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Correlations of 25-hydroxyvitamin D3 level in patients with ulcerative colitis with inflammation level, immunity and disease activity

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Abstract. – OBJECTIVE: To investigate the correlations between 25-hydroxyvitamin D3 (25-OHD3) level in patients with ulcerative colitis (UC) and inflammation level, immunity, disease activity.

PATIENTS AND METHODS: The serum level of 25-OHD3, inflammation status, immunity level and disease activity in patients (n=122) with UC in our hospital from 2015 to October 2017 were evaluated and analyzed.

RESULTS: The levels of inflammatory factors [C-reactive protein (CRP) and tumor necrosis factor-α (TNF-α)] in low 25-OHD3 group were higher than those in non-low 25-OHD3 group (p<0.01 and p<0.05), and both expressions of CRP and TNF-α in patients presented linearly negative correlations with the level of 25-OHD3 (r^2=0.8351, r^2=0.7298). There were no significant differences in the levels of immunoglobulin G (IgG) and complement C3 in low 25-OHD3 group compared with those in non-low 25-OHD3 group (p>0.05). There was an overall decreasing trend of 25-OHD3 level as disease activity increased, and there were statistically significant differences in the levels of 25-OHD3 in each group in remission period and mild, moderate and severe activity periods. The disease activity score of patients showed a linearly negative correlation with the level of 25-OHD3 (r^2=0.8465). The level of 25-OHD3 in the observation group (treated with mesalazine combined with vitamin D) was increased with the time of medication, and the level was higher than that in the control group (treated with mesalazine only). CRP, TNF-α, and disease activity score in the observation group were decreased with the time of medication, and the level was lower than that in the control group.

CONCLUSIONS: The level of 25-OHD3 in UC patients is linearly correlated with the level of inflammation and disease activity. At the same time, combined treatment with vitamin D improves the reducing level of inflammation and limits the disease activity. Therefore, 25-OHD3 can be used in the assessment of the level of inflammation and disease activity, and as a potential tool in the treatment.

Key Words

Ulcerative colitis, 25-OHD3, Inflammation, Immunity, Disease activity.

Introduction

Ulcerative colitis (UC) is a kind of inflammatory bowel disease (IBD), and its lesion occurs around the whole colon[1]. The possible pathogenesis is now considered to be associated with inflammation and immune disorders[2-5]. The major clinical manifestations of UC are hematochezia, abdominal pain, increased frequency of defecation, etc. The treatment is mainly definitive therapy because of its unclear pathogenesis, including the alleviation of symptoms and discomfort of the patient, the maintenance of a remission state. However, so far there has been no effective treatment regimen yet[6-8]. C-reactive protein (CRP) represents a type of protein produced under the stress of the body. As a non-specific inflammatory marker, it facilitates the protection against external invasion and cleans up the "garbage" generated in the body in order to protect it[9]. The main function of vitamin D is to regulate calcium-phosphorus metabolism. In addition, studies[10-12] have found that it is associated with immunoregulation and participates in the occurrence and development of a variety of IBDs. Although vitamin D

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was involved in the development of UC, there are no detailed reports on the specific correlation. This study aimed to elucidate the relationship between vitamin D and UC, and it provided another choice for the diagnosis and treatment of UC.

Patients and Methods

Patients

The serum level of 25-OHD3, inflammation level, immunity level and disease activity in patients (n=122) with UC in our hospital from 2015 to October 2017 were detected, among which there were 78 men and 54 women with an average age of (43.6±10.77) years old.

Testing Methods

25-OHD3 was detected by electrochemiluminescence, and 25-OHD3 < 20 ng/mL was treated as low 25-OHD3. TNF-α was detected by enzyme-linked immunosorbent assay (ELISA) and immunological transmission turbidimetry was used to detect CRP, IgG, and complement C3.

Assessment of Disease Activities

Mayo scoring system was used to evaluate the activity of UC (evaluation items: endoscopy, defecating frequency, hematochezia, and physician evaluation). Score ≤ 2 points: clinical remission, 3-5 points: mild activity, 6-10 points: moderate activity, and 11-12 points: severe activity.

Grouping and Treatment

Patients with low 25-OHD3 were randomly divided into the control group (n=39, treated with mesalazine only) and the observation group (n=38, treated with mesalazine combined with vitamin D). Mesalazine Enteric-coated Tablets were orally taken for 4 times a day (1 g each time), and vitamin D twice a day, 400 units each time (1 pill).

