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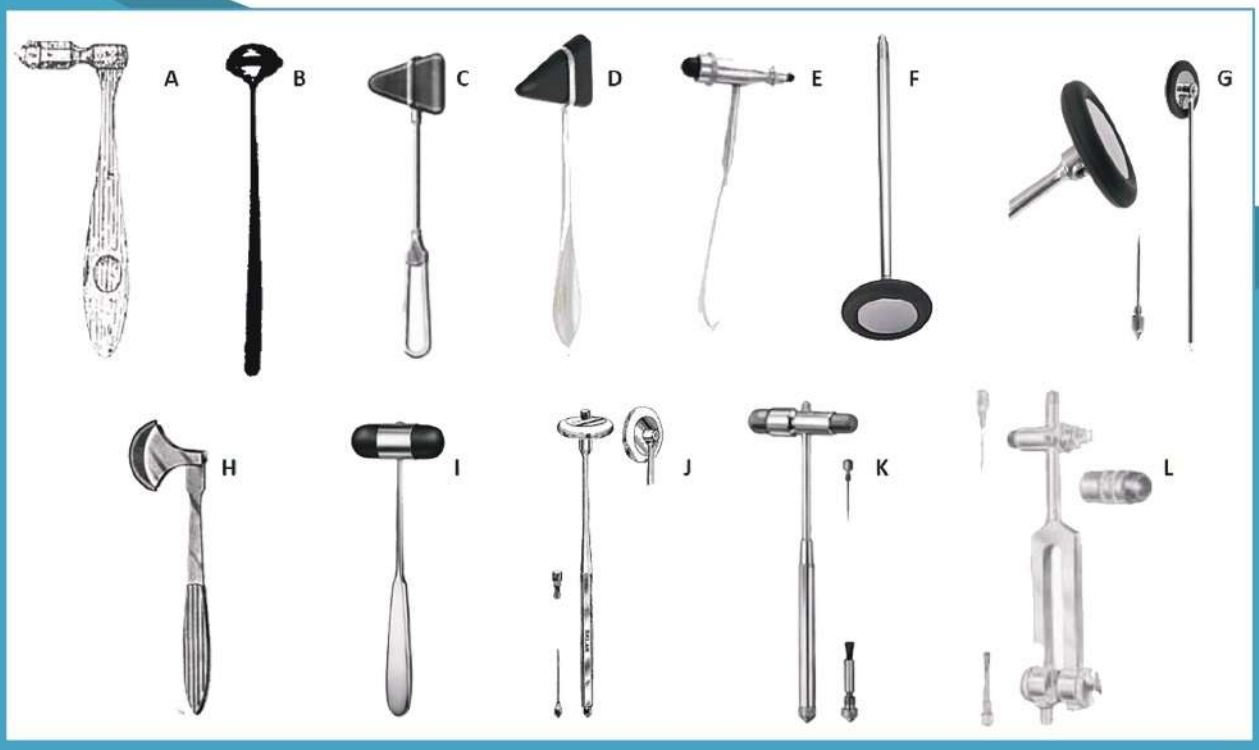
# Headache Medicine

SOCIEDADE BRASILEIRA DE CEFALEIA
*Brazilian Headache Society*



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# Headache Medicine

## Scientific Publication of the Brazilian Headache Society

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## CONTENTS

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## CONSELHO EDITORIAL



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# Sociedade Brasileira de Cefaleia – SBCe
## filiada à International Headache Society – IHS

Av. Tenente José Eduardo n° 453, sala 203
27323-240 Barra Mansa - RJ - Brasil
Fone:+55 (24) 9 8847-9980 www.sbcefaleia.com.br
secretaria@sbcefaleia.com.br
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# Do we know all the triggers of migraine?

## Conhecemos todos os gatilhos da enxaqueca?

Raimundo Pereira Silva-Néto [1]

Scientific Editor, Headache Medicine [1]

Migraine trigger is understood as any factor that is temporally associated with the development of migraine attacks. These triggers can be single or multiple for the same patient. In order to study these triggers, a recent meta-analysis analyzed 85 published articles and found 420 unique triggers that triggered headache attacks in only 86% of migraine patients[1].

