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ARAŞTIRMA / RESEARCH

Upper gastrointestinal endoscopy findings of patients with B12 deficiency

B12 vitamin eksikliği olan hastalarda üst gastrointestinal endoskopi bulguları

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Abstract

Purpose: Vitamin B12 deficiency is highly prevalent. It may be caused by malabsorption or low intake and may trigger macrocytic anemia, neuropsychiatric and clinical symptoms. We aimed to detect the endoscopic evidence for vitamin B12 deficiency in the patients who referred to our clinic.

Material and Methods: We retrospectively scanned the patients referred to Celal Bayar University, Faculty of Medicine, Department of Gastroenterology for vitamin B12 deficiency and underwent upper gastrointestinal endoscopy for this reason from May 2014 to May 2016. We examined all other reasons that might cause vitamin B12 deficiency for all patients and excluded those with other pathologies or receiving medication.

Results: The patients' mean age was 48.13 and 56.7% of them were female. The control group had a mean age of 48.6. The control group had a mean age of 48.6. Of the patients with vitamin B12 deficiency, 24.3% had no pathology in the stomach or duodenum, while 86.4% presented no pathology in the duodenum. Thirty-four percent of the control group had no pathology in the stomach or duodenum. Eighty-two percent of the cases presented normal duodenal endoscopy findings.

Conclusion: Vitamin B12 deficiency is a highly prevalent pathology that may lead to a series of clinical symptoms including neuropsychiatric and hematological symptoms. Treatment provides a notably positive response, and its etiology is important for treatment. The present study found no significant difference between the age- and gender-relevant control group and the patient group in terms of gastritis and duodenal pathologies.

Key words: B12 vitamin, cobalamin, endoscopy.

Öz

Amaç: B12 vitamin eksikliği sık gözlenir. Emilim ya da alım azlığı nedeniyle oluşabilir. Makrositer anemi, nöropsikiyatrik bulgular ile kilinik bulgular verebilir. Polikliniğimize başvuran hastalarda B12 vitamin eksikliğinde endoskopi bulgularını saptamak istedik.

Gereç ve Yöntem: 2014 Mayıs ve 2016 Mayıs ayları arasında Celal Bayar Üniversitesi Tıp Fakültesi Gastroenteroloji Bilim Dalı'na B12 vitamin eksikliği nedeniyle yönlendirilen ve bu nedenle üst gastrointestinal sistem endoskopisi uygulanan hastalar retrospektif olarak tarandı. Tüm hastalarda B12 vitamin eksikliğine neden olabilecek diğer sebepler gözden geçirildi ve ek patolojileri saptanan ya da ilaç kullanımı olan hastalar çalışma dışı bırakıldı.

Bulgular: Hastaların yaş ortalaması 48.13 olarak saptandı. 56.7%' si kadındı. Kontrol grubunun yaş ortalaması 48.6 olarak saptandı. Kontrol grubunun yaş ortalaması 48.6 olarak saptandı. B12 vitamin eksikliği hastalarının 24.3%' ünde hem mide hem de duodenumda patoloji saptanmaz iken, 86.4%' ünde duodenumda patoloji saptanmamıştır. Kontrol grubunun 34%' ünde hem mide hem de duodenumda patoloji saptanmamıştır. Olguların 82%' inde duodenum endoskopi bulguları olağan bulunmuştur.

Sonuç: B12 vitamin eksikliği toplumda sık görülen, nöropsikiyatrik ve hematolojik bulgular gibi klinik semptomlara neden olabilen bir patolojidir. Tedavi ile belirgin cevap alınır ve etiyolojisi tedavi açısından önemlidir. Çalışmamızda yaş-cinsiyet uyumlu kontrol grubu ile karşılaştırılan hasta grubunda gastrit ve duodenal patolojiler açısından anlamlı bir farklılık saptanmamıştır.

Anahtar kelimeler: B12 vitamini, kobalamin, endoskopi.

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INTRODUCTION

Vitamin B12 deficiency was first defined in 1948 and then immediately shown to play a role in the development of pernicious anemia. The high prevalence of vitamin B12 deficiency, also known as cobalamin, has lead to an increasing number of studies in this field. Later, this deficiency was demonstrated as a prevalent cause of macrocytic anemia and found to be associated with a group of neuropsychiatric disorders.

