/regeneration therapy method as a new holistic approach for celiac disease: Two case reports

Mustafa Yasar*, Bulent Uysal, Teoman Alpay Demirel

RTM Clinic, Izmir, Turkey

ABSTRACT

Background: Celiac disease (CD) is a widespread disorder caused by an intolerance to gluten which is a protein found in many foods in genetically susceptible individuals. The disease is characterized by small-intestinal mucosal injury and nutrient malabsorption. Currently, in spite of a life-long gluten-free diet is the effective and available treatment option for patients with CD, the widespread use of wheat-derived gluten in the food industry limits the effectiveness of treatment. Therefore, it is needed to perform further studies on non-dietary therapies which solve the causes of the disease. The Remember/Regeneration Therapy Method (RTM) is a novel holistic medicine approach that targets physiopathological changes in quadruplet body structures and includes various complementary methods such as acupuncture, ozone therapy, and phytotherapy, etc. in different combinations which are determined depending on the disease.

Case Presentation: We present two celiac cases that were serologically diagnosed and successfully healed with the RTM without a significant side effect.

Conclusion: RTM may provide consistent results for CD and similar diseases by using combinations of various holistic medicine methods in different doses, durations, and sessions. The identification of epigenetically regulated genes related to CD may be promising to develop epigenetic drugs for disease management. For that purpose, further scientific studies that contain the aforementioned features are needed.

ARTICLE HISTORY

Received February 02, 2020

Accepted April 03, 2020

Published May 17, 2020

KEYWORDS

cognitive function, diet, brain questionnaires, brain-targeted beverage.

Background

Celiac disease (CD) is a widespread disorder characterized by small-intestinal mucosal injury and nutrient malabsorption. It is caused by an intolerance to gluten which is a protein found in many foods. Also, genetic predisposition is one of the main characters of CD [1]. Many scientific studies have demonstrated that CD is a disease that involves various epigenetic mechanisms as well as its genetic aspects. [2-4]

Currently, a life-long gluten-free diet is an effective and available treatment option for patients with celiac disease. But, the widespread use of wheat-derived gluten in the food industry limits the effectiveness of life-long gluten diet [5]. Therefore, many scientific studies that target various issues related to the disease such as non-dietary therapies, gluten tolerization, and immunomodulation and immune cell-targeted therapies have been performed by considering the pathological mechanisms of the disease [6]. Alternative options were investigated in order to find curative medical approaches. It has been demonstrated that alternative and complementary medicine methods such as acupuncture and phytotherapeutic agents have beneficial effects on CD [7,8].

On the other hand, the links between epigenetic mechanisms and CD have recently become the subject of scientific research [9]. Novel scientific discoveries in the sciences of biology and

genetics have demonstrated that inheritance has a whole new dimension beyond the genes, not in the structure of the DNA. In this new dimension of inheritance called epigenetics, it has been shown that changes can be transferred to new generations [10,11]. The importance of epigenetic modifications in long-term memory performance has been demonstrated in the most extensive and comprehensive study on DNA methylation. The processes such as chromatin remodeling, histone modifications, and non-coding RNA are also other important changes that belong to epigenetic mechanisms [12].

The Remember/Regeneration Therapy Method (RTM) is a holistic approach which consists of diagnostic and treatment systems that include mainly phytotherapy and different combinations of various complementary and traditional medical methods such as acupuncture, cupping therapy, hirudotherapy, ozone therapy, etc. Phytotherapy is the main and pivot part of the RTM while the other treatment modalities are used to support its effects. In phytotherapeutic applications of RTM, two main groups of phytotherapeutics called "Remember Herbs" and "Regeneration Herbs" are used. According to the RTM, diseases are seen as the reflection of epigenetic changes in the phenotype resulting from the gene-environment mismatch. The treatment strategy is based on the recovery of health by essentially improving the deteriorating structures. It has been considered that the pathological process of a disease

Contact Mustafa Yasar, M.D. ✉ drmustafa.yasar@rtmclinic.com.tr 📍 RTM Clinic, Izmir, Turkey.

