GSC Advanced Research and Reviews

eISSN: 2582-4597 CODEN (USA): GARRC2

Cross Ref DOI: 10.30574/gscarr

Journal homepage: https://gsconlinepress.com/journals/gscarr/

(RESEARCH ARTICLE)

Check for updates

Evaluation of nitric oxide and uric acid in patients with headache

Asmaa Hamza Radeef *

Department of Clinical Biochemistry, Hammurabi College of Medicine, University of Babylon, Babylon, Iraq.

GSC Advanced Research and Reviews, 2025, 22(02), 138-141

Publication history: Received on 08 January 2025; revised on 15 February 2025; accepted on 18 February 2025

Article DOI: https://doi.org/10.30574/gscarr.2025.22.2.0058

Abstract

Backgrounds: Headache, a painful sensation in the head or neck, can be categorized as primary, tension-type, and cluster headaches. Factors influencing nitric oxide levels, such the eNOS gene mutation and uric acid, may result in endothelial dysfunction. This study intends to evaluate these parameters.

Objectives: Assess the factors that may affect the levels of nitric oxide, which is the main mediator of endothelial dysfunction.

Material and Methods: The study includes 40 individuals who suffer from headaches and 40 healthy volunteers who are matched in terms of age and gender. eNOS enzyme concentration, as well as the measurement of blood levels of nitric oxide and uric acid.

Results: The headache group exhibited a substantially decreased serum nitric oxide concentration ($P < 0.05$) than the control group. Additionally, the serum uric acid level in the headache group is significantly lower than that of the control group.
In the headache group, there was a substantial positive correlation between the serum level of NO and the serum uric acid concentration ($r = 0.307$, $P < 0.01$).

Conclusion: The study suggests a role of endothelial dysfunction in the pathogenesis of migraine with the GG genotype of eNOS gene as a distinct risk factor for developing migraine.

Keywords: Headache; Endothelial Nitric Oxide Synthase; Nitric Oxide; Uric Acid And Endothelial Dysfunction

1. Introduction

Headache is a symptom that is indicative of discomfort in the head or neck region [1]. It is generally classified into primary headaches, which include tension-type headache, migraine, and cluster headache, and secondary headache disorders [2]. Primary headaches are not associated with any identifiable pathology.

The level of endothelial derived NO can be affected by several factors, of which transition point mutation on seventh exon (G894T, rs1799983) in the eNOS gene, and this is related to depression in the production of NO [3]. Uric acid was reported to inhibit the production of NO and may confer endothelial dysfunction in hyperuricemic individuals [4].

The primary objective of this study is to assess the factors that may affect the levels of nitric oxide, which is the main mediator of endothelial dysfunction.

* Corresponding author: Asmaa Hamza Radeef

Copyright © 2025 Author(s) retain the copyright of this article. This article is published under the terms of the Creative Commons Attribution Liscense 4.0.

2. Subjects and Methods

The study comprised a total of 80 participants, with 40 serving as control subjects and 40 experiencing headaches. The control group consisted of forty healthy persons devoid of chronic illnesses, matched to the patient groups by age and gender.

After elucidating the study objectives and obtaining written informed consent from all participants, we commenced the collection of baseline demographic and clinical data by interviews utilizing the study questionnaire. The questionnaire encompassed information regarding medical history, familial headache history, medication usage, tobacco consumption, and alcohol intake. Blood pressure (systolic and diastolic), weight, and height (for the calculation of body mass index). The study utilized many measurements to examine the attributes of headaches, including the age of onset. The primary criterion employed in this study to assess headache severity is the Headache Impact Test (HIT-6), a questionnaire with predetermined scores for each response. Individuals with hypertension, diabetes mellitus, renal or hepatic problems, previous stroke or transient ischemic attack, myocardial infarction, systemic lupus erythematosus, tobacco use, sickle cell anemia, or women undergoing estrogen or progesterone therapy were excluded from this study.

