ISSN 2077-8333 (print)
ISSN 2311-4088 (online)

ЭПИЛЕПСИЯ и пароксизмальные состояния

15 лет С ВАМИ

2024 Том 16 №2

EPILEPSY AND PAROXYSMAL CONDITIONS

2024 Vol. 16 №2

https://epilepsia.su

https://doi.org/10.17749/2077-8333/epi.par.con.2024.169
ISSN 2077-8333 (print)
ISSN 2311-4088 (online)

Evaluation of the effects of sodium valproate on plasma homocysteine, folate and vitamin B12 levels in epileptic patients

A. Aman-Mohammady, D. Qujeq, P. Saadat, K. Hajian-Tilaki

Babol University of Medical Sciences (GMJH+F6G, Babol, Mazandaran Province, Iran)

Corresponding author: *Payam Saadat, E-mail: sepanta1968@yahoo.com*

SUMMARY

Objective: to investigate the effects of sodium valproate on plasma concentrations of homocysteine, folate and vitamin B12 levels in epileptic patients with long-standing tonic-clonic seizures compared to newly diagnosed epileptic patients and healthy controls.

Material and methods. The study included 90 participants (mean age 36.30±12.83 years, the majority (58.89%) were males) divided into three groups: 30 non-epileptic people (control Group 1), 30 newly diagnosed epileptic patients (Group 2), and 30 patients with long-term tonic-clonic seizures epilepsy (Group 3). In Group 3, patients received sodium valproate therapy. All subjects underwent clinical and neurological examinations. Differences in plasma levels of homocysteine, folic acid and vitamin B12 in three groups were investigated after 6 months of follow-up.

Results. Homocysteine level in Groups 2 and 3 was increased; for Group 2 it was significantly higher than for Groups 3 and 1 (p=0.001). Plasma folate level in Groups 2 and 3 was decreased; for Group 3 it was significantly higher than for Group 2 and lower than for Group 1 (p=0.001). Vitamin B12 level in Groups 2 and 3 was decreased, but the difference was not significant (p=0.090). In Groups 1 and 2, a significant correlation was observed between the indicators.

Conclusion. Sodium valproate administration might disrupt the homeostatic level of homocysteine, folate and vitamin B12 and cause irregularity of their plasma contents in epileptic patients with long-standing tonic-clonic seizures.

KEYWORDS

Newly diagnosed epileptic seizures, long-standing epilepsy, sodium valproate, folate, homocysteine, vitamin B12.

ARTICLE INFORMATION

Received: 13.09.2023. **Revision received:** 02.02.2024. **Accepted:** 09.04.2024. **Published:** 30.06.2024.

Conflict of interests

The authors declare no conflict of interest regarding this publication.

Funding

The project was funded by Babol University of Medical Sciences as MSc thesis of A. Aman-Mohammady in clinical biochemistry (Project No. 9542933).

Authors' contribution

A. Aman-Mohammady – study performing, text writing;
D. Qujeq – study design, text writing;
P. Saadat – text writing;
K. Hajian-Tilaki – results analysis

For citation

Aman-Mohammady A., Qujeq D., Saadat P., Hajian-Tilaki K. Evaluation of the effects of sodium valproate on plasma homocysteine, folate and vitamin B12 levels in epileptic patients. *Epilepsia i paroksizmal'nye sostoania / Epilepsy and Paroxysmal Conditions.* 2024; 16 (2): 104–109 (in Russ.). https://doi.org/10.17749/2077-8333/epi.par.con.2024.169.

Оценка влияния вальпроата натрия на уровни гомоцистеина, фолата и витамина B12 в плазме крови у больных эпилепсией

А. Аман-Мохаммади, Д. Куджек, П. Саадат, К. Хаджиан-Тилаки

Бабольский университет медицинских наук (GMJH+F6G, Баболь, провинция Мазандаран, Иран)

Для контактов: *Пайам Саадат, E-mail: sepanta1968@yahoo.com*

РЕЗЮМЕ

Цель: изучить влияние вальпроата натрия на концентрации гомоцистеина, фолата и витамина B12 в плазме крови у больных с длительно присутствующей эпилепсией с тонико-клоническими приступами в сравнении с пациентами с впервые диагностированной эпилепсией и контрольной группой.

