Folic Acid Levels in a Sample of Portuguese Psychiatric Outpatients

Níveis de Ácido Fólico numa Amostra de Doentes Psiquiátricos Portugueses em Ambulatório

Joana Abreu Lopes[1]

Autor Correspondente:
Joana Lopes [joana.lopes@hvfx.pt]

ABSTRACT

INTRODUCTION: There is substantial evidence of the association between mental disorders and low folic acid levels. The aim of this study was to evaluate the prevalence of folic acid deficiency in a sample of Portuguese psychiatric outpatients.

METHODS: The study was retrospective and included 428 psychiatric outpatients with a diagnosis of depression or non-affective psychosis, for whom folic acid levels had been measured as part of routine blood tests. Folic acid levels from other hospital patients from the same time period were also registered.

RESULTS AND DISCUSSION: The prevalence of folic acid deficiency in this sample is 18%. Non-psychiatric hospital patients with risk factors for folic acid deficiency have a prevalence of 15% of folic acid deficiency. Men and younger patients have lower folic acid levels, with statistical significance, and the prevalence of deficit reached 26%.

CONCLUSION: The elevated frequency of folic acid deficiency in this sample of patients shows that folic acid levels should be routinely assessed in every patient with depression or psychosis, in order to avoid maintenance of symptoms and treatment resistance.

KEYWORDS: Folic Acid; Folic Acid Deficiency; Depression; Portugal; Psychotic Disorders

RESUMO

INTRODUÇÃO: *Há múltiplas evidências da associação entre doenças mentais e baixos níveis de ácido fólico. O objetivo deste estudo foi avaliar a prevalência da deficiência de ácido fólico numa amostra de doentes da consulta externa de psiquiatria.*

MÉTODOS: *O estudo foi retrospetivo e incluiu 428 doentes da consulta externa de psiquiatria com os diagnósticos de depressão ou de psicose não afetiva, nos quais os níveis de ácido fólico tinham sido avaliados em análises de rotina. Foram também registados os níveis de ácido fólico de outros doentes do hospital, no mesmo período temporal.*

1. Serviço de Psiquiatra, Hospital Vila Franca de Xira, Vila Franca de Xira, Portugal.

Recebido/*Received*: 19/07/2016 - Aceite/*Accepted*: 01/08/2016

RESULTADOS E DISCUSSÃO: *A prevalência de deficiência de ácido fólico nesta amostra foi de 18%. Os doentes não psiquiátricos com fatores de risco para deficiência de ácido fólico tiveram uma prevalência de 15% de deficiência. Nos homens e em doentes mais jovens os níveis de ácido fólico foram significativamente mais baixos, a prevalência de deficiência atingiu os 26%.*

CONCLUSÃO: *A alta frequência de deficiência de ácido fólico nesta amostra de doentes comprova que os níveis de ácido fólico devem ser avaliados sistematicamente em doentes da consulta de psiquiatria com diagnósticos de depressão ou psicose, para evitar persistência de sintomas e resistência ao tratamento.*

PALAVRAS-CHAVE: *Ácido Fólico; Deficiência de Ácido Fólico; Depressão; Portugal; Transtornos Psicóticos*

INTRODUCTION

Folic acid is a vitamin involved in one-carbon transfer (methylation) reactions, necessary for the production of monoamine neurotransmitters, phospholipids and nucleotides. There is substantial evidence of the association between mental disorders and low folic acid levels.[1] Decreased folic acid levels have also been associated with lowered response rates to treatment and place patients at higher risk of relapse.[2]

It has been hypothesized that in mental illness, a combination of decreased appetite, decreased absorption and increased utilization of folate results in folate depletion.[3] Mental illness is also commonly associated with alcohol excess, which is known to impair folate absorption and deplete stores of folate. Both of these factors could confound the relationship between folate and psychiatric illness, so that the direction of cause and effect remains unclear.[4]