3. Methodology

3.1. Collection of the blood

Blood samples were obtained from both patient and control subjects using 5 mL disposable syringes while they were seated. The blood in the tubes containing gel was allowed to coagulate at ambient temperature for 10-15 minutes. The sample was subsequently centrifuged at 2000 × g for roughly 10 to 15 minutes. The resultant sera were aliquoted and preserved at -20˚C until analysis was conducted.

3.2. Determination of serum nitric oxide level

The nitrate and nitrite contents of a specific sample were measured using the Total Nitric Oxide Assay Kit. The traditional Griess reagent was used to detect both the nitrates and the total amount of nitrite after nitrate reductase transformed the nitrate in the sample into nitrite [5].

3.3. Determination of serum level of Uric acid

Uric acid was measured by uricase method as prescribed earlier by Carl and Edward [6].

4. Results

The student's t-test of the study subjects' demographic features showed non-significant statistical differences between migraine and headache group regarding gender distribution, age, BMI as shown in table 1.

Table 1 Demographic features of the study groups

	Headache	**Control**	**P value**
Men	15 (34 %)	14 (36 %)	0.82
Women	25 (32 %)	26 (31 %)	
Age (years)	34.45 ± 7.2	37.15 ± 8.3	0.063
BMI (kg/m2)	22.56 ± 2.73	24.34 ± 2.9	0.09

4.1.1. BMI: body mass index

The level of study parameters in the control and headache groups was illustrated in table 2. In comparison to the control group, the headache group exhibited a substantially reduced serum concentration of nitric oxide ($P < 0.05$).

Additionally, the serum uric acid level in the headache group is significantly lower than that of the control group.

Table 2 the mean ±SD in the level of study biochemical parameters in headache and control groups

Parameter	Group	N	Mean ± SD	95% CI
Serum conc. of NO (µM)	Headache group	40	65.44 ± 19.10 *	56.25 – 71.69
	Control group	40	79.11 ± 19.39	72.91 - 85.32
Serum conc. of uric acid (µM)	Headache group	40	6.02 ± 2.3 *	4.7 – 6.6
	Control group	40	8.5 ± 3	– 9.5

Significant difference according to t-test between headache group versus control group; * P < 0.05

Pearson's correlations were implemented to assess potential correlations between biochemical parameters. The serum level of NO and serum uric acid concentration in the headache group exhibited a significant positive correlation (r =0.307, P <0.01), as illustrated in Figure 1.

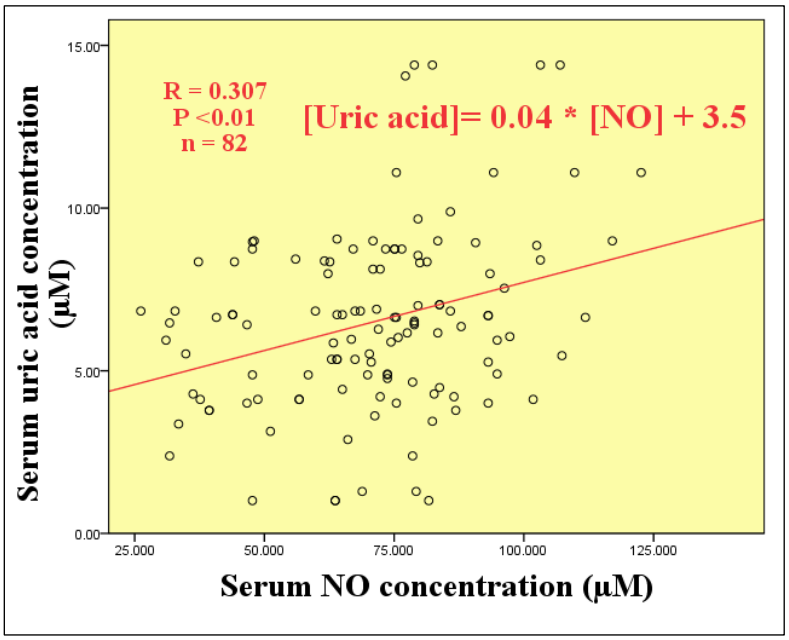

Figure 1 Correlation between serum uric acid values and serum level of nitric oxide (NO) in headache group