Материал и методы. В исследование включены 90 участников (средний возраст 36,30±12,83 года, большинство (58,89%) составляли мужчины), которые были разделены на три группы: 30 человек, не страдающих эпилепсией (контрольная 1-я группа), 30 больных с впервые выявленной эпилепсией (2-я группа) и 30 пациентов с длительно присутствующей эпилепсией с тонико-клоническими приступами (3-я группа). В 3-й группе больные получали вальпроат натрия. Все участники исследования прошли клиническое и неврологическое обследование. Различия в уровнях гомоцистеина, фолиевой кислоты, витамина B12 в плазме крови в трех группах исследовали через 6 мес наблюдения.

Результаты. Зарегистрирован повышенный уровень гомоцистеина во 2-й и 3-й группах; во 2-й группе он был достоверно выше, чем в 3-й и 1-й группах (p=0,001). Уровень фолатов в плазме во 2-й и 3-й группах оказался снижен; в 3-й группе он был достоверно выше, чем во 2-й группе, и ниже, чем в 1-й группе (p=0,001). Снижение уровня витамина B12 во 2-й и 3-й группах было недостоверно (p=0,090). В 1-й и 2-й группах наблюдалась значимая корреляция между показателями.

Заключение. Введение вальпроата натрия может нарушить гомеостатические уровни гомоцистеина, фолата и витамина B12 и вызвать их колебания в сыворотке крови у больных с длительно присутствующей эпилепсией с тонико-клоническими приступами.

КЛЮЧЕВЫЕ СЛОВА

Впервые диагностированная эпилепсия, длительно присутствующая эпилепсия, вальпроат натрия, фолат, гомоцистеин, витамин B12.

ИНФОРМАЦИЯ О СТАТЬЕ

Поступила: 13.09.2023. **В доработанном виде:** 02.02.2024. **Принята к печати:** 09.04.2024. **Опубликована:** 30.06.2024.

Конфликт интересов

Авторы заявляют об отсутствии необходимости раскрытия конфликта интересов в отношении данной публикации.

Финансирование

Проект профинансирован Бабольским университетом медицинских наук в качестве магистерской диссертации А. Аман-Мохаммади по клинической биохимии (проект № 9542933).

Вклад авторов

Аман-Мохаммади А. – проведение исследования, написание текста;
Куджек Д. – планирование исследования, написание текста;
Саадат П. – написание текста;
Хаджиан-Тилаки К. – анализ результатов

Для цитирования

Аман-Мохаммади А., Куджек Д., Саадат П., Хаджиан-Тилаки К. Оценка влияния вальпроата натрия на уровни гомоцистеина, фолата и витамина B12 в плазме крови у больных эпилепсией. *Эпилепсия и пароксизмальные состояния.* 2024; 16 (2): 104–109. https://doi.org/10.17749/2077-8333/epi.par.con.2024.169.

INTRODUCTION / ВВЕДЕНИЕ

Epilepsy is a common neurological disease caused by a transient electrical brain disorder that leads to sudden and repeated attacks (various types of seizures), short-term, accompanied by changes in the state of consciousness or abnormal movements. It may sometimes be accompanied by complete seizures or local muscle spasms, and depending on the nature and type of attacks, it may be associated with loss of consciousness [1, 2]. All aspects of this disease are not well known and cannot be cured, but epileptic attacks can be controlled with some treatment methods, including drug treatments with anti-epileptic drugs [3].

There is a wide range of antiepileptic drugs with different mechanism, pharmacology, pharmacokinetics and important side effects. One of these drugs is sodium valproate (SV),

which is an 8-carbon branched-chain fatty acid and has been used as a broad-spectrum drug since 1970 as one of the first-line anticonvulsant drugs [4].

SV, like other anticonvulsant drugs, has side effects, such as, if prescribed for a long time, the metabolism of folate and vitamin B12 is affected, and by increasing the plasma level of homocysteine (Hcy), they lead to cerebrovascular disorders [5]. Hcy, as an amino acid containing sulfur, plays a role in methionine metabolism, and folic acid and vitamin B12 are necessary for the remethylation of Hcy to methionine, So that the reduction of each of them may lead to an increase in the level of Hcy and a decrease in methionine [6].

