ORIGINAL ARTICLE

DOI: 10.4274/eamr.galenos.2018.30922
Eur Arch Med Res 2019; 35 (2): 66-70

Is there any Relationship Between Acquired Premature Ejaculation and Blood Vitamin B12 or Folic Acid Levels?

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Abstract

Objective: To investigate the relationship between acquired premature ejaculation (PE) and serum vitamin B12 or folic acid levels.

Methods: A total of 93 patients with acquired PE and 69 controls without PE were included the study. All patients fulfilling the criteria of the International Society for Sexual Medicine Committee were considered to have acquired PE. Serum vitamin B12 and folic acid levels were evaluated in all men included in the study.

Results: Compared to controls, vitamin B12 levels were lower in patients with acquired PE (336.5±142.9 pg/mL vs. 356.0±162.5 pg/mL); however, there was no statistically significant difference between the two groups (p=0.576). There was no significant difference in folic acid levels between patients with acquired PE and controls (7.5±3.4 ng/mL vs. 7.3±3.1 ng/mL, p=0.853).

Conclusion: There is no relationship between serum vitamin B12 and folic acid levels and acquired PE. The evaluation of these vitamins should not be recommended to explore the etiology and risk factors of acquired PE.

Keywords: Intravaginal ejaculation latency time, premature ejaculation, vitamin B12, folic acid

INTRODUCTION

Premature ejaculation (PE) is the most common sexual dysfunction in men (1). Although its prevalence varies according to different criteria, this rate is reported as 4-39% (2). In a cross-sectional study carried out in Turkey, the prevalence of PE was found to be 20% (3). However, despite these high prevalence rates, the definition and subtypes of PE are still ongoing. According to the definition made by the International Society for Sexual Medicine (ISSM) in 2014, lifelong PE was defined as "ejaculation which always or nearly always occurs prior to or within about one minute of vaginal penetration from the first sexual experiences" and acquired PE was defined as "a clinically significant and bothersome reduction in latency time, often to about 3 minutes or less". According to this definition, "the inability to delay ejaculation on all or nearly all vaginal penetrations" and "negative personal consequences, such as distress, bother, frustration and/or the avoidance of sexual intimacy" defined as PE (4). In addition to these definitions, Waldinger (5) classified two distinct subgroups as natural variable PE and subjective PE. Natural variable PE is defined as "PE not always occurring and not seen in every sexual intercourse" and subjective variable is defined as "subjective perception of PE while actually having a normal or even extended ejaculation time". However, these two subgroups are not considered within the PE definition. Basile Fasolo et al., (6) reported that acquired PE was more common (14.8% vs. 4.5%) than lifelong PE, whereas Serefoglu et al., (7) reported that lifelong PE was more common (62.5% vs. 16.1%).

Although the underlying causes of lifelong PE are usually acquired neurobiological dysfunctions, correctable medical pathologies

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Cite this article as: Canat HL, Değirmentepe RB, Can O, Atalay HA, Alkan İ, Çulha MG, Özbir Sait. Is there any Relationship Between Acquired Premature Ejaculation and Blood Vitamin B12 or Folic Acid Levels?. Eur Arch Med Res 2019; 35 (2): 66-70

Received: 08.01.2018
Accepted: 28.01.2018

are often included in the etiology of acquired PE. Some of these pathologies are anxiety (8), psychological or relational problems (8), erectile dysfunction (ED) (9), chronic prostatitis (10), hyperthyroidism (11) and various drugs (12). For these reasons, the treatment response in acquired PE to is better than lifelong PE (13, 14). It has been reported by many authors that anxiety is an important risk factor for acquired PE (15, 16). It has been shown that anxiety activates the sympathetic nervous system, thereby reducing the ejaculatory threshold as the ejaculation emission phase occurs earlier (15). It is also known that nitric oxide and serotonergic neurotransmitters play a role in the ejaculatory cascade and that pathological condition or drugs affecting this cascade may affect the duration of ejaculation (15).

Vitamin B12 and folic acid are essential vitamins, which are necessary for various metabolic functions in the central nervous system and have regulatory roles on mood. In the deficiency of vitamin B12 and folic acid, methylation of neurotransmitters such as serotonin and dopamine is impaired and hyperhomocysteinemia occurs. As a result of these two conditions, mental disorders such as anxiety and depression may develop (17). It is also known that vitamin B12 plays a complementary role in the metabolism of serotonin and nitric oxide (18, 19). In addition, folic acid deficiency was associated with decreased 5-hydroxytryptamine (5-HT) activity and weak response to selective serotonin reuptake inhibitors (SSRIs) has been shown (20).

This study was planned to compare the levels of vitamin B12 and folic acid in patients with acquired PE and healthy controls.