Research on the association of folic acid deficiency and mental illness dates back to the 1960s with studies showing reduced folic acid levels in psychiatric patients, the frequency varying from one quarter to one third of the populations studied.[1] In a study made in Israel published in 2005, 30% of psychiatric inpatients had folate deficiency, compared with 2.5% in the control group.[4] A study made with 70 Spanish psychiatric inpatients in 2009 also showed significantly lower levels of folate in patients when compared with controls.[5]

A meta-analysis published in 2007 showed a significant relationship between folate status and depression, which remained after controlling for potential confounding factors - age, nutritional status and co-morbid alcohol disorders.[6] A meta-analysis published in 2016 showed that folate deficiency is associated with schizophrenia diagnosis.[7]

The aim of this study is to evaluate the prevalence of folic acid deficiency in a sample of Portuguese psychiatric outpatients and to correlate it with demographic factors.

METHODS

The study was retrospective, from April 2013 to December 2015, and included 428 psychiatric outpatients with a diagnosis of depression (unipolar, bipolar) or non-affective psychosis (schizophrenia, delusional disorder, transient and acute psychosis) for whom folic acid levels had been measured as part of routine blood tests in the outpatient clinic. Folic acid was measured in plasma by immunoassay, levels below 3 ng/mL were considered deficient.

Folic acid levels from other hospital patients from the same time period were also gathered a total of 1271 patients, to serve as comparison. These were from inpatients and outpatients from neurology, internal medicine, surgery and gastroenterology, whose doctors requested folic acid levels for clinical reasons.

The statistical analysis was made with IBM SPSS Statistics 24.

RESULTS

Psychiatric patients' mean age was 48, 75% of the sample were women and 70% had a diagnosis of depression. Mean folic acid levels was 6.5 ng/mL. Values were lower in men, patients with psychosis and patients younger than 48 (patients were divided in two groups using as a cut off the mean age of 48, for analysis purposes). The global prevalence of folic acid deficiency was 18%, with a maximum of 26% in men and in patients younger than 48, and a minimum of 12% in older patients (Table 1). These differences were statistically significant, but when sex and age were controlled, there were no significant differences in folic acid levels between depression and psychosis patients, as the differences found were due to different demographics in different diagnostic groups (Table 2).

Non-psychiatric hospital patients for whom folic acid was measured served as a comparison group. Their mean folic acid level was 7.8 ng/mL, younger patients

TABLE 1. Results in psychiatric patients.

	Mean age	Mean folic acid level	Student's t test	Folic acid deficient (<3)
Total (428)	48 y	6.5		18%
Men (109)	44	4.9	(t – -4.586)	26%
Women (319)	50	7.0	(p – 0.000)	16%
Younger than 48 (195)		5.3	(t – 4.752	26%
Older than 48 (233)		7.5	(p – 0.000)	12%
Psychosis (129)	44	5.5	(t – 3.082)	23%
Depression (299)	50	6.9	(p – 0.002)	16%

TABLE 2. Analysis of regression of folic acid levels.

Folic acid levels by:	β	SE	t	p
Sex	-1.607	.562	-2.857	.004
Age	.065	.015	4.393	.000
Diagnostic	-.441	.538	-.819	.413

TABLE 3. Non psychiatric patients' results.

Controls	Mean age	Mean folic acid level	Student's t test	Folic acid deficient
Total (1271)	61	7.8		15%
Men (542)	61	7.6	(t – -1.148	15%
Women (728)	60	8.0	p – NS	15%
Younger than 48 (297)		5.9	(t – -6.734	27%
Older than 48 (972)		8.3	p – 0.000)	11%

also had lower levels, with a statistically significant difference, but there was no statistically significant difference in levels between men and women. The prevalence of folic acid deficiency was 15%, with a maximum of 27% in patients younger than 48 (Table 3).