Epilepsy is prevalent in about half to one percent of the world's population, and almost 80% of its cases are reported in developing countries [7]. Its prevalence in Iran has been about 5% higher than the statistics of similar countries, while in terms of geographical region, the highest frequency has been reported in the center of the country, then the east and finally the north of the country [8].

SV is one of the most widely used and common drugs used by epilepsy patients and is reported to be one of the first common drugs used in these patients. Therefore, this study was conducted to investigate its effect on the plasma levels of Hcy, folate and vitamin B12, and as a result, controlling side effects and ultimately helping patients recover.

Objective – to investigate the effects of SV on plasma concentrations of homocysteine, folate and vitamin B12 levels in epileptic patients with long-standing tonic-clonic seizures compared to newly diagnosed epileptic patients and healthy controls.

MATERIAL AND METHODS / МАТЕРИАЛ И МЕТОДЫ

This descriptive-analytical study was conducted in the population of epilepsy patients referred to Ayatollah Rouhani Hospital in Babol between November 2015 and January 2018. A total of 90 people were studied.

Participants / Участники

The inclusion criteria were defined as patients who were suffering from epilepsy at the time of the study, and the exclusion criteria were defined as age less than 20 years, pregnancy, heart, liver and kidney disorders, suffering from cancer, taking supplements containing folate and vitamin B12 and hyperlipidemia.

The control group (Group 1) consisted of 30 healthy people without epilepsy and without diagnosis of neurological disorder. According to the available sampling method and the inclusion criteria, 30 patients with newly diagnosed epilepsy who did not take SV (Group 2) and 30 patients with long-term epilepsy with tonic-colonic seizures under SV treatment (Group 3) were selected and included in the study.

Healthy people (Group 1) included 12 men and 18 women with an average age of 36.30±12.80 years. The newly diagnosed group (Group 2) included 13 men and 17 women with an average age of 36.76±12.91 years. The group of patients with long-term epilepsy (Group 3) included 12 men and 18 women with an average age of 35.56±12.77 years and an average duration of the disease of 6 months (**Table 1**).

Ethical aspects / Этические аспекты

The researchers complied with the requirements of the Helsinki Declaration of the World Medical Association (Fortaleza, Brazil, 2013). The study was approved by the local Ethics Committee (MUBABOL.REC.1395.179-3570). The samples were collected with the consciously written consent of patients.

Methods of plasma analysis / Методы анализа плазмы

Differences in plasma Hcy, folate and vitamin B12 concentrations in studied patients after 6 months of follow-up were analyzed. Blood (5 ml) was collected from the veins of fasting and resting patients, and plasma was isolated. Standard biochemical kits were used to detect plasma concentrations of Hcy, folate and vitamin B12 according to the manufacturer's instructions.

Statistical analyses / Статистический анализ

SPSS Statistics 18 (IBM Inc., USA) was used for all statistical analyses. Data are presented as mean ± standard deviation. Parameters that were not normally distributed, including folate, vitamin B12, and Hcy, were log-transformed before analysis. Comparisons between groups were performed using analysis of variance (ANOVA). The Pearson's test was used to assess the correlation of the parameters.

Table 1. Descriptive statistics of healthy controls, newly diagnosed epileptic patients and patients with long-standing tonic-clonic seizures following sodium valproate therapy

Таблица 1. Описательная статистика здоровых лиц контрольной группы, пациентов с впервые диагностированной эпилепсией и больных с длительно присутствующей эпилепсией с тонико-клоническими приступами, принимающих вальпроат натрия

Parameter / Параметр	Group / Группа		
	1 (control) / 1 (контрольная) (n=30)	2 (without therapy) / 2 (без терапии) (n=30)	3 (with therapy) / 3 (с терапией) (n=30)
Gender, n (%) / Пол, n (%)			
male / мужской	12 (40.0)	13 (43.3)	12 (40.0)
female / женский	18 (60.0)	17 (56.7)	18 (60.0)
Age, years / Возраст, лет	36.30±12.8	36.76±12.91	35.56±12.77

RESULTS / РЕЗУЛЬТАТЫ

In **Table 2**, the comparison of mean plasma concentrations of Hcy, folic acid and vitamin B12 of healthy controls, newly diagnosed patients and long-standing tonic-clonic seizures epileptic patients after SV therapy is shown. The plasma folate levels in Group 3 (following SV treat¬ment) were significantly higher than those in Group 2 (without SV treatment) and significantly lower than those Group 1 (p=0.001). Hcy level in Group 2 was significantly higher than in Group 3 (following SV treatment) and in the control group (p=0.001). The level of B12 was also higher in healthy people than in patients, and while it was reported higher in Group 2 (without SV therapy) than in Group 3 (with SV therapy), the difference between the groups was not significant (p=0.090).