Statistical Analysis

Statistical Product and Service Solutions (SPSS) 19.0 software (IBM Corp. Released 2010. IBM SPSS Statistics for Windows, Armonk, NY, USA) was used to process the data, and they were represented as mean ± standard deviation. p<0.05 suggested that the difference in comparison was statistically significant.

Results

Correlation Between the 25-OHD3 Level and the Inflammation Level

The levels of inflammatory factors (CRP and TNF-α) in low 25-OHD3 group were higher than those in non-low 25-OHD3 group (p<0.01 and p<0.05) (Table I).

Correlation Between the 25-OHD3 Level and the Immune Level in UC Patients

There were no significant differences in the levels of IgG and complement C3 between low 25-OHD3 group and non-low 25-OHD3 group (p>0.05) (Table II).

Correlation Between the 25-OHD3 Level and Disease Activity in UC Patients

The 25-OHD3 level was increased as disease activity was reduced. There were significant differences of 25-OHD3 level in each group in remission period and mild, medium, and severe activity periods (Table III).

Table I. Correlation between the 25-OHD3 level and the inflammation level.

Inflammatory factor	Low 25-OHD3 group (n=77)	Non-low 25-OHD3 group (n=45)
CRP (μg/mL)	10.12±3.28	3.46±1.02*
TNF-α (μg/mL)	4.15±1.56	2.12±0.33#

Note: *: p<0.01, #: p<0.05

Table II. Correlation between the 25-OHD3 level and the immune level in UC patients.

Immune factor	Low 25-OHD3 group (n=77)	Non-low 25-OHD3 group (n=45)
IgG (mg/mL)	14.82±4.32	12.75±3.79[a]
Complement C3 (mg/mL)	1.21±0.32	1.91±0.29[a]

Note: [a]: p>0.05

Table III. Correlation between the 25-OHD3 level and disease activity in UC patients.

Disease activity	The level of 25-OHD3 (ng/mL)
Remission period	25.49±8.02
Mild activity period	17.23±7.96[b]
Moderate activity period	14.52±6.77[b,c1]
Severe activity period	7.68±3.01[b,c2,d]

Note: [b]: Compared with the remission period, $p<0.01$. [c1]: Compared with mild activity period, $p<0.01$. [c2]: Compared with medium activity period, $p<0.01$. [d]: Compared with severe activity period, $p<0.01$.

Correlation Analyses of the 25-OHD3 Level With the Levels of Inflammatory Factors (CRP and TNF-Ð)

The expressions of CRP and TNF-α in patients were linearly negatively correlated with the 25-OHD3 level (r^2=0.8351, r^2=0.7298) (Figures 1, 2).

Correlation Analysis Between the 25-OHD3 Level and the Disease Activity Score in Patients with UC

The disease activity score of patients was also linearly negatively related with the 25-OHD3 level (r^2=0.8465) (Figure 3).

Changes of 25-OHD, CRP, TNF-α, and Disease Activity Score With Time After Treatment in the Observation Group and the Control Group

The level of 25-OHD3 in the observation group was increased with the time of medication and was higher than that in the control group. CRP, TNF-α, and disease activity score in the observation group was decreased with the time of medication and was lower than that in the control group (Figures 4-7).

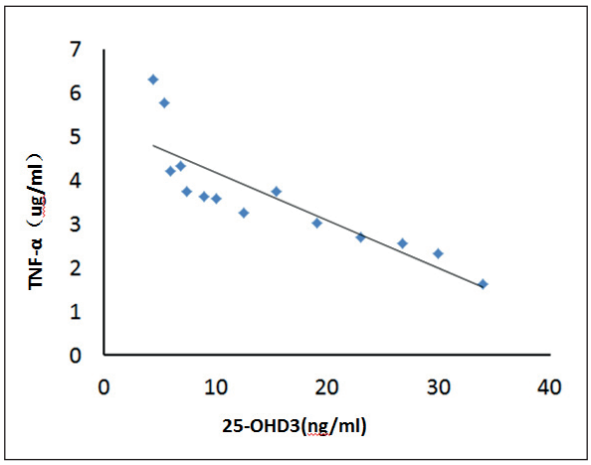

Figure 2. Correlation analysis between the 25-OHD3 level and the level of inflammatory factor TNF-α. r^2 = 0.7298.