Low intake or a disorder through the chain of absorption may trigger vitamin B12 deficiency. Vitamin B12 is absorbed in two significant ways. The passive absorption takes place directly through the jejunum and ileum. However, an intrinsic gastric factor is required for the active absorption mechanism. The physiological amount of vitamin B12 in food is absorbed in this way. The vitamin B12 in food disengages during the gastric digestion. It forms a stable complex with the gastric protein R. That complex is digested in the duodenum, and the vitamin B12 disengages again. Free vitamin B12 then binds to the intrinsic factor released in combination with HCL from glycoprotein and parietal cells. When the B12-IF complex (the cubam complex) arrives at the distal ileum, it binds to the specific receptors on the surface of the mucosa and gets absorbed by them[1,2].

The presence of chronic autoimmune gastritis and helicobacter pylori (HP) are two contemporary debates and subjects of research, causing the absorption disorder[3]. Patients develop malabsorption due to the chronic autoimmune gastritis, also known as type-A atrophic gastritis. Consequently, it leads to a deficiency of vitamins and essential elements[4]. In the literature, in our region there is not enough data about gastrointestinal pathologies in the vitamin B12 deficiency. Therefore, we decided to examine the prevalence of pathologies in the upper gastrointestinal endoscopy among the patients referred to our clinic due to a vitamin B12 deficiency and find out whether it was necessary to carry out an endoscopy for all patients with vitamin B12 deficiency in our region. In conclusion; if we detected the endoscopy should not be performed to the all patients, we can avoid unnecessary medical costs and time loss. In case of requirement of endoscopy, we think that the endoscopic approach for these patients become more important.

MATERIAL AND METHODS

Patients

Celal Bayar University, Department of Gastroenterology provides health services, primarily in city of Manisa and its counties. Also, due to the proximity of the location; a significant amount of patients are come from the İzmir, Aydın and Balikesir regions. Medical history of the patients, their laboratory findings and imaging records are recorded by Probel software system. Probel software system is used for 4 years. We retrospectively scanned the patients referred to Celal Bayar University, Faculty of Medicine, Department of Gastroenterology for vitamin B12 deficiency and underwent upper gastrointestinal endoscopy for this reason from May 2014 to May 2016.

We scan 1712 patient's endoscopy results. 52 patients had vitamin B12 deficiency. In all patients, other reasons that may cause vitamin B12 deficiency were reviewed (low intake of protein or food of animal origin, pancreatic insufficiency, vegetarian diet, small bowel resection, Chron, and history of gastrectomy). We excluded the patients with a history that might lead to vitamin B12 deficiency, additional pathologies, diet and/or drug intake (proton-pump inhibitors, H2 receptor antagonists). The patients who excluded from the study; 3 patients had a history of gastrectomy, 6 patients Chron Disease, 6 patients were using proton-pump inhibitors. The control group included the patients who underwent an endoscopy due to a family history of stomach cancer or who received an endoscopy by their own will despite the absence of a relevant medical history. The study was approved by the local ethics committee. The ethics committee's approval was granted from Celal Bayar University, Medical School, local ethics committee on June 29, 2016 with no. 20478486-259.

Examination

The endoscopy procedures included in the study were performed by Assoc. Prof. Elmas Kasap who educated with 4 years of internal medicine and 3 years of Gastroenterology. We examined all other reasons that might lead to vitamin B12 deficiency for all patients and excluded those with other pathologies, comorbidities, or receiving medication. All endoscopy findings were reviewed from the reports.

Identification

Vitamin B12 levels of the patients were scanned retrospectively from Probel System. In our hospital vitamin B12 levels are working with Access Immunoassay system. The blood samples of patients are studied immediately. The interval of 126-505 pg/ml was assumed to indicate normal B12 levels for the patients. Values less than 126 pg/ml were considered pathological for the vitamin B12 deficiency.

Statistical analysis

We analyzed the data for groups with the SPSS (Statistical Package for the Social Sciences) Statistics 21.0 software. After statistical analyses, $p \leq 0.05$ was considered to indicate statistical significance. After statistical analyses, $p \leq 0.05$ was considered to indicate statistical significance. Between vitamin B12 deficiency and control group, we compared these data: gender, age, endoscopic findings (Pangastritis, antral gastritis, intestinal metaplasia, atrophic gastritis, gastric cancer and duodenum pathological findings) and HP.