In **Table 3** and **Figure 1**, correlations between mean plasma concentrations of Hcy, folate, and vitamin B12 in healthy controls, newly diagnosed patients, and long-standing tonic-clonic seizures epileptic patients who have undergone SV therapy are demonstrated.

DISCUSSION / ОБСУЖДЕНИЕ

The current study determined SV impact on plasma levels of Hcy, folate and vitamin B12 B12 in long-standing

Table 2. Comparsion between mean plasma levels of homocystein, folic acid, and vitamin B12 in healthy controls, newly diagnosed epileptic patients and patients with long-standing tonic-clonic seizures following treatment with sodium valproate

Таблица 2. Сравнение средних уровней гомоцистеина, фолиевой кислоты и витамина B12 в плазме крови у здоровых лиц контрольной группы, пациентов с впервые диагностированной эпилепсией и больных с длительно присутствующей эпилепсией с тонико-клоническими приступами, принимающих вальпроат натрия

Parameter / Параметр	Group / Группа			p
	1 (control) / 1 (контрольная) (n=30)	2 (without therapy) / 2 (без терапии) (n=30)	3 (with therapy) / 3 (с терапией) (n=30)	
Homocystein, μmol/l // Гомоцистеин, мкмоль/л	8.20±0.50	11.77±0.76	9.57±0.32	0.001
Folic acid, ng/ml // Фолиевая кислота, нг/мл	15.07±0.70	1.70±0.60	4.85±0.65	0.001
Vitamin B12, pg/ml // Витамин B12, пг/мл	368.65±26.81	330.85±13.30	310.47±12.83	0.090

Table 3. Correlation between mean plasma levels of homocystein, folic acid and vitamin B12 in healthy controls, newly diagnosed epileptic patients and patients with long-standing tonic-clonic seizures following treatment with sodium valproate

Таблица 3. Корреляция между средними уровнями гомоцистеина, фолиевой кислоты и витамина B12 в плазме крови у здоровых лиц контрольной группы, пациентов с впервые диагностированной эпилепсией и больных с длительно присутствующей эпилепсией с тонико-клоническими приступами, принимающих вальпроат натрия

Group / Группа	Parameter / Параметр	Homocystein, μmol/l // Гомоцистеин, мкмоль/л		Folic acid, ng/ml // Фолиевая кислота, нг/мл		Vitamin B12, pg/ml // Витамин B12, пг/мл	
		r*	p	r*	p	r*	p
1 (control) / 1 (контрольная)	Homocystein, μmol/l // Гомоцистеин, мкмоль/л	–	–	–0.45	0.01	0.17	0.36
	Folic acid, ng/ml // Фолиевая кислота, нг/мл	–0.45	0.01	–	–	0.14	0.44
	Vitamin B12, pg/ml // Витамин B12, пг/мл	0.17	0.36	0.14	0.44	–	–
2 (without therapy) / 2 (без терапии)	Homocystein, μmol/l // Гомоцистеин, мкмоль/л	–	–	–0.39	0.02	–0.51	0.004
	Folic acid, ng/ml // Фолиевая кислота, нг/мл	–0.39	0.02	–	–	0.59	0.001
	Vitamin B12, pg/ml // Витамин B12, пг/мл	–0.51	0.004	0.59	0.001	–	–
3 (with therapy) / 3 (с терапией)	Homocystein, μmol/l // Гомоцистеин, мкмоль/л	–	–	0.18	0.33	0.16	0.93
	Folic acid, ng/ml // Фолиевая кислота, нг/мл	0.18	0.33	–	–	0.08	0.64
	Vitamin B12, pg/ml // Витамин B12, пг/мл	0.16	0.93	0.08	0.64	–	–