Discussion

Vitamin D is a kind of steroid derivative that is absorbed mainly through the intestinal tract. Since UC appears in the whole colon, it may affect the absorption of vitamin D, causing vitamin D deficien-

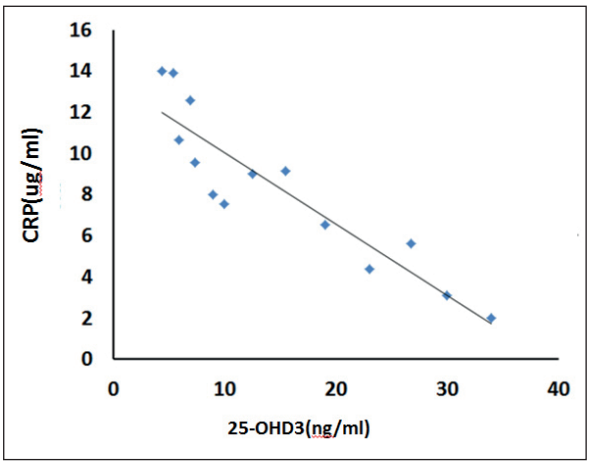

Figure 1. Correlation analysis between the 25-OHD3 level and the level of inflammatory factor CRP. r^2 = 0.8351.

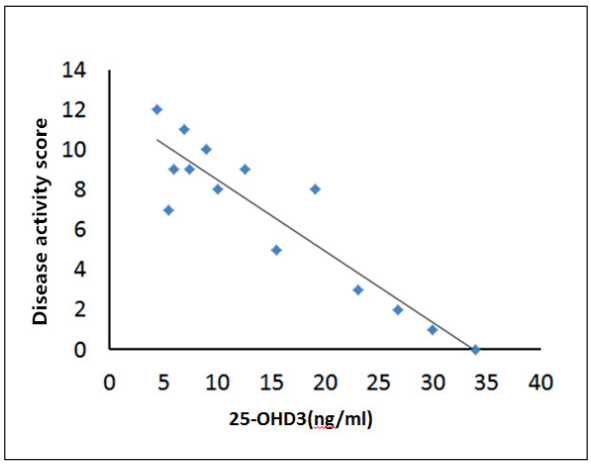

Figure 3. Correlation analysis between the 25-OHD3 level and the disease activity score in patients with UC r^2 = 0.8465.

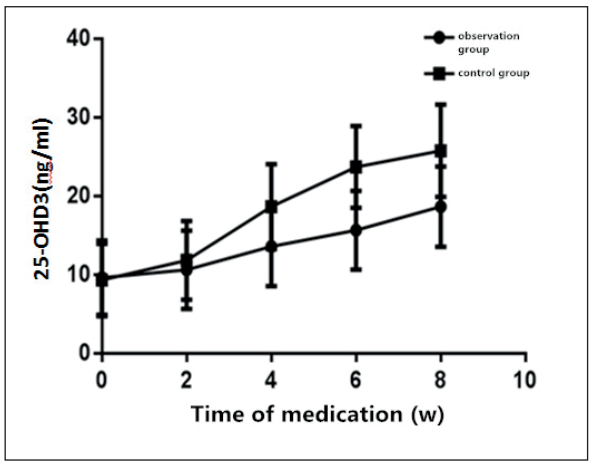

Figure 4. Changes of 25-OHD with time after treatment in the observation group and the control group.

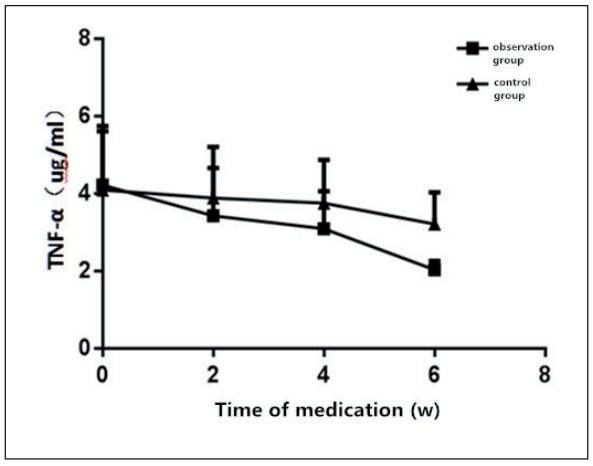

Figure 6. Changes of TNF-α with time after treatment in the observation group and the control group.