RESULTS

We included 37 patients based on their endoscopy reports; the patients were referred due to the vitamin B12 deficiency and they had no associated comorbidity and/or drug intake. The control group included 44 patients who underwent an endoscopy due to a family history of stomach cancer or who received an endoscopy by their own will despite the absence of a medical history. The patients with vitamin B12 deficiency had a mean age of 48.1 years. The control group had a mean age of 48.6 years. No statistically significant difference was observed between the two groups in terms of mean age ($p=0.86$). 56.7% (n=21) of the patients with vitamin B12 deficiency were female. 54.5% (n=24) of the patients within the control group were female. No statistically significant difference was observed between the two groups ($p=0.51$) (Table 1).

Of the patients with vitamin B12 deficiency, 9 patients (24.3%) had no pathology in the stomach or duodenum, while 32 (86.4%) presented no pathology in the duodenum. Thirty-four percent (n=15) of the control group had no pathology in the stomach or duodenum. Eighty-two percent of the cases presented normal duodenal endoscopy findings. We compared the patients without an endoscopic finding in both groups and found no statistically significant difference between them ($p=0.43$). Also, there was no significant difference between the cases with symptoms in the duodenum in both groups ($p=0.64$). Of the 28 vitamin B12 deficiency patients with at least one symptom in the stomach or duodenum, 53.8% (n=15) were female. In the control group, 52% (n=15) of the 29 vitamin B12 deficiency patients with at least one symptom in the stomach or duodenum were female.

29.7% (n=11) of the patients had pangastritis, and 63.6% (n=7) of them were female. Four pangastritis patients had duodenitis, and one had Forrest III duodenal ulcer. We detected pangastritis in 14% (n=6) of the control group, 34% (n=2) of whom were female. Two patients had duodenitis as a comorbidity. No statistically significant difference was observed between the two groups in terms of the prevalence of pangastritis ($p=0.67$).

35.1% of the patients with vitamin B12 deficiency presented antral gastritis. 53.8% (n=7) of them were female. The patients with antral gastritis had no accompanying duodenal pathology. 43.1% (n=19) of the control group had antral gastritis. Fifty-eight percent (n=11) of them were female. Within the control group, five of the antral gastritis patients had duodenitis and one had duodenal ulcer. No statistically significant difference was observed between the two groups in terms of antral gastritis rates ($p=0.93$).

Of the patients with vitamin B12 deficiency, 3 had intestinal metaplasia (IM) and atrophic gastritis (AG), while 1 patient had stomach cancer. Those patients had no accompanying duodenal pathology. Four patients within the control group had IM and AG as comorbidities (Table 2).

As regards the HP in both groups, 22% (n=8) of the patients with vitamin B12 deficiency and 27.2% (n=12) of the control group were HP positive. There was no significant difference between the two groups ($p=0.37$) (Table 1).

Table 1. Baseline patient characteristics

Variable	B12 deficient (n = 37)	Controls (n = 44)	P-value
Age (yr)	48.1	48.6	0.89
Gender (M:F)	16:21	20:24	0.51
H pylori infection (+/-)	8:29	12:32	0.37

Table 2. Endoscopy findings

	B12 deficient (%)	Controls (%)	P-value
Normal	24.3	34	0.43
Duodenum pathological findings	13	18	0.64
Pangastritis	29.7	14	0.67
Antral Gastritis	35.1	43.1	0.93
Others*	11	9	

* Intestinal metaplasia, atrophic gastritis, gastric cancer

DISCUSSION

The importance of vitamin B12 was first demonstrated in 1984 as part of the pernicious anemia treatment, and it has since been subject to research in a variety of contexts including neuropsychiatric and hematological diseases with an established significance. Prevalence of vitamin B12 deficiency is 3% in patients aged 20 to 39 years. Vitamin B12 deficiency increases with age. In developing countries, deficiency is much more common, starting in early life [5,6]. The average age of our patients with vitamin B12 deficiency is 48.1. Inadequate intake and malabsorption are the two most prevalent causes of this deficiency. Identification of its absorption mechanism is important in revealing the etiology of vitamin B12 deficiency[1]. When examining the causes of vitamin B12 deficiency, in the recent studies inadequate intake was not as high as expected. Andres et al. showed that among 172 elderly patients with vitamin B12 deficiency, only 2% accounted for inadequate intake[7]. This data increases the importance of malabsorption.