Some of these triggers are noteworthy, such as odors. In an experimental study, Silva-Néto et al[2] exposed two groups of patients, one with migraine; and another with other primary headaches. Headache attacks were triggered by odor only in patients with migraine, corresponding to 34.7% of the sample, but in none with other primary headaches.

When studying the triggers, we must look at some of their particularities. First, the frequency with which they are found, for example, stress, odor, prolonged fasting or sleep deprivation are cited by most migraine patients. Second, the potency of causing pain, that is, the likelihood of the patient having a headache attack after exposure. Investigating triggers and clarifying the patient is critical. When he/she identifies any trigger of his pain, there will be a change in behavior in response to that factor[3].

What is the percentage of migraine attacks that occur without any triggers? This is a frequent question from neurologists and patients. According to the meta-analysis shown, 14% of patients did not identify any triggers[1]. We do not yet know if there are migraine attacks in the absence of any triggering factors or if these factors are unknown.

Is the patient able to identify all triggering factors of their migraine attacks? Would neuronal hyperexcitability make the patient more vulnerable to external and internal factors? There are many unanswered questions. Therefore, future studies need to be conducted to clarify these doubts.

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***Correspondence**
Raimundo Pereira Silva-Néto
Universidade Federal do Delta do Parnaíba, Avenida São Sebastião, 2819, Fátima, Parnaíba, PI, 64001-020, Brasil.
Tel. + 55 3237-2104.
E-mail: neurocefaleia@terra.com.br

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# The impact of anxiety and depression on migraine patients' journey to a tertiary headache center

## Impacto da ansiedade e depressão na jornada dos pacientes com enxaqueca a um centro de cefaleia terciário

Érica C Santos [1,2]
Juliane P P Mercante, PhD [3]
André M S Silva, MD [4]
Rosana T Miyazaki [5]
Pamella F Daud [2]
Arao B Oliveira, PhD [3]
Mario F P Peres, PhD [1,3]

[1] Universidade de São Paulo, Faculdade de Medicina, Instituto de Psiquiatria, São Paulo, Brazil.
[2] Universidade de São Paulo, Faculdade de Neurociência e Comportamento, Instituto de Psicologia, São Paulo, Brazil.
[3] Hospital Israelita Albert Einstein, São Paulo, Brazil.
[4] Universidade de São Paulo, Faculdade de Medicina, Departamento de Neurologia São Paulo, Brazil.
[5] Universidade de São Paulo, Faculdade de Medicina, Instituto de Psiquiatria, São Paulo, Brazil.

## ABSTRACT

**Objective:** To evaluate the role of psychiatric comorbidity in the number of diagnostic procedures, acute and preventive pharmacological treatments, and non-pharmacological interventions in migraine patients experienced before visiting a tertiary headache center in São Paulo, Brazil. **Methods:** We conducted a retrospective, observational study of 465 consecutive patients diagnosed with migraines and evaluated in a specialized tertiary headache center in São Paulo, Brazil. We collected the data based on medical chart reviews and a self-administered questionnaire routinely performed during the first medical visit. Two standardized instruments were used for the diagnosis of depression and anxiety, respectively: the Patient Health Questionnaire-9 (PHQ-9) and the Generalized Anxiety Disorder (GAD-7). **Results:** We studied 465 patients diagnosed with migraines. The patients' mean age was 37.3 years (313.1), and 72.7% of patients were women. The average age of headache onset was 17.1 years (311.4) before the first appointment at our tertiary headache center, and 51.7% of patients had chronic migraines. Most patients (65.8%) had a PHQ-9 ≥ 5, indicating at least some depressive symptoms, whereas 152 patients (34.2%) were considered depressed (PHQ-9 ≥ 9). Anxiety symptoms were observed in 68.2% of patients based on the GAD-7 instrument, and 209 patients (47.0%) were diagnosed with anxiety (GAD-7 ≥ 8). Chronic migraines were more common than episodic migraines among patients with psychiatric comorbidity: 63.2% of depressive patients, 61.2% of anxious patients, and 43.5% of patients without any psychiatric disorder. Most patients underwent laboratory tests and brain imaging (62.4% and 70.5%, respectively) in a similar proportion among subgroups with and without anxiety or depression. Non-pharmacological treatment was frequent in all subgroups, and 342 patients (73.5%) performed at least one modality. Overall, acupuncture was the most common non-pharmacological treatment (55.2% of patients), and we found no difference between the subgroups. Depressive and anxious patients more frequently underwent psychotherapy (54.2% and 50.8%, respectively) when compared to patients with neither depression nor anxiety (34.7%). Depression was associated with a reduced likelihood of previous physiotherapy (OR 0.39, CI 0.16 – 0.99). Patients with severe anxiety used 10.7 times more medicines than non-severe patients. **Conclusion:** Depressed patients underwent more psychotherapy than non-depressed patients, although they had a reduced chance of previous physiotherapy. Anxiety was also associated with previous psychotherapy and a risk of 10.7 times of using acute pharmacological treatment, which may lead to issues related to analgesic abuse. Anxiety and depression affect the journey of patients with migraines before arriving at a tertiary headache center.