Note. ** Pearson's correlation.*

Примечание. ** Корреляция Пирсона.*

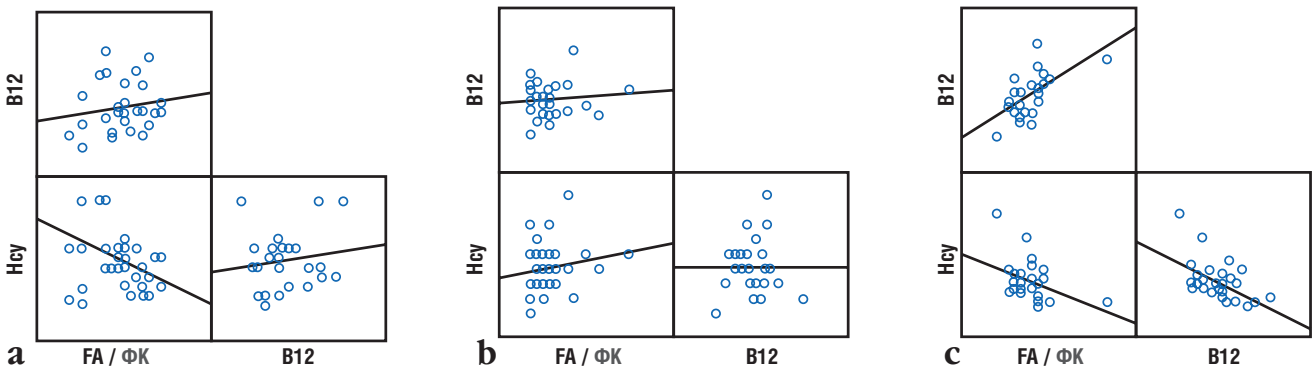

Figure 1. Correlations between mean plasma concentrations of homocystein (Hcy), folic acid (FA), and vitamin B12: **a** – in healthy controls (Group 1); **b** – in newly diagnosed epileptic patients without therapy (Group 2); **c** – in patients with long-standing tonic-clonic seizures following treatment with sodium valproate (Group 3)

Рисунок 1. Корреляции между средними концентрациями гомоцистеина (Hcy), фолиевой кислоты (ФК) и витамина B12 в плазме крови: **a** – у здоровых лиц (1-я группа); **b** – у пациентов с впервые диагностированной эпилепсией без терапии (2-я группа); **c** – у больных с длительно присутствующей эпилепсией с тонико-клоническими приступами, принимающих вальпроат натрия (3-я группа)

tonic-clonic seizures epileptic patients following SV therapy compared to newly diagnosed epileptic patients and healthy controls. The main findings were a decrease in folate level, but Hcy levels elevated in patients with long-standing tonic-clonic seizures epilepsy (Group 3) compared to Groups 1 and 2. It is likely that SV could effect on the acidic properties of the digestive tract and the buffering system. These changes might effect on folate precursor enzymes and reduces folate absorption. Also, it may affect folate synthesizing pathway. Considering that vitamin B12 plays a role in the transport and storage mechanism of folate, by reducing vitamin B12 folate metabolism also fails. Vitamin B12 plays a role as a cofactor of methyl transferase [9–12].

But the reason for the elevation of Hcy level may be due to decreased folate levels. Because of the reduction of folate, the transfer of methyl group from Hcy to methionine is not done [10]. Folate is an important component in many biochemical and physiological reactions in the body. The amount of Hcy might remain high as folate level decreases. Also, with the reduction of vitamin B12, a disruption of the methyl group is caused.

On the other hand, elevated serum Hcy may be due to decreased vitamin B12 and folate, because vitamin B12 and folate are essential in the conversion of Hcy to the metabolite methionine. This may be the mechanism by which SV increases serum Hcy levels due to interference with feeding, absorption and renal excretion. These results indicate that SV interacts with folate and vitamin B12 metabolism.

Our results indicate that the plasma contents of Hcy, folic acid and vitamin B12 could be dependent risk factors for epilepsy, agreeing with previous studies [5, 9]. Current findings demonstrated lower contents of sera folate and vitamin B12 contents in newly diagnosed epileptic patients and long-standing tonic-clonic seizures epileptic patients treated with SV, which was attributed to direct relationship between folate and vitamin B12 levels. But our results demonstrated higher levels of serum Hcy levels in newly diagnosed epileptic patients, which was attributed to inverse relationship between Hcy, folate and vitamin B12 contents.