© 2020 The Authors. This is an open access article under the terms of the Creative Commons Attribution NonCommercial ShareAlike 4.0 (<https://creativecommons.org/licenses/by-nc-sa/4.0/>).

can potentially be reversed by RTM, considering the epigenetic changes. It has been clinically observed that epigenetic changes and irregularities improved when appropriate treatment protocols were applied, as in the RTM [13].

Case Presentation

In the current study, two cases with CD are presented. The patients received a specific mixture called RTM phytotherapeutics in RTM Clinic, Izmir, Turkey. All complaints, clinical and laboratory findings of the patients were healed within 8-16 months following the beginning of treatment. At the end of the 5-year and 3-year follow-up period, respectively in Case 1 and Case 2, no relapse has been detected in neither of the cases.

Case 1

Case 1 was a 13 years old female with CD and was suffering from the disease for 1.5 years. There was no family history and no stress factor which trigger the disease. The case was cured with RTM phytotherapeutics consisting of different herbal extracts.

The following RTM phytotherapeutics were used for Case 1 for 16 months;

- o DVD.SNO, 3*2 (A mixture with thistle)
- o ISY.CP, 3*2 (A mixture with nettle leaf)
- o ARD.REM, 3*1 (A mixture with juniper fruit)
- o SDS.X, 3*1 (St. John's wort extract)

Case 2

Case 2 was a 9-year-old female with CD and was suffering from the disease for 4 months. There is no family history and no stress factors which trigger the disease. The case was cured with RTM phytotherapeutics.

The following RTM phytotherapeutics were used for Case 2 for 8 months;

- o DVD.ARD, 2*1 (A mixture with thistle and Juniper fruit)
- o DVD.SNO, 2*3 (A mixture with thistle)
- o ISY.CP, 2*3 (A mixture with nettle leaf)
- o KiD MiX, 3*1

We presented the results of two cases with CD following the RTM. In this article, the recovery process of two patients with CD after RTM, after long-lasting conventional treatments will be discussed.

Follow up period and the diagnostic results

Both patients were called for follow up periodically, and physical examination and other practices were performed. Clinical findings or complaints were not observed during the follow-up period of 5 and 3 years in Case 1 and 2, respectively. Briefly, both cases were completely healed with RTM within 16 and 8 months, respectively (Table 1). Also, the healing process was supported by the improvement in antibodies (Table 2 and 3).

Also, there were no side effects caused by RTM so patients did not interrupt the treatment. The therapy exhibited a desirable safety outline and was associated with a good response rate of 100% within 8 to 16 months.

Limitations

In this study, we could not use molecular methods to explain the mechanism of action of RTM in terms of epigenetic regulation. Since the cases were out of control of our clinic before RTM, they came to us without epigenetic analysis. Therefore, we could not show the possible mechanism of the epigenetic process. The fact that the study was a retrospective study also contributed to this limitation.

Discussion

Celiac disease, or gluten enteropathy, is caused by a sensitivity to the gliadin fraction of gluten [14]. Therefore, the analysis of antibodies against gliadin has been a significant improvement in the diagnosis of the disease. The antigliadin tests shows high variability in terms of sensitivities and specificities. It has been shown that immunoglobulin (Ig)G-based antigliadin (AGA) tests were generally poor in both parameters while the IgA-based test was poorly sensitive but more specific. Whereas, the IgA endomysium (EMA-IgA) and tissue transglutaminase (TTG-IgA) tests have been shown to be both highly sensitive and specific with values for both parameters exceeding 95% in most studies [15]. But it is considered that such screening tests cannot replace intestinal biopsy that is the gold standard for diagnosis of CD [16]. In the current study, we aimed to demonstrate the efficacy of the RTM against CD by presenting the improvement in results of antigliadin, transglutaminase and endomysial antibody testing following the RTM. For the same purpose, we presented the disappearing of the complaints in each case by comparing the change in patient's complaints before and after treatment to show clinic recovery. During the RTM, antibodies and existing complaints of patients decreased and normalized gradually. Moreover, these cases still maintain their improved state over a long period of follow-up. Another important point is that patients discontinued diet therapy after the RTM and still have no complaints. Despite intense scientific studies, there is no curative and effective treatment against CD. Therefore, it seems that a life-long gluten-free diet is the single and most effective treatment option for CD currently. On the other hand, dietary therapy does not improve the quality of life completely even if it reduces the clinical complaints of the patients. Because, although people around the patients consume all kinds of food with pleasure, they are deprived of it. Whatever the treatment is, it should also normalize patients' food consumption and this should be what is expected of an ideal treatment. This can only be achieved with treatment protocols that have a new and different perspective, and RTM is a set of protocols emerged from this different point of view. Another point we can consider is that the RTM complies with "*primum non nocere*" which is the basic notion in medicine according to the results in both cases.