cy[13-15]. UC represents an immune related disease, and its occurrence and development are closely related to inflammation and immunity. Vitamin D has been confirmed[15-17] to be associated with the immune development of a variety of diseases, including rheumatoid disease, diabetes, cancer, and so on. Studies have also found that more than half of the UC patients are low in vitamin D. Therefore, we investigated the correlations of vitamin D with factors including inflammation level, immune level, and disease activity in UC patients, in order to further determine the correlation between vitamin D and UC. At the same time, curative effects between vitamin D combined with mesalazine therapy and mesalazine therapy alone were compared, so as to investigate whether vitamin D supplements can promote the treatment and remission of UC[18,19]. In this study, the levels of inflammatory factors (CRP and TNF-α) in low 25-OHD3 group were higher than those in non-low 25-OHD3 group ($p<0.01$ and $p<0.05$), and the expressions of CRP and TNF-α in patients showed linearly negative correlations with the level of 25-OHD3 ($r^2=0.8351$, $r^2=0.7298$). CRP is a nonspecific inflammatory marker, while TNF-α is an inflammatory mediator. Their levels are both associated with 25-OHD, the correlations of which were linearly negative. Therefore, 25-OHD3 can be used as an indicator to predict the UC inflammation level. There were no significant differences of IgG and complement C3 levels between non-low and low 25-OHD3 groups ($p>0.05$). The levels of IgG and complement C3 were both correlated with the immune condition. There were no correlations of the two with 25-OHD3 in UC patients. There was an

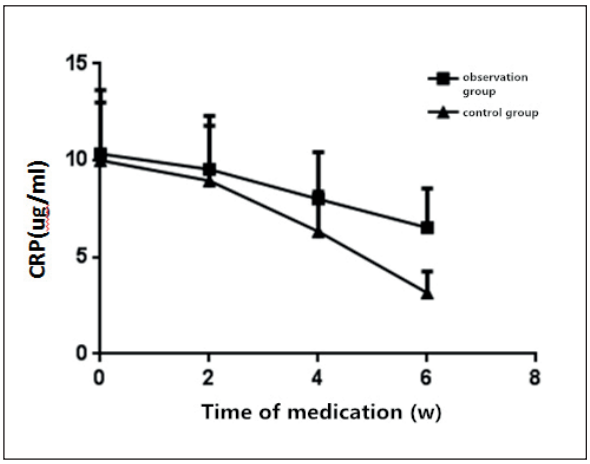

Figure 5. Changes of CRP with time after treatment in the observation group and the control group.

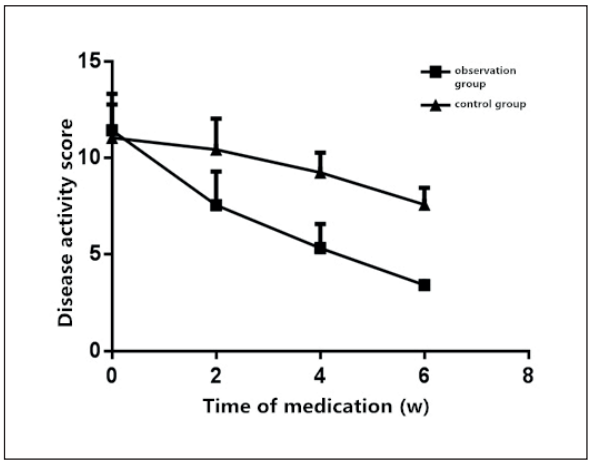

Figure 7. Changes of disease activity score with time after treatment in the observation group and the control group.

overall decreasing trend in the level of 25-OHD3, while the disease activity was elevated. Of note, we found that the disease activity score of patients had a linearly negative correlation with the level of 25-OHD3 (r^2=0.8465). The results show that 25-OHD3 is closely related to the disease activity of UC patients, which can be used as an indicator for predicting the disease activity. We propose the possible mechanism of the severe intestinal lesions of patients in disease activity period, which markedly affect the vitamin D absorption, leading to the decreasing level of vitamin D. Our data on the levels of 25-OHD3, CRP, TNF-α, and disease activity score in the observation group suggest that vitamin D can be used to evaluate the condition of the disease and favor the treatment of UC to reduce the level of inflammation.

Conclusions

The level of 25-OHD3 in UC patients is linearly correlated with the levels of inflammation and disease activity. At the same time, the combination treatment involving vitamin D significantly reduces the levels of inflammation and restricts the disease activity, which provides the academic basis for the future diagnosis and therapy.

Conflict of Interests:

The Authors declare that they have no conflict of interests.

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