Anyway, the mechanism underlying the effects of SV effect on folate and vitamin B12 content remains to be recognized. Therefore, additional basic and clinical studies should be managed to verify these results.

The present study demonstrated that taking SV is meaningfully connected with decreased serum levels of folate and tendency to decrease vitamin B12. This observation correlates with the finding of other researchers who had reported a significant decreased serum levels of vitamins B12 and folate in epileptic patients [5, 13, 14]. Our results agree with other researchers' reports [6]. But our findings indicate that receiving SV is meaningfully connected with increased serum levels of Hcy in epileptic patients. This findings agrees with most of clinical studies results [13, 15, 16], but is inconsistent with the findings of other researchers [17].

Study limitations / Ограничения исследования

The study had certain limitations. Our sample size was small. Besides, we did not analyze plasma concentrations of other biochemical markers such as lipid profiles, because SV may cause alterations in these variables. Additionally, we did not take into account plasma hormone concentrations such as thyroid hormones.

Acknowledgements / Благодарности

The authors thank for support the Vice-Chancellor of Research and Technology of Babol University of Medical Sciences and the Development and Research Unit of Ayatollah Rouhani Hospital of Babol.

CONCLUSION / ЗАКЛЮЧЕНИЕ

Administration of SV reduces the plasma contents of folate. It might disrupt the homeostatic level of Hcy and vitamin B12 and cause irregularity of their plasma contents in newly diagnosed and long-standing epileptic patients.

REFERENCES / ЛИТЕРАТУРА:

1. Alvim M.K., Coan A.C., Campos B.M., et al. Progression of gray matter atrophy in seizure-free patients with temporal lobe epilepsy. *Epilepsia*. 2016; 57 (4): 621–9. https://doi.org/10.1111/epi.13334.
2. Dugbartey A.T., Barimah K.B. Traditional beliefs and knowledge base about epilepsy among university students in Ghana. *Ethn Dis.* 2013; 23 (1): 1–5.
3. Eadie M.J. Shortcomings in the current treatment of epilepsy. *Expert Rev Neurother.* 2012; 12 (12): 1419–27. https://doi.org/10.1586/ern.12.129.
4. Chateauvieux S., Morceau F., Dicato M., Diederich M. Molecular and therapeutic potential and toxicity of valproic acid. *J Biomed Biotechnol.* 2010; 2010: 479364. https://doi.org/10.1155/2010/479364.
5. Linnebank M., Moskau S., Semmler A., et al. Antiepileptic drugs interact with folate and vitamin B12 serum levels. *Ann Neurol.* 2011; 69 (2): 352–9. https://doi.org/10.1002/ana.22229.
6. Tamura T., Aiso K., Johnston K.E., et al. Homocysteine, folate, vitamin B-12 and vitamin B-6 in patients receiving antiepileptic drug monotherapy. *Epilepsy Res.* 2000; 40 (1): 7–15. https://doi.org/10.1016/s0920-1211(00)00101-7.
7. Bell G.S., Neligan A., Sander J.W. An unknown quantity – the worldwide prevalence of epilepsy. *Epilepsia.* 2014; 55 (7): 958–62. https://doi.org/10.1111/epi.12605.
8. Sayehmiri K., Tavan H., Sayehmiri F., et al. Prevalence of epilepsy in Iran: a meta-analysis and systematic review. *Iran J Child Neurol.* 2014; 8 (4): 9–17.
9. Bochyńska A., Lipczyńska-Łojkowska W., Gugała-Iwaniuk M., et al. The effect of vitamin B supplementation on homocysteine metabolism and clinical state of patients with chronic epilepsy treated with carbamazepine and valproic acid. *Seizure.* 2012; 21 (4): 276–81. https://doi.org/10.1016/j.seizure.2012.01.013.
10. Cahill V., McCorry D., Soryal I., Rajabally Y.A. Newer anti-epileptic drugs, vitamin status and neuropathy: a cross-sectional analysis. *Rev Neurol.* 2017; 173 (1–2): 62–6. https://doi.org/10.1016/j.neurol.2016.09.008.
11. Ni G., Qin J., Fang Z., et al. Increased homocysteine levels in valproate-treated patients with epilepsy: a meta-analysis. *BMJ Open.* 2014; 4 (7): e004936. https://doi.org/10.1136/bmjopen-2014-004936.
12. Yu W.H., Ho Y.L., Huang P.T., et al. The Phosphorylation state of GSK3β serine 9 correlated to the development of valproic acid-associated fetal cardiac teratogenicity, fetal VPA syndrome, rescued by folic acid administration. *Cardiovasc Toxicol.* 2016; 16 (1): 34–45. https://doi.org/10.1007/s12012-015-9316-0.
13. Aslan K., Bozdemir H., Unsal C., Güvenc B. The effect ofantiepileptic drugs on vitamin B12 metabolism. *Int J Lab Hematol.* 2008; 30 (1): 26–35. https://doi.org/10.1111/j.1751-553X.2007.00910.x.
14. Gorjipour F., Asadi Y., Osguei N.K., et al. Serum level of homocysteine, folate and vitamin-B12 in epileptic patients under carbamazepine and sodium valproate treatment: a systematic review and meta-analysis. *Iran Red Crescent Med J.* 2013; 15 (3): 249–53. https://doi.org/10.5812/ircmj.9690.
15. Huemer M., Ausserer B., Graninger G., et al. Hyperhomocysteinemia in children treated with antiepileptic drugs is normalized by folic acid supplementation. *Epilepsia.* 2005; 46 (10): 1677–83. https://doi.org/10.1111/j.1528-1167.2005.00264.x.
16. Sener U., Zorlu Y., Karaguzel O., et al. Effects of common anti-epileptic drug monotherapy onserum levels of homocysteine, vitamin B12, folic acid and vitamin B6. *Seizure.* 2006; 15 (2): 79–85. https://doi.org/10.1016/j.seizure.2005.11.002.
17. Ono H., Sakamoto A., Mizoguchi N., Sakura N. The C677T mutation in the methylenetetrahydrofolate reductase gene contributes to hyperhomocysteinemia in patients taking anticonvulsants. *Brain Dev.* 2002; 24 (4): 223–6. https://doi.org/10.1016/s0387-7604(02)00004-9.