**Keywords:** Migraine; Headache; Anxiety; Depression; Psychiatric Comorbidity.

***Correspondence**
Mario Fernando Prieto Peres
E-mail: marioperes@usp.br

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## RESUMO

**Objetivo:** Avaliar o papel da comorbidade psiquiátrica no número de procedimentos diagnósticos, tratamentos farmacológicos agudos e preventivos e intervenções não farmacológicas em pacientes com enxaqueca experimentados antes de visitar um Centro Terciário de Cefaleia em São Paulo, Brasil. **Métodos:** Realizamos um estudo retrospectivo observacional de 465 pacientes consecutivos diagnosticados com enxaqueca e avaliados em um centro especializado em cefaleia terciária em São Paulo, Brasil. Coletamos os dados com base em revisões de prontuários médicos e em um questionário autoaplicado rotineiramente realizado durante a primeira consulta médica. Dois instrumentos padronizados foram utilizados para o diagnóstico de depressão e ansiedade, respectivamente: o Questionário de Saúde do Paciente-9 (PHQ-9) e o Transtorno de Ansiedade Generalizada (GAD-7). **Resultados:** Foram estudados 465 pacientes com diagnóstico de enxaqueca. A idade média dos pacientes foi de 37,3 anos (3 13,1) e 72,7% dos pacientes eram mulheres. A idade média do início da dor de cabeça foi de 17,1 anos (3 11,4) antes da primeira consulta em nosso Centro Terciário de Cefaleia, e 51,7% dos pacientes apresentavam enxaqueca crônica. A maioria dos pacientes (65,8%) apresentou um PHQ-9 ≥ 5, indicando pelo menos alguns sintomas depressivos, enquanto 152 pacientes (34,2%) foram considerados deprimidos (PHQ-9 ≥ 9). Os sintomas de ansiedade foram observados em 68,2% dos pacientes com base no instrumento GAD-7, e 209 pacientes (47,0%) foram diagnosticados com ansiedade (GAD-7 ≥ 8). As enxaquecas crônicas foram mais comuns que as enxaquecas episódicas em pacientes com comorbidade psiquiátrica: 63,2% dos pacientes depressivos, 61,2% dos ansiosos e 43,5% dos pacientes sem nenhum transtorno psiquiátrico. A maioria dos pacientes foi submetida a exames laboratoriais e imagens cerebrais (62,4% e 70,5%, respectivamente) em proporção semelhante entre os subgrupos com e sem ansiedade ou depressão. O tratamento não farmacológico foi frequente em todos os subgrupos e 342 pacientes (73,5%) realizaram pelo menos uma modalidade. No geral, a acupuntura foi o tratamento não farmacológico mais comum (55,2% dos pacientes), e não encontramos diferença entre os subgrupos. Pacientes depressivos e ansiosos foram submetidos a psicoterapia com mais frequência (54,2% e 50,8%, respectivamente) quando comparados aos pacientes sem depressão nem ansiedade (34,7%). A depressão foi associada a uma probabilidade reduzida de fisioterapia prévia (OR 0,39, IC 0,16 - 0,99). Pacientes com ansiedade grave usavam 10,7 vezes mais medicamentos do que pacientes não graves. **Conclusão:** Pacientes deprimidos foram submetidos a mais psicoterapia do que pacientes não deprimidos, embora tivessem uma chance reduzida de fisioterapia anterior. A ansiedade também foi associada à psicoterapia anterior e a um risco de 10,7 vezes do uso de tratamento farmacológico agudo, o que pode levar a questões relacionadas ao abuso de analgésicos. Ansiedade e depressão afetam a jornada de pacientes com enxaqueca antes de chegarem a um Centro Terciário de Cefaleia.