5. Discussion

Nitric oxide is recognized as a powerful naturally occurring substance that widens blood vessels, and it plays a role in transmitting and increasing sensitivity to pain. The pathophysiology of migraine is intricately involved in its development, resulting in an instant headache in all individuals with migraines and occasionally in those who are healthy. Furthermore, the freed nitric oxide (NO) plays a crucial role in the hemodynamic alterations associated with cortical spreading depression (CSD) [7]. Migraine patients exhibit a heightened sensitivity to nitric oxide (NO) in their arteries. Furthermore, NO plays a regulatory function in the production of neuropeptides, such as calcitonin gene-related peptide, by commencing a neurogenic inflammatory process [8].

A hypothesis suggesting that blood vessels in migraine sufferers may be overly sensitive to nitric oxide (NO) due to a lack of functional autonomic regulation is postulated and supported by studies that describe an elevated cerebrovascular reactivity to hypercapnia [9]. Silva et al. observed that endothelial function and vascular responsiveness to NO were within the usual range [10].

6. Conclusion

The low serum level of nitric oxide results from low serum level of endothelial nitric oxide synthase and the well positively correlated serum level of endothelial nitric oxide synthase with IMT and FMD predict a role of endothelial dysfunction in reducing the NO serum level.

Compliance with ethical standards

Disclosure of conflict of interest

Author declared that there are no conflicts of interest.

Statement of ethical approval

The Ethical Committee in Hammurabi College of Medicine authorized the protocol.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

References

[1] Stovner LJ, Hagen K, Jensen R, Katsarava Z, Lipton RB, Scher AI, Steiner TJ, Zwart JA. The global burden of headache: a documentation of headache prevalence and disability worldwide. Cephalalgia. 2007 Mar;27(3):193-210.

[2] Turner DP, Smitherman TA, Black AK, Penzien DB, Porter JA, Lofland KR, Houle TT. Are migraine and tension-type headache diagnostic types or points on a severity continuum?: an exploration of the latent taxometric structure of headache. Pain. 2015 Jul;156(7):1200.

[3] Toriello M, Oterino A, Pascual J, Castillo J, Colás R, Alonso-Arranz A, Ruiz-Alegría C, Quintela E, Montón F, Ruiz-Lavilla N. Lack of association of endothelial nitric oxide synthase polymorphisms and migraine. Headache: The Journal of Head and Face Pain. 2008 Jul;48(7):1115-9.

[4] Khosla UM, Zharikov S, Finch JL, Nakagawa T, Roncal C, Mu W, Krotova K, Block ER, Prabhakar S, Johnson RJ. Hyperuricemia induces endothelial dysfunction. Kidney international. 2005 May 1;67(5):1739-42.

[5] Miles AM, Wink DA, Cook JC, Grisham MB. Determination of nitric oxide using fluorescence spectroscopy. InMethods in enzymology 1996 Jan 1 (Vol. 268, pp. 105-120). Academic Press.

[6] Carl A, Edward R. Tietz text book of clinical Biochemistery and Molecular Diagnostics; 4th.

[7] Myers DE. Potential neurogenic and vascular roles of nitric oxide in migraine headache and aura. Headache: The Journal of Head and Face Pain. 1999 Feb;39(2):118-24.

[8] Holzer P, Jocic M. Cutaneous vasodilatation induced by nitric oxide-evoked stimulation of afferent nerves in the rat. British journal of pharmacology. 1994 Aug;112(4):1181.

[9] Müller M, Marziniak M. The linear behavior of the system middle cerebral artery flow velocity and blood pressure in patients with migraine: lack of autonomic control?. Stroke. 2005 Sep 1;36(9):1886-90.

[10] Silva FA, Rueda-Clausen CF, Silva SY, Zarruk JG, Guzmán JC, Morillo CA, Vesga B, Pradilla G, Florez M, López-Jaramillo P. Endothelial function in patients with migraine during the interictal period. Headache: The Journal of Head and Face Pain. 2007 Jan;47(1):45-51.