

Effects of vitamin B12 on olfactory functions

Running title: Olfaction, Vitamin B12

Ahmet Baki^{1*}, Selçuk Gündoğar²

¹Başakşehir Çam and Sakura City Hospital, Department of otorhinolaryngology, İstanbul/Turkey

²Uskudar State Hospital, Department of internal medicine

*Corresponding Author: Ahmet Baki, Başakşehir Çam and Sakura City Hospital, Department of otorhinolaryngology, İstanbul/Turkey.

Received date: December 09, 2021: Accepted date: January 20, 2022: Published date: January 28, 2023

Citation: Ahmet Baki, Selçuk Gündoğar. (2023). Effects of vitamin B12 on olfactory functions. *Journal of Clinical Otorhinolaryngology* 5(1); DOI: 10.31579/2692-9562/061

Copyright: © 2023, Ahmet Baki. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Abstract

Objective: To evaluate the effects of vitamin B12 on olfactory functions.

Materials and Methods: The smell scores of 48 patients with vitamin B12 deficiency were compared before and after the treatment. The patients followed in the internal medicine were referred to the otolaryngology for the smell test. Smell test was done to the patients before the treatment. After three month of treatment, patients whose vitamin B12 levels reached normal limits were given a smell test.

Results: There were 28 female and 20 male patients in the study. The ages of the patients participating in the study ranged from 24 to 45, and the mean age was 33.9±5.4 years. While the threshold, identification, and total score values of the patients were 2,45±0,5, 3,52±0,5, and 2,98±0,34, respectively, after treatment, 4,7±0,94, 5,32±0,7, and 5,02±0,66. A statistically significant difference was found in the comparison of scores before and after treatment. (p=0.001)

Conclusion: Vitamin B12 treatment provides an improvement in olfactory functions.

Keywords: Vitamin B12; smell test; olfactory function

Introduction

Olfaction plays an important role in our daily lives, and olfactory dysfunction causes a significant decrease in the quality of life. Approximately 20% of the general population complains about olfactory dysfunction, and 5% of these individuals are anosmic [1]. Psychophysical and electrophysiological tests are often used to evaluate olfaction function. Even though psychophysical tests are generally used for the clinical evaluation of people with smell dysfunction, electrophysiological tests are mostly used for further investigation [2]. The Connecticut Chemosensory Clinical Research Center (CCCRC) olfactory test evaluates the butanol threshold and smell identification [3]. It is validated for the analysis of smell capacity in the Turkish society [4]. It is easy to prepare, cheap, and simple to administer [4]. Because vitamin B12 is not produced in the body, it must be taken from the diet [5]. Vitamin B12 deficiency may be due to insufficient intake, as in vegetarians; however, malabsorption is an essential factor for deficiency [5]. The relation of

vitamin B12 deficiency to neurological symptoms has been shown for a long time [5]. Subacute combined degeneration of the spinal cord is the best manifestation of the neurological findings of vitamin B12 deficiency. The dorsal and lateral columns of the spinal cord are affected in this disease. In the case of vitamin B12 deficiency, neurological symptoms such as paresthesia, sensory ataxia, fatigue in the lower extremities, dementia, and optic atrophy can be seen. Rarely, extrapyramidal symptoms such as cerebellar ataxia, dystonia, and chorea may also be seen [6]. Previous studies showed that vitamin B12 deficiency might lead to deficiency in olfactory functions [7]. In this study, we aimed to analyze the olfactory function with the CCCRC olfactory test in individuals with isolated vitamin B12 insufficiency and to reveal the changes in the olfactory level after vitamin B12 replacement therapy.

Materials and Methods

This study included 48 patients with vitamin B12 insufficiency was conducted between June and December 2019. The participants were

selected from the internal medicine clinic on the basis of their vitamin B12 testing and then referred to the ENT clinic for olfactory testing. A detailed history was taken from all the patients, and a routine ear, nose, and throat examination was also performed. Patients with nasal septum deviation, acute or chronic rhinosinusitis, active upper respiratory tract infection, nasal polyposis, history of nasal surgery, allergic rhinitis, smoking, systemic diseases (e.g., diabetes mellitus, hypothyroidism, hypertension, chronic renal failure, and chronic liver failure), neurological diseases, <18 years of age, pregnancy, female menopause, and a history of head trauma were excluded. Participants using drugs (e.g., diuretics, calcium channel blockers, statins, angiotensin-converting enzyme inhibitors, antidepressants, and local or systemic steroids) that could affect olfactory function were also excluded. Participants' liver dysfunction, folate deficiency, hypothyroidism, hemolysis, myelodysplasia, antimetabolite drugs, etc. they had no such situation. Vitamin B12 levels, with values <197 ng/l considered as vitamin B12 insufficiency. Patients with neurological symptoms were given hydroxocobalamin 1 mg IM 3x/week for 2 weeks and then every 2 months for life. At the end of the first month, patients whose vitamin B12 levels reached the normal range were re-tested for smell. (Normal range is 197-771 ng/l) [8]. The olfactory test scores calculated before (pre-replacement group) and after vitamin B12 replacement (post-replacement group) were compared with each other. The study was approved by the local ethics committee (protocol number: 42, date: 17/04/2019). The patients provided written informed consent.

Smell assestant

The CCCRC test comprises of a butanol threshold and an identification as already reported [4]. It was administered pre- treatment and in the 12th week post-treatment.

Butanol threshold test

The participants were given two glass bottles of the same color and uniform view, one of which contained water and the other a dilute concentration of butanol during the test. They were then ordered to close one nostril and place the tip of the first bottle quickly below the other one. The second bottle was then sampled in a similar manner, and the participant had to select which of the bottles contained something other than water. If the selection was incorrect, a more potent concentration of

butanol was submitted along with the bottle having only water. Possible scores ranged from 0–9, but scores ≥7 were scored as 7 per the olfactory test protocol. For the final score, the average of both nostril scores was taken.

Identification test

Cinnamon, Vicks, chocolate, Turkish coffee, peanut butter, carbonate, soap, and baby powder were added to opaque bottles. The ability to sniff out Vicks showed unimpaired trigeminal nerve function, and all the subjects easily recognized it; therefore, it was not added to the final score. Possible scores ranged from 0 to 7. For the final score, the average of both nostril scores was taken.

Total score

Scores for the butanol threshold and identification tests were later averaged to reach a total score, which was classified as defined by Cain et al [9].

Statistics

Statistical Package for the Social Sciences 22 program was used for statistical analysis. The suitability of parameters to normal distribution was evaluated by Shapiro-Wilks test. Descriptive statistical methods (mean and standard deviation) were determined when evaluating the study data. Wilcoxon Signed Rank test was used to evaluate the dependent non-parametric data. One-way Analysis of variance test was used to compare the groups in terms of stages. P<0.05 was considered statistically significant.

Results

There were 28 female and 20 male patients in the study. The ages of the patients participating in the study ranged from 24 to 45, and the mean age was 33.9±5.4 years. While the threshold, identification, and total score values of the patients were 2,45±0,5, 3,52±0,5, and 2,98±0,34, respectively, after treatment, 4,7±0,94, 5,32±0,7, and 5,02±0,66. A statistically significant difference was found in the comparison of scores before and after treatment. (p=0.001). While before treatment B12 vitamin levels was 139,56±10,8 ng/L after treatment 548,3±29,2 ng/l.

	Pre-treatment			Post-treatment			p
	N	Min-Max	Mean±SD	N	Min-Max	Mean±SD	
Threshold score	48	2-3	2,45±0,5	48	3-6	4,7±0,94	0,001
Idetification score	48	3-4	3,52±0,5	48	4-6	5,32±0,7	
Total score	48	2,5-3,5	2,98±0,34	48	3,5-6	5,02±0,66	
Vitamin B12	48	120-165	139,56±10,8	48	500-599	548,3±29,2	
<i>Wilcoxon test, N:Patient number, Min:Minimum, Max:Maximum, SD:Standart deviation, p≤0.05</i>							

Table 1: Comparison of scores before and after treatment

Discussion

Olfactory dysfunction may occur because of conductive or sensorineural problems. Conductive dysfunction may occur because of nasal pathologies, whereas sensorineural dysfunction may develop owing to the olfactory receptor and subsequent central pathways [10]. This study reports that vitamin B12 insufficiency is associated with smell abnormality. Mean olfactory test scores are significantly increased in

people with vitamin B12 insufficiency after a vitamin B12 replacement protocol. The number of patients with anosmia and hyposmia decreased after vitamin B12 replacement therapy. Previous studies have shown that vitamin B12 deficiency affects the central and peripheral nervous system. The most common neurological disorder as a result of vitamin B12 deficiency is peripheral neuropathy. Also is, subacute combined degeneration well-known and common neurological disorder in vitamin B12 deficiency [11]. Acute chorea, cerebral ischemia, infratentorial and

supratentorial leukoencephalopathy are rare diseases that occur as a result of vitamin B12 deficiency [12]. It has been shown that olfactory functions improve after B12 deficiency treatment in a very few cases with olfactory dysfunction (13). Our study shows the positive effect of vitamin B12 treatment on olfactory functions. The pathophysiologic mechanisms of vitamin B12 deficiency in the nervous system are unclear. It is claimed to occur as a result of insufficient remethylation of homocysteine to methionine. The pathophysiological mechanisms of vitamin B12 deficiency in the nervous system are unclear. However, insufficient remethylation of homocysteine to methionine and excessive propionyl-CoA formation lead to degenerative conversion of methylmalonyl-coenzyme A (CoA) to succinyl-CoA, resulting in a decrease in the supply of methyl groups [14]. As a result of deteriorated fatty acids and a defect in the methylation of myelin basic protein, the myelin sheath, which is a component of the nervous system synthesis, deteriorates. In addition, increased plasma homocysteine concentrations can have a direct toxic effect on neurons [15]. Another study claimed that olfactory dysfunction was caused by vitamin B12 deficiency and high homocysteine levels leading to myelin damage in the olfactory nerve [16]. It has been shown that the olfactory threshold is positively correlated with the vitamin B12 level [16]. Chronic rhinosinusitis, infectious diseases and trauma are the most important causes of olfactory functions. Heaton et al reported that involvement of the nervous system in 40% of patients with vitamin B12 deficiency [17].

In addition to neurological, metabolic, and endocrinological diseases, toxic factors and drugs can cause deterioration in olfactory functions [18]. In our study, we performed a smell test on patients with vitamin B12 deficiency.

Conclusion

Vitamin B12 deficiency causes various neurological disorders as well as olfactory dysfunction. Vitamin B12 treatment provides improvement in olfactory functions. Further studies may be needed to add vitamin B12 therapy to the treatment protocol in patients with olfactory disorders.

Compliance with Ethical Standards:

Financial disclosure: There is no financial support.

Conflict of Interest: There is no conflict of interest in this article.

Ethical approval: All procedures performed in studies involving human participants were by the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study protocol was approved by the ethical research committee of the *Zeynep Kamil Women's and Children's Disease Training and Research Hospital* in Istanbul,

Informed consent: Routine informed consent was obtained from all patients before the hospitalization and also informed consent from the individuals of the control group was obtained in the study. There is no support source that requires confirmation.

References

- Mullol J, Alobid I, Mariño-Sánchez F, et al. (2012). Furthering the understanding of olfaction, prevalence of loss of smell and risk factors: a population-based survey (OLFACAT study). *BMJ Open*.

- Evren C, Yiğit VB, Çınar F. (2015). Subjective assessment of olfactory function. *Kulak Burun Bogaz İhtis Derg.* 25:59-64.
- Cain WS, Gent JF, Goodspeed RB, Leonard G. (1988). Evaluation of olfactory dysfunction in the connecticut chemosensory clinical research center. *Laryngoscope.* 98:83-88.
- Veyseller B, Ozucer B, Karaaltın AB, Yildirim Y, Degirmenci N, Aksoy F, Ozturan O. (2014). Connecticut (CCRC) olfactory test: normative values in 426 healthy volunteers. *Indian J Otolaryngol Head Neck Surg.* 66:31-34.
- Miller A, Korem M, Almog R, Galboiz Y. (2005). Vitamin B12, demyelination, remyelination and repair in multiple sclerosis. *J Neurol Sci.* 233:93-97.
- Shyambabu C, Sinha S, Taly AB, Vijayan J, Koor JM. (2008). Serum vitamin B12 deficiency and hyperhomocystinemia: a reversible cause of acute chorea, cerebellar ataxia in an adult with cerebral ischemia. *J Neurol Sci.* 273:152-154.
- Doty RL, Bromley SM, Panganiban WD. (2006). Olfactory function and dysfunction. In: Bailey BJ, Johnson JT, eds. *Head and Neck Surgery—Otolaryngology*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins. 289-305.
- (Dr Diana Krezelewski – GP, Laura Catt – Prescribing Interface Advisor, In consultation with Dr Moorby – Haematologist Sherwood Forest Hospital November 2018. Review November 2021 extended to March 2022).
- Cain WS, Gent JF, Goodspeed RB, Leonard G. (1988). Evaluation of olfactory dysfunction in the connecticut chemosensory clinical research center. *Laryngoscope.* 98:83-88.
- Veyseller B, Ozucer B, Degirmenci N, Gurbuz D, Tambas M, Altun M, Aksoy F, Ozturan O. (2014). Olfactory bulb volume and olfactory function after radiotherapy in patients with nasopharyngeal cancer. *Auris Nasus Larynx.* 41:436-40
- Reynolds E. (2006). Vitamin B12, folic acid, and the nervous system. *Lancet Neurol.* 5:949-960.
- Su S, Libman RB, Diamond A, Sharfstein S. (2000). Infratentorial and supratentorial leukoencephalopathy associated with vitamin B12 deficiency. *J Stroke Cerebrovasc Dis.* 9:136-138.
- Malkarnekar NA, Behere RV, Bhandary RP, Praharaj SK, Sharma PS. (2014). Olfactory perceptual abnormality associated with vitamin B12 deficiency. *Psychosomatics.* 55:310-311.
- Torsvik I, Ueland PM, Markestad T, Bjorke-Monsen AL. (2013). Cobalamin supplementation improves motor development and regurgitations in infants: Results from a randomized intervention study. *Am J Clin Nutr.* 98:1233-1240.
- Gupta PK, Garg RK, Gupta RK, et al. (2014). Diffusion tensor tractography and neuropsychological assessment in patients with vitamin B12 deficiency. *Neuroradiology.* 56:97-106.
- Serhan Derin, Sabri Koseoglu, Cem Sahin and Murat Sahan. (2016). Effect of vitamin B12 deficiency on olfactory function. *International Forum of Allergy & Rhinology, Vol.*
- Heaton EB, Savage DG, Brust JC, Garrett TJ, Lindenbaum J. (1991). Neurologic aspects of cobalamin deficiency. *Medicine (Baltimore).* 70:229-245.
- Huart C, Eloy P, Rombaux P. (2013). Olfaction. In: Onerci TM, ed. *Nasal Physiology and Pathophysiology of Nasal Disorders*. Berlin: Springer. 113-137.