**Descritores:** Enxaqueca, Dor de Cabeça, Ansiedade, Depressão, Comorbidade Psiquiátrica.

## INTRODUCTION

Migraine is a common chronic neurological disease and a leading cause of disability worldwide, affecting daily and social activities (1). In a study on the global burden of disease, migraine had an average prevalence of 14% and was the second highest contributor of DALYs (disability-adjusted life-years) (2). In Brazil, the population-based prevalence of migraine varies from 10.7% to 22.1% (3), and in tertiary care centers, migraines represent 38% of all headaches (4).

Anxiety and mood disorders are the psychiatric comorbidities most often associated with migraines. These conditions are 2 to 10 times more common in patients with migraines than in the general population, which increases the complexity of their medical management (5, 6). Patients with migraines and comorbid anxiety and/or depression experience higher medical costs when compared to patients with no comorbidities (7) due to resource utilization, including medical visits, diagnostic tests, and therapeutic interventions (8, 9). Additionally, migraineurs are less optimistic and more pessimistic than non-migraneurs, which may also influence their medical care seeking (10).

Patients with anxiety use health care services for medical consultations, emergencies, and examinations more often than individuals without mental disorders (12.5 3 8.1 vs. 2.4 3 2.6 visits/year) (11). In earlier surveys, anxiety and mood disorders were consistently associated with substantial impairments in both productive roles (e.g., work absenteeism, work performance, unemployment, and underemployment), social roles (e.g., social isolation, interpersonal tensions, and marital disruption) (12, 13), and greater stigma (14). Stigma is a significant aspect of mental and neurological conditions (15). It is a process involving labeling, separation, knowledge and emphasis of stereotypes, prejudice, and discrimination in the context in which power is exercised over disadvantaged members of a social group (16).

Tertiary headache centers usually manage more difficult patients, including those with medical and psychiatric comorbidities (5). Information regarding the patient journey to a specialty headache care center is

limited, and the influence of psychiatric comorbidity on the migraine patient journey is unknown.

In this study, we aimed to assess the role of psychiatric comorbidity on the number of diagnostic procedures, preventive and acute pharmacological treatments, and non-pharmacological interventions migraine patients experienced before visiting a tertiary headache center, in São Paulo, Brazil. We hypothesized that anxiety and depression increase the number of previous diagnostic tests and treatment experiences.

# METHODS

## Study design

We conducted a retrospective, observational study of 465 consecutive patients with migraine diagnoses based on the International Classification of Headache Disorders – 3rd edition (ICHD-3). The patients were evaluated in a specialized tertiary headache center from March to July 2017, in São Paulo, Brazil. We collected the data through medical chart reviews and a self-administered questionnaire routinely used during initial medical visits. The study was conducted in accordance with local laws and was approved by the local ethics committee.

## Eligibility criteria

Inclusion criteria were adult patients of both sexes over 18 years of age who were undergoing initial consultations at a tertiary headache center in São Paulo. Exclusion criteria included patients under 18 years, patients unable to provide reliable information, and patients with significant cognitive deficits or associated dementia.

## Patient characteristics

We collected the following patient characteristics: sociodemographic variables, headache characteristics, previous diagnostic methods, clinical history, and treatments previously used. Additionally, we used two standardized instruments to diagnose depression and anxiety, respectively: the Patient Health Questionnaire-9 (PHQ-9) and Generalized Anxiety Disorder (GAD-7).

## Instruments and variable definitions

We defined patients with chronic migraines as having headaches more than 15 days per month for at least 3 months; patients with episodic migraines had headaches fewer than 15 days per month.

To evaluate previous diagnostic methods qualitatively, we asked patients if they had undergone at least one of the following: laboratory test, cranial computed tomography, cranial magnetic resonance, electroencephalogram, and polysomnography.

Regarding previous treatments, we asked patients if they had undergone at least one of the following: acupuncture, psychotherapy, physiotherapy, botulinum toxin, meditation, preventive medicines, and acute medicines.