DISCUSSION AND CONCLUSION

The prevalence of folic acid deficiency in this sample was 18%, similar to the prevalence obtained in other studies, but data are not comparable as the methodology, criteria for patient selection, methods of measurement and definitions of folic acid deficiency vary considerably. Non-psychiatric hospital patients had a prevalence of 15%. These patients are, however, at high risk for folic acid deficiency, as they have diagnosis such as macrocytic anaemia, liver cirrhosis, malabsorption or dementia. The conclusion to be drawn from these results is that psychiatric patients with depression or psychosis are also a high risk group for folic acid deficiency.

Men, younger patients and non-affective psychosis patients had lower folic acid levels when compared with women, older patients and patients with diagnosis of depression, and the difference was statistically significant. However, when sex and age were controlled, there was no difference in folic acid levels between depression and psychosis patients – as patients with psychosis are usually younger and more frequently male.

In non-psychiatric patients only age was a risk factor for folic acid deficiency, with younger patients having lower levels of folic acid and higher percentages of folic acid deficiency. In this group of patients, male sex was not a risk factor for folic acid deficiency when age is controlled.

The differences found may be explained by the higher prevalence of risk factors for folic acid deficiency in younger and in male patients, accentuated in mental illness - poor nutrition, alcohol abuse, medication with mood-stabilizing anticonvulsants.

The elevated frequency of folic acid deficiency in this sample shows that folic acid levels should be routinely assessed in every patient with depression or psychosis, in order to avoid maintenance of symptoms and treatment resistance.

ACKNOWLEDGMENTS

I would like to thank Dr. Luís Silva, director of the Clinical Pathology Department of Hospital de Vila Franca de Xira, for his help in gathering the data necessary for this article.

CONFLICTS OF INTEREST: The authors have no conflicts of interest to declare.

FINANCING SUPPORT: This work has not received any contribution, grant or scholarship.

CONFIDENTIALITY OF DATA: The authors declare that they have followed the protocols of their work center on the publication of data from patients.

CONFLITOS DE INTERESSE: Os autores declaram não ter qualquer conflito de interesse na realização do presente trabalho.

PROTEÇÃO DE PESSOAS E ANIMAIS: Os autores declaram que os procedimentos seguidos na elaboração do presente trabalho estão em conformidade com as normas das comissões de investigação clínica e de ética, bem como da declaração de Helsínquia e da Associação Médica Mundial.

FONTES DE FINANCIAMENTO: Não houve qualquer fonte de financiamento na realização do presente trabalho.

CONFIDENCIALIDADE DOS DADOS: Os autores declaram ter seguido os protocolos da sua instituição acerca da publicação de dados de doentes.

REFERENCES

1. Simon N, Young J. Folate and depression—a neglected problem. Psychiatry Neurosci. 2007;32:80-2.
2. Lazarou C, Kapsou M. The role of folic acid in prevention and treatment of depression: an overview of existing evidence and implications for practice. Complement Ther Clin Pract. 2010;16:161-6.
3. Alpert J, Fava M. Nutrition and depression: the role of folate. Medscape Psychiatry Mental Health eJ. 1997;2 [accessed 2016 Mar 1]. Available: http://www.medscape.com/viewarticle/431514.
4. Lerner V, Kanevsky M, Dwolatzky T, Rouach T, Kamin R, Miodownik C . Vitamin B12 and folate serum levels in newly admitted psychiatric patients. Clin Nutr. 2006;25:60-7.
5. Trujillo F, Raya J, Monzón J, Rodriguez-Martos T, Salinas M, Martin-Santos T, et al. Serum folate, vitamin B12, and homocysteine in acute patients with schizophrenia, depression, or bipolar disorder. Eur Neuropsychopharmacol. 2009; 19:S344-5.
6. Gilbody S, Lightfoot T, Sheldon T. Is low folate a risk factor for depression? A meta-analysis and exploration of heterogeneity. Epidemiol Community Health. 2007;61:631-7.
7. Wang D, Zhai JX, Liu DW. Serum folate levels in schizophrenia: a meta-analysis. Psychiatry Res. 2016;235:83-9.