In this context, pangastritis and corpus gastritis, generally observed with the involvement of the parietal region, are associated with the malabsorption[8]. Autoimmune gastritis frequently accompanies the gastritis cases progressing with parietal cell involvement. Acid secretion decreases in the stomach. Those patients frequently exhibit antibodies against parietal cells and the intrinsic factor in the serum. The cases of gastritis with antral involvement display a low number of autoimmune components, normal acid secretion, and high HP[9,10].

Dholakia et al. studied old patients with vitamin B12 deficiency and reported that patients with normal endoscopic evidence exhibited the same characteristics with the control group. Although the patients with vitamin B12 deficiency had a lower rate of gastritis than the control group, they had a notably high level of gastric atrophy[11].

The present study detected pangastritis in 29.7% of the patients with vitamin B12 deficiency. This rate was 14% for the control group. Comparing both groups, the high rate of pangastritis in the vitamin B12 deficiency might be associated with the involvement of parietal cells and reduced release of the intrinsic factor. However, this difference was not statistically significant. The present study detected antral gastritis in 35.1% of the patients with vitamin B12 deficiency, which was observed in 43.1% of the control group. Yet no statistically significant difference was observed between the two groups in terms of antral gastritis rates.

Of the patients with vitamin B12 deficiency, 3 had IM and AG, while 1 patient had stomach cancer. Moreover, four patients within the control group had IM and AG as comorbidities. Nevertheless, no statistically significant difference was observed between the two groups in terms of IM and AG presence.The HP has been demonstrated to be related to duodenal ulcer and atrophic gastritis, which accompany hypochlorhydria and cause B12 malabsorption. This leads us to question a possible relationship between the HP and vitamin B12 deficiency. A study by Sarari et al. supports this

relationship. They detected HP-positive gastritis in 71.7% of the patients, and 67.4% of them had pernicious anemia[3]. Kaplan et al. administered HP eradication treatment to 77 HP-positive pernicious anemia patients. Thirty-one patients returned back to normal B12 levels. This constitutes an evidence for the relationship between the vitamin B12 deficiency and HP[12]. A literature review by Perez-Perez found, contrary to what was expected, that HP positivity was significantly higher in the age- and gender-relevant control group in the context of the vitamin B12 deficiency ($p<0.0001$)[9]. Similarly, a prospective study by Fong et al. reported HP positivity in 3 (11%) of 28 patients with pernicious anemia, while 20 (71%) of 28 patients within the age- and gender-relevant control group were HP-positive[13]. As regards the HP in both groups, 22% of the patients with vitamin B12 deficiency and 27.2% of the control group were HP positive. No statistically significant difference was observed between the two groups ($p=0.37$).

The present study found normal endoscopic findings of the duodenum in 86.4% of the patients with vitamin B12 deficiency and 82% of the control group. Unless the endoscopic evidence for vitamin B12 deficiency implies celiac disease such as other accompanying vitamin deficiencies, we do not see the duodenal biopsy as essential. The present study found no significant difference between the age- and gender-relevant control group and the patient group in terms of HP, gastritis or duodenal pathologies. Further studies with greater sample sizes may reveal different results.

Vitamin B12 deficiency is a highly prevalent pathology that may lead to a series of clinical symptoms including neuropsychiatric and hematological symptoms. Treatment provides a notably positive response, and its etiology is important for treatment. The present study found no significant difference between the age- and gender-relevant control group and the patient group in terms of HP or duodenal pathologies. Unless the endoscopic evidence for vitamin B12 deficiency implies celiac disease such as other accompanying vitamin deficiencies, we do not see the duodenal biopsy as essential. Although gastritis is more prevalent in patients with vitamin B12 deficiency, this high prevalence is not of statistical significance. Further studies with greater sample sizes may reveal different results.

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