METHODS

This single-center, prospective, observational study was performed in accordance with the and Helsinki Declaration and informed consent of the patient. This study by approved to the decision of the Ethics Committee of Clinical Researches of İstanbul Okmeydanı Training and Research Hospital of the University of Health Sciences (approval no: 963). One hundred and sixty-two patients who applied to the andrology outpatient clinic between January 2017 and June 2017 were analyzed. The study included 93 patients with acquired PE and 69 controls without any PE symptoms. Inclusion criteria were as follows: between the ages of 20 and 60, having a permanent and heterosexual relationship within the last 6 months, and having acquired PE according to the 2014 ISSM criteria (4). Patients with a) lifelong PE, b) chronic disease or psychiatric and neurological disorder that may affect sexual function, c) history of pelvic/perineal trauma or surgery, d) active urinary tract infection or chronic prostatitis, e) SSRI, alpha blocker, phosphodiesterase type 5 inhibitor and anticholinergic drug use and f) supplementary vitamin B12 or folic acid use were excluded from the study.

All participants were questioned with a Turkish version of the PE Diagnostic Tool (PEDT) form (21). In all participants, partner-assisted intravaginal ejaculation latency time (IELT) was recorded with a stopwatch. The validated Turkish version of International Index of Erectile Function-5 (IIEF-5) was used to evaluate the erectile function (22, 23). Patients with severe and moderate ED according to the IIEF-5 score were not included in the study. Body mass index (BMI), partner age, frequency of sexual intercourse, smoking and alcohol consumption and various comorbidities were recorded.

For the evaluation of vitamin B12 and folic acid levels, blood samples were obtained between 8:00 and 10:00 am after 8-10 hours of night fasting.

All statistical analyzes were performed using SPSS 22 (IBM Co., Armonk, NY, USA). Mean, standard deviation, median, minimum, maximum and frequency values were used for descriptive statistics of the data. The distribution of variables was analyzed by Kolmogorov-Smirnov test. Independent Samples t-test and Mann-Whitney U test were used for quantitative analysis of independent data and chi-square test was used for the analysis of qualitative independent data.

RESULTS

Of the 162 men included in the study, 93 had acquired PE. The remaining 69 men constituted the control group. Demographic and clinical characteristics of the study population are given in Table 1. There was no difference between the mean age of the patients with acquired PE and controls (40.0±7.2 vs. 40.6±4.8, p=0.876). Similarly, no difference was observed between the two groups in terms of partner age, BMI and frequency of monthly sexual intercourse. There was no difference between two groups in terms of smoking, alcohol consumption and various comorbidities (diabetes mellitus, cardiovascular disease, hypertension, dyslipidemia). The IIEF-5 score was not different between the two groups (22.5±6.4 vs. 22±4.2, p=0.912).

The mean PEDT score was 15.3±3.6 in the PE group and 9.9±4.7 in the control group (p<0.001). As expected, mean IELT was significantly lower in the acquired PE group compared to the control group (32.3±22.4 sec. vs. 221.7±166.5 sec., p<0.001) (Table 2).

Mean folic acid levels were 7.5±3.4 ng/mL in the PE group and 7.3±3.1 ng/mL in the control group. This difference was

not statistically significant (p=0.853). Vitamin B12 levels were lower in the acquired PE group, but no statistically significant difference was observed between the two groups (336.5±142.9 pg/mL vs. 356.0±162.5 pg/mL, p=0.576) (Table 2).

DISCUSSION

Studies on somatic and neurobiological factors to explain the etiology of PE have increased in the last two decades. While unexplained neurobiological dysfunctions are suggested in the etiology of life-long PE, the etiology of acquired PE often includes causes with better response to medical therapy (14). In our study, we planned to study only patients with acquired PE to demonstrate the association between PE and vitamin B12 and folic acid levels.

Folic acid and vitamin B12 have important roles in 5-HT, dopamine and noradrenaline metabolism (19, 24). It is known that serotonergic, dopaminergic and adrenergic neurons play a role in the complex mechanism of ejaculation control (25). Folic acid supplementation has been shown to increase the level of 5-hydroxyindolacetic acid, the main metabolite of 5-HT in cerebrospinal fluid (26). It is thought that these vitamins may be effective in the treatment of PE, especially if the relationship between folic acid or vitamin B12 can be demonstrated. However, in our study, no statistically significant difference was observed between two groups, although vitamin B12 level was lower in patients with acquired PE. Another study from Turkey has shown a significant relationship between vitamin B12 and PE (27). However, in this study, patients with acquired PE or lifelong PE were not mentioned separately and this study was conducted with lower number of patients.