We defined depression based on the Patient Health Questionnaire–9 (PHQ-9), which is designed for use with adults to assess and monitor the severity of depression according to the Diagnostic and Statistical Manual of Mental Disorders (17) and International Classification of Diseases, 10th Edition, diagnostic criteria (ICD-10) (18, 19). The PHQ-9 includes nine items that evaluate symptoms related to depressed mood, anhedonia (loss of interest or pleasure in doing things), problems with sleep, tiredness or lack of energy, change in appetite or weight, feelings of guilt or uselessness, concentration problems, feeling slow or restless, and suicidal thoughts. Final scores are calculated by adding each response ("not all," "several days," "more than half the days," and "almost every day") and are classified into five depression severity groups: 0-4: none; 5-9: mild; 10-14: moderate; 15-19: moderately severe; 20-27: severe. However, based on a previous Brazilian study that defined a score of 9 as the best point of accuracy, and to assess depression as a dichotomized variable, we divided the patients into two groups: with depression if their PHQ-9 scores were greater than or equal to 9, and without depression if their scores were less than 9 (20).

Anxiety was defined based on the Generalized Anxiety Disorder (GAD-7) scale, which consists of seven items arranged on a 4-point Likert scale (0: not at all; 1: several days; 2: more than half the days; 3: nearly every day). Final scores are divided into four groups: 0-4: minimal or no anxiety; 5-9: mild; 10-14: moderate; 15-21: severe. (21). In our study, we consider a GAD-7 score greater than or equal to 8 an anxiety diagnosis.

## Statistical analysis

For subgroup comparison in a univariate analysis, we used the qui-square test or Fisher's exact test. To identify variables independently related to depression and anxiety symptoms, we categorized patients in four steps. Initially, we defined two groups: patients with depression and patients without depression. Next, we performed a logistic regression to identify association of previously performed exams and previously used treatments with both groups. We then categorized patients as having anxiety or not, and performed a new logistic regression to study the same variable's association with anxiety. Finally, we performed a third logistic analysis to consider the severe anxiety and severe depression subgroups. We used IBM SPSS Statistics version 25 software (IBM, Armonk, New York, USA) and considered a two-sided $P < 0.05$ statistically significant.

# RESULTS

## Sample characteristics

We studied 465 patients with migraine diagnosis; their characteristics are summarized in Table 1. Their mean age was 37.3 years (313.1), and 72.7% of patients were women. The patients' average age at headache onset was 17.1 years (311.4) before the first appointment

**Table 1.** Patients characteristics with migraine.

| Sociodemographic and clinical characteristics | N or years | % or SD |
|---|---|---|
| Age (Mean 3 SD, n=462) | 37.3 | 13.1 |
| Duration of migraine in years (Mean 3 SD, n=462) | 17.2 | 11.4 |
| Gender (n=462) | | |
| Men | 126 | 27.3 |
| Women | 336 | 72.7 |
| Religion (n=239) | | |
| Yes | 204 | 85.4 |
| Without religion | 35 | 14.6 |
| Migraine type | | |
| Chronic | 240 | 51.7 |
| Episodic | 224 | 48.3 |
| Patient Health Questionnaire - 9 (PHQ-9) (n=445) | | |
| Minimal or none (score 0-4) | 152 | 34.2 |
| Mild (score 5-9) | 152 | 34.2 |
| Moderate (score 10-15) | 75 | 16.9 |
| Moderately severe (score 15-19) | 35 | 7.9 |
| Severe (score 20-27) | 31 | 7.0 |
| General Anxiety Disorder - 7 (GAD-7) (n=445) | | |
| None (score 0-4) | 139 | 31.2 |
| Mild (score 5-9) | 144 | 32.4 |
| Moderate (score 10) | 93 | 20.9 |
| Severe (score 15-21) | 69 | 15.5 |
| Final mood diagnosis (n=445) | | |
| Depression (PHQ-9≥9) | 152 | 34,2 |
| Anxiety (GAD-7≥8) | 209 | 47.0 |
| Depression and anxiety (PHQ-9≥9 and GAD-7≥8) | 131 | 28.2 |
| No depression or anxiety (PHQ-9<9 and GAD-7<8) | 237 | 50.9 |
| Medical comorbidities (n=465) | | |
| Rhinitis | 180 | 50.7 |
| Sinusitis | 175 | 49.3 |
| Gastritis | 173 | 48.7 |
| Kidney stone | 66 | 18.6 |
| Polycystic ovary | 58 | 16.3 |
| Hypertension | 39 | 11.0 |
| Endometriosis | 22 | 6.2 |
| Fibromyalgia | 21 | 5.9 |
| Any medical comorbities (n=465) | 355 | 76.3 |
| Tabacco use (n=435) | 30 | 6.5 |
| Alcohol use (n=465) | 214 | 46.0 |

SD: Standard deviation.

at our tertiary headache center, and 51.7% of patients had chronic migraines.

Most patients (65.8%) had a PHQ-9 ≥ 5, indicating at least some depressive symptoms, whereas 152 patients (34.2%) were considered depressed (PHQ-9 ≥ 9) (Table 1). Symptoms of anxiety were observed in 68.2% of patients, based on their GAD-7 scores, and 209 patients (47.0%) were diagnosed with anxiety (GAD-7 ≥ 8). Depression and anxiety were simultaneously diagnosed in 131 patients (28.2%), and 237 patients (50.9%) had neither anxiety nor depression. Other self-reported medical conditions were common: 76.3% of patients had comorbidities, such as gastritis, sinusitis, hypertension, kidney stones, fibromyalgia, and polycystic ovarian syndrome (Table 1).

We divided the patients into 4 subgroups: depression, anxiety, depression and anxiety, and neither depression nor anxiety. The characteristics evaluated in comparison were migraine type, previous diagnoses methods, and previous non-pharmacological and pharmacological treatments.

Chronic migraines were more common than episodic migraines among patients with psychiatric comorbidities: 63.2% of depressive patients, 61.2% of anxious patients, and 43.5% of patients without any mood disorder experienced chronic migraines (Table 2).

Most patients underwent laboratory tests and brain imaging (62.4 and 70.5%, respectively) in a similar proportion among subgroups with or without anxiety or depression (Table 2). One-third of patients underwent an electroencephalogram before first evaluation (Table 2).

Non-pharmacological treatment was frequent in all subgroups, and 342 patients (73.5%) performed at least one modality. Overall, acupuncture was the non-pharmacological treatment most commonly done (55.2% of patients) without difference between all subgroups. Depressive and anxious patients (54.2% and 50.8%, respectively) more frequently underwent psychotherapy compared to patients with neither depression nor anxiety (34.7%) (Table 2). We found no differences among the subgroups for other treatment modalities, such as physiotherapy, botulinum toxin, nerve blocks, and meditation.

Regarding pharmacological treatments, most patients in all subgroups used preventive and acute treatments (Table 2), although the proportion of acute medicine usage was slightly higher than that of preventive medicine, even in subgroups with mood disorders. Depressed patients took preventive medications more often compared to non-depressed patients (67.1% vs. 59.8%).

## Multivariate analysis

Logistic regression was performed to identify factors associated with depression and anxiety. Depressed patients were more likely to be female (OR 8.18, CI 2.82 – 23.75), had more chronic migraines (OR 4.25, 1.90-9.50), and had undergone more psychotherapy (OR 2.56, CI 1.15 – 5.66) than non-depressed patients (Table 3). In addition, depression was associated with a reduced likelihood of having previously undergone physiotherapy (OR 0.39, CI 0.16 – 0.99). Anxiety was also associated with female gender (OR 3.07, CI 1.36 – 6.95), chronic migraines (OR 3.91, CI 1.90 – 8.04), and previous psychotherapy (OR 2.18,

**Table 2.** Comparison based in the presence of anxiety and depression

| Patients (n=465) | Depression (D) N= 152 | | Anxiety (A) N=209 | | D + A N=131 | | Without D or A N=237 | | All patients N=465 | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | N | % |
| **Migraine Type*** | | | | | | | | | | |
| Chronic | 96/152 | 63.2 | 128/209 | 61.2 | 84/131 | 64.1 | 103/237 | 43.5 | 240 | 51.7 |
| Episodic | 56/152 | 36.8 | 81/209 | 38.8 | 47/131 | 35.9 | 134/237 | 56.5 | 224 | 48.3 |
| **Previous test** | | | | | | | | | | |
| Laboratory tests | 100/152 | 65.7 | 134/209 | 64.1 | 86/131 | 65.6 | 156/237 | 65.8 | 290 | 62.4 |
| Cranial CT | 92/152 | 60.5 | 130/209 | 62.2 | 85/131 | 64.9 | 130/237 | 54.9 | 260 | 55.9 |
| Cranial MRI | 94/152 | 61.8 | 126/209 | 60.3 | 84/131 | 64.1 | 133/237 | 56.1 | 259 | 55.7 |
| Cranial CT or MRI | 112/152 | 73.7 | 154/209 | 73.7 | 98/131 | 74.8 | 168/237 | 70.9 | 328 | 70.5 |
| EEG | 57/152 | 37.5 | 80/209 | 38.3 | 49/131 | 37.4 | 83/237 | 35.0 | 163 | 35.1 |
| **Non-pharmacological treatments** | | | | | | | | | | |
| Any non-pharmacological | 119/152 | 78.3 | 164/209 | 78.5 | 105/131 | 80.2 | 178/237 | 75.1 | 342 | 73.5 |
| Acupuncture | 81/141 | 57.4 | 117/196 | 59.7 | 73/122 | 59.8 | 116/226 | 51.3 | 233 | 55.2 |
| Psychotherapy* | 77/142 | 54.2 | 100/197 | 50.8 | 70/123 | 56.9 | 78/225 | 34.7 | 178 | 42.2 |
| Physiotherapy | 39/141 | 27.7 | 60/196 | 30.6 | 32/122 | 26.2 | 69/223 | 30.9 | 129 | 30.8 |
| Botulinum Toxin | 22/141 | 15.6 | 31/196 | 15.8 | 21/122 | 17.2 | 36/225 | 16.0 | 67 | 15.9 |
| Nerve Blockade | 35/141 | 24.8 | 44/196 | 22.4 | 28/122 | 23.0 | 47/224 | 21.0 | 91 | 21.7 |
| Meditation | 19/141 | 13.5 | 34/196 | 17.3 | 16/122 | 13.1 | 41/225 | 18.2 | 75 | 17.8 |
| **Pharmacological treatments** | | | | | | | | | | |
| Preventive medicines | 102/152 | 67.1 | 132/209 | 63.2 | 84/122 | 64.1 | 144/235 | 61.3 | 276 | 59.6 |
| Acute medicines | 103/152 | 67.8 | 139/209 | 66.5 | 88/131 | 67.2 | 150/235 | 63.8 | 289 | 62.4 |

* numbers in bold present results with difference statistically significant (p<0.05). D: Depression; A: Anxiety.

**Table 3.** Multivariate analysis for presence of depression

| Variables | B | Wald | OR | 95% Confidence interval | p-value |
|---|---|---|---|---|---|
| Age (years) | -0.05 | 5.34 | 0.95 | 0.92 – 0.99 | 0.021 |
| Female | 2.10 | 14.95 | 8.18 | 2.82 – 23.75 | 0.000 |
| Having religion | 0.60 | 1.41 | 1.82 | 0.68 – 4.88 | 0.235 |
| Disease duration (years) | 0.03 | 2.05 | 1.03 | 0.99 – 1.08 | 0.152 |
| Chronic migraine | 1.45 | 12.48 | 4.25 | 1.90 – 9.50 | 0.000 |
| Alcohol use | 0.49 | 1.62 | 1.63 | 0.77 – 3.46 | 0.202 |
| Tobacco use | 0.40 | 0.35 | 1.48 | 0.40 – 5.47 | 0.552 |
| Presence of any comorbidity | 0.35 | 0.46 | 1.42 | 0.51 – 3.92 | 0.499 |
| Cranial MRI | 0.44 | 1.04 | 1.55 | 0.67 – 3.60 | 0.308 |
| Cranial CT | -0.13 | 0.09 | 0.88 | 0.39 – 1.99 | 0.759 |
| Laboratory tests | -0.06 | 0.02 | 0.94 | 0.42 – 2.10 | 0.877 |
| EEG | ,0.14 | 0.11 | 1.16 | 0.50 – 2.69 | 0.737 |
| Acupuncture | 0.06 | 0.03 | 1.07 | 0.49 – 2.31 | 0.869 |
| Psychotherapy | 0.94 | 5.34 | 2.56 | 1.15 – 5.66 | 0.021 |
| Physiotherapy | -0.92 | 3.97 | 0.40 | 0.16 – 0.99 | 0.046 |
| Botulinum toxin | 0.29 | 0.30 | 1.34 | 0.47 – 3.78 | 0.582 |
| Nerve Blockade | -0.39 | 0.66 | 0.67 | 0.26 – 1.74 | 0.417 |
| Meditation | -0.82 | 2.77 | 0.44 | 0.17 – 1.16 | 0.096 |
| Preventive medicines | -0.71 | 2.16 | 0.49 | 0.19 – 1.27 | 0.141 |
| Acute medicines | 0.41 | 0.83 | 1.51 | 0.62 – 3.67 | 0.362 |

* numbers in bold present results with difference statistically significant (p<0.05)

CI 1.07 – 4.47). In addition, anxious patients were less likely to undergo laboratory tests (OR 0.40, CI 0.19 – 0.85).

Furthermore, we performed a logistic regression to determine whether severe depression (65 patients) and severe anxiety (69 patients) were associated with the same variables. We found that severe depression was also associated with chronic migraines (OR 4.72, CI 1.53 – 14.56) and female gender (OR 4.62, CI 13-18) and tended to be associated with previous psychotherapy (OR 2.72, CI 0.96-7.69). The inverse relationship between depression and previous physiotherapy was not found in the severe group. Severe anxiety was also associated with fewer laboratory tests (OR 0.23, CI 0.09 – 0.60) and chronic migraines (OR 3.15, CI 1.20 – 8.23). In addition, we found that severe anxiety patients used 10.7 times more acute medication than non-severe anxiety patients (OR 10.71, CI 2.60 – 44.08).

## DISCUSSION

In our study of migraine patients at a tertiary headache center, we found depressive symptoms in 65.8% of patients and a depression prevalence of 34.2%. The prevalence of anxiety was 47.0%, whereas 68.2% of patients had some anxiety symptoms. Anxiety and depression were present simultaneously in 28.2% of patients, (Table 1) and these conditions were strongly associated with chronic migraines and female gender. These results align with recent studies that reported high prevalence of the same psychiatric comorbidities in patients with chronic migraines (1, 5, 6, 22, 23). The analysis of previous patient journeys showed that depressive patients underwent more psychotherapy and less physiotherapy than non-depressed patients, whereas anxiety was associated with a higher probability of undergoing psychotherapy, but a lower probability of undergoing laboratory tests. Additionally, severe anxiety increased the risk of using acute medication by 10.7 times. Patients with migraines frequently have multiple medical visits before arriving at a tertiary center. Reported on primary care provided by non-specialists and found that headache patients had an average of 3 health care providers prior to consultation with a specialist, with an average of 11 years of pain duration (24). In our tertiary headache center, the mean headache duration was 17.1 years (311.4) before the first appointment, and most patients had already performed non-pharmacological treatments and used preventive medicine. Therefore, considering the high prevalence of mood symptoms in migraineurs, non-specialists should be trained in the management of psychiatric comorbidities in headache disorders to improve the patient journey.

Regarding ancillary tests performed during headache diagnosis, cranial computed tomography and magnetic resonance imaging permit the exclusion of certain secondary causes of headaches, such as brain masses and vascular diseases, but their usefulness is significantly reduced in patients with chronic headaches. We consider the previous cranial imaging undergone by 70% of our patients to be quite unwarranted, as is the high frequency of previous Electroencephalogram (EEG) (one-third of our patients had undergone at least one), which is usually unnecessary for migraine patients. A detailed evaluation of other symptoms indicative of secondary headaches should always be considered, so excessive and costly tests may be precluded in patients with evident migraine criteria unless other warning signs are present (25).

We expected more migraine patients with psychiatric comorbidities to have undergone diagnostic tests than those without comorbidities, as observed in previous reports (5, 26), but our study did not confirm these findings. This could be due to a trend among primary physicians of asking tests for most headache patients, regardless of