About the authors

Amene Aman-Mohammady – Student, Student Research Committee, Babol University of Medical Sciences (Babol, Iran).

Durdi Qujeq – Professor, Department of Clinical Biochemistry, Faculty of Medicine, Babol University of Medical Sciences (Babol, Iran). ORCID ID: https://orcid.org/0000-0003-1344-9344; WoS ResearcherID: H-2445-2019; Scopus Author ID: 6603540605.

Payam Saadat – Associate Professor of Neurology, Mobility Impairment Research Center, Health Research Institute, Clinical Research Development Unite of Rouhani Hospital, Babol University of Medical Sciences (Babol, Iran). ORCID ID: https://orcid.org/0000-0002-5150-4757; Scopus Author ID: 56346081500. E-mail: sepanta1968@yahoo.com.

Karimollah Hajian-Tilaki – Professor, Department of Biostatistics and Epidmiology, School of Medicine, Babol University of Medical Sciences (Babol, Iran). ORCID ID: https://orcid.org/0000-0001-6830-1916; Scopus Author ID: 6603011396.

Сведения об авторах

Амен Аман-Мохаммади – студент, Студенческий исследовательский комитет, Бабольский университет медицинских наук (Баболь, Иран).

Дурди Куджек – профессор, кафедра клинической биохимии, медицинский факультет, Бабольский университет медицинских наук (Баболь, Иран). ORCID ID: https://orcid.org/0000-0003-1344-9344; WoS ResearcherID: H-2445-2019; Scopus Author ID: 6603540605.

Пайам Саадат – доцент, врач-невролог, Исследовательский центр двигательных нарушений, Научно-исследовательский институт здравоохранения, Центр клинических исследований и разработок больницы Рухани, Бабольский университет медицинских наук (Баболь, Иран). ORCID ID: https://orcid.org/0000-0002-5150-4757; Scopus Author ID: 56346081500. E-mail: sepanta1968@yahoo.com.

Каримолла Хаджиан-Тилаки – профессор, кафедра биостатистики и эпидемиологии, Школа медицины, Бабольский университет медицинских наук (Баболь, Иран). ORCID ID: https://orcid.org/0000-0001-6830-1916; Scopus Author ID: 6603011396.