RTM is a holistic medicine that describes the anatomical and physiological aspects of physiopathological changes in quadruplet body structures (QBSs), which is a unique treatment system where phytotherapy is at the center and integrated with traditional and complementary applications. In the RTM, diseases are seen as the reflection of epigenetic changes in the phenotype resulting from the gene-environment mismatch. The treatment strategy is based on the recovery of health by

essentially improving the deteriorating structures. Considering that many of the epigenetic changes which lead to disease can potentially be reversed, it has been clinically observed that epigenetic changes and irregularities improved when appropriate treatment protocols were applied, as in the RTM. Thus, firstly, these extraordinary and abnormal conditions that lead to the gene-environment mismatch should be eliminated, and secondly, previous normal physiological processes should be reminded to the body. The name of RTM comes from the special treatment strategy that is composed of proper combinations of regenerative and remember phytotherapeutic agents and holistic medicine methods [13].

Phytotherapy is the main and pivot part of the RTM while the other treatment modalities are used to support the effect of phytotherapy. Moreover, in phytotherapeutic applications of RTM, two main groups of phytotherapeutics called "Remember Herbs" and "Regeneration Herbs" which consist of different amounts of various medical herbs are used [13]. Many phytochemicals have been shown to affect through epigenetic regulation on some conditions such as cancer chemoprevention and metabolic syndrome [17,18].

Nowadays, many chronic inflammatory diseases have been shown to be associated with epigenetic mechanisms [19]. Epidemiological studies have emphasized the link between perinatal factors such as breastfeeding, cesarean delivery, and antibiotic use, and the increased risk for inflammatory bowel disease and/or celiac disease. So, it is considered that changes in the development and composition of the intestinal microbiota, as well as epigenetic changes, may be the key mechanisms through which the perinatal environment determines susceptibility to intestinal inflammatory disorders [20]. Scientific discussions about epigenetic remedies that are used for inflammatory skin disorders still maintain up-to-date [21]. Therefore, it seems reasonable to consider a similar scientific discussion for CD, which exhibits a strong inflammatory process. RTM has ameliorated 2 cases with CD completely without any side effect, and any relapse has not been detected after a period of 5 and 3 year-follow-up for each case respectively. These results may likely be related to the effects of RTM on epigenetic modification.

Conclusion

As a conclusion, the RTM therapeutics were well tolerated by both patients with CD, and no side effects were observed. Clinically, the recovery of patients' health in a short period, and effective treatment without any side effects gave us new hopes for CD in the future.

Identification of epigenetically regulated genes related to CD may be promising in order to develop epigenetic drugs for disease management. However, further functional studies might be required to determine epigenetically regulated genes in CD.

Declaration of Interest

The author declares no conflicts of interest.

References

- [1] Kagnoff MF. Celiac disease: pathogenesis of a model immunogenetic disease. *J Clin Invest* 2007;117(1):41-9.
- [2] Bascuñán-Gamboa KA, Araya-Quezada M, Pérez-Bravo F. MicroRNAs: an epigenetic tool to study celiac disease. *Rev Esp Enferm Dig* 2014;106(5):325-33.
- [3] Kocsis D, Béres N, Veres G, Szabó D, Müller KE, Arató A, et al. Genetic and epigenetic aspects of celiac disease. *Orv Hetil* 2014;155(3):83-8.
- [4] Serena G, Yan S, Camhi S, Patel S, Lima RS, Sapone A, et al. Proinflammatory cytokine interferon- γ and microbiome-derived metabolites dictate epigenetic switch between forkhead box protein 3 isoforms in coeliac disease. *Clin Exp Immunol* 2017;187(3):490-506.
- [5] Hassan K, A-Kader H. Celiac disease: the search for adjunctive or alternative therapies. *Expert Rev Gastroenterol Hepatol* 2014;8(3):313-21.
- [6] Alhassan E, Yadav A, Kelly CP, Mukherjee R. Novel nondietary therapies for celiac disease. *Cell Mol Gastroenterol Hepatol* 2019; 8(3):335-45.
- [7] Zevallos VF, Herencia LI, Chang F, Donnelly S, Ellis HJ, Ciclitira PJ. Gastrointestinal effects of eating quinoa (*Chenopodium quinoa* Willd.) in celiac patients. *Am J Gastroenterol* 2014;109(2):270-8.
- [8] Ohlsen BA. Acupuncture and a gluten-free diet relieve urticaria and eczema in a case of undiagnosed dermatitis herpetiformis and atypical or extraintestinal celiac disease: a case report. *J Chiropr Med* 2011;10(4):294-300.
- [9] Bascuñán-Gamboa KA, Araya-Quezada M, Pérez-Bravo F. MicroRNAs: an epigenetic tool to study celiac disease. *Rev Esp Enferm Dig* 2014; 106(5):325-33.
- [10] Skinner MK. Role of epigenetics in developmental biology and transgenerational inheritance. *Birth Defects Res C Embryo Today* 2011; 93(1):51-5.
- [11] Sharma A. Systems genomics analysis centered on epigenetic inheritance supports development of a unified theory of biology. *J Exp Biol* 2015; 218(Pt 21):3368-73.
- [12] Holliday R. Epigenetics: A historical overview. *Epigenetics* 2006; 1(2):76-80.
- [13] Yasar M. The therapy protocol remember regeneration therapy method: an overview of new to approach diseases. *J Complement Med Res* 2019; 10(1):68-80.
- [14] Chartrand LJ, Seidman EG. Celiac disease is a life-long disorder. *Clin Invest Med* 1996; 19:357-61.
- [15] ID Hill. What are the sensitivity and specificity of serologic tests for celiac disease? do sensitivity and specificity vary in different populations? *Gastroenterology* 2005;128(4 Suppl 1):25-32.
- [16] Chartrand LJ, Agulnik J, Vanounou T, Russo PA, Baehler P, Seidman EG. Effectiveness of anti gliadin antibodies as a screening test for celiac disease in children. *CMAJ* 1997;157(5):527-33.
- [17] Thakur VS, Deb G, Babcook MA, Gupta S. Plant phytochemicals as epigenetic modulators: role in cancer chemoprevention. *AAPS J* 2014;16(1):151-63.
- [18] Kirk H, Cefalu WT, Ribnicky D, Liu Z, Eilertsen KJ. Botanicals as epigenetic modulators for mechanisms contributing to development of metabolic syndrome. *Metabolism* 2008;57(7 Suppl 1):16-23.
- [19] Ray G, Longworth MS. Epigenetics, DNA organization, and inflammatory bowel disease. *Inflamm Bowel Dis* 2019;25(2):235-47.

- [20] Ley D, Desseyn JL, Mischke M, Knol J, Turck D, Gottrand F. Early-life origin of intestinal inflammatory disorders. *Nutr Rev* 2017;75(3):175-87.
- [21] Vanden Berghe W, Haegeman G. Epigenetic remedies by dietary phytochemicals against inflammatory skin disorders: myth or reality? *Curr Drug Metab* 2010;11(5):436-50.