It has been shown in several studies that anxiety and depression and PE have a bidirectional relationship (28-31). In particular, it is stated that anxiety reduces the time of ejaculation by affecting the emission phase by activation of sympathetic nervous system. In our study, there was no significant difference in the evaluation

Table 1. Demographic and clinical characteristics of the study population

	Acquired PE group (n=93)		Control group (n=69)		p
	Mean ± SD median (range)		Mean ± SD median (range)		
	n - %		n - %		
Age (year)	40.0±7.2	41 (21-59)	40.6±4.8	40 (23-60)	0.876
Partner age (year)	35.3±7.2	35 (21-44)	34.0±4.2	36 (26-48)	0.156
BMI (kg/m^2)	27.5±4.4	27 (17.5-43)	27.9±3.4	26.4 (18-37.6)	0.531
Sexual intercourse frequency (month)	6.3±3.1	6 (3-16)	7.2±4.1	6 (2-17)	0.323
Smoking	41-44.08%		35-50.7%		0.331
Alcohol consumption	10-10.7%		9-13.04%		0.234
IIEF-5 score	22.5±6.4	22 (15-23)	22±4.2	20 (14-25)	0.912
Comorbidities					
DM	7-7.5%		4-5.7%		0.715
Hypertension	7-7.5%		6-8.6%		0.753
CVD	2-2.1%		2-2.8%		0.876
Dyslipidemia	4-4.3%		4-5.7%		0.445

PE: Premature ejaculation, SD: Standard deviation, BMI: Body mass index, IIEF-5: International Index of Erectile Function-5, DM: Diabetes mellitus, CVD: Cardiovascular disease

Table 2. Evaluation of premature ejaculation and folic acid and vitamin B12 levels

	Acquired PE group (n=93)		Control group (n=69)		p
	Mean ± SD median (range)		Mean ± SD median (range)		
	n - %		n - %		
IELT (second)	32.3±22.4	25.6 (0-124)	221.7±166.5	221.7 (82-876)	<0.001
PEDT score	15.3±3.6	15 (7-23)	9.9±4.7	10 (3-14)	<0.001
Vitamin B12 (pg/mL)	336.5±142.9	316.6	356.0±162.5	289.9	0.576
Folic acid (ng/mL)	7.5±3.4	6.9	7.3±3.1	6.9	0.853

PE: Premature ejaculation, SD: Standard deviation, IELT: Intravaginal ejaculatory latency time, PEDT: Premature ejaculation Diagnostic Tool, IIEF-5: International Index of Erectile Function-5

of depression in both groups. In a study conducted with hospital anxiety and depression scale, a significant relationship was found between PE and anxiety (32). In our study, a direct interpretation about the relationship between folic acid and vitamin B12 and anxiety-PE relationship cannot be made between patients with acquired PE and controls, as anxiety was not questioned in our study.

Nitric oxide has an important role in the relationship between sympathetic nervous system and ejaculation (15). In addition to 5-HT metabolism, folic acid and vitamin B12 are known to be complementary factors in nitric oxide metabolism (33, 34). As a result of the studies to be carried out in the future, it may be possible to prolong the time of ejaculation with folic acid and vitamin B12 supplements.

One of the risk factors for acquired PE is ED. In a prevalence study conducted with 12,333 men from three countries, the rate of ED in men with PE was 31.9% and this rate was reported to be 11.8% in men without PE (35). In our study, no significant difference was observed between IIEF-5 scores and PE. Jannini et al., (36) stated that ED and PE could be the cause of each other (36). The reason for no correlation between IIEF-5 scores and PE in our study might be due to patients with moderate and severe ED were not included in our study and only patients with acquired PE complaints were included.

In the evaluation of PE, IELT alone may not be sufficient for diagnosis. Therefore, various questionnaires were developed. PEDT was used in our study and this questionnaire has the largest database (21). In addition, IELT was measured with a stopwatch and the mean time was 221.7 seconds (3.7 min) in healthy males. In two multicenter studies, including Turkey, the median IELT in the general population was measured as 5.4 min and 6.0 min, respectively (37, 38).

In our study, no significant difference was observed between two groups in terms of demographic characteristics. Age, partner age, frequency of sexual intercourse, smoking and alcohol consumption were similar in both groups. Gao et al., (14) showed a relationship between acquired PE and high BMI. However, there was no significant relationship between BMI and PE in our study.

Study Limitations

There are several limitations in our study. First, healthy men in the control group may not represent the general population. Second, the number of patients in both groups is relatively low. Our results need to be confirmed by large-scale studies. In addition, the lack of the evaluation of the anxiety and partner's sexual dysfunction, which are among the etiologies of PE, is one of the main limitations of the study.

CONCLUSION

In our study investigating the relationship between acquired PE and vitamins B12 and folic acid, it was shown that both vitamins were not associated with PE. However, large-scale clinical and observational studies are needed to demonstrate this relationship indirectly through psychoneuroendocrine routes.

Ethics

Ethics Committee Approval: The study was approved by the University of Health Sciences İstanbul Okmeydanı Training and Research Hospital Ethics Committee (approval number: 963).

Informed Consent: Informed consent from was patient.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: H.L.C., R.B.D., O.C., Concept: H.L.C., Design: H.L.C., Data Collection or Processing: H.L.C., R.B.D., O.C., H.A.A., İ.A., M.G.C., S.Ö., Analysis or Interpretation: H.A.A., İ.A., M.G.C., S.Ö., Literature Search: H.L.C., R.B.D., Writing: H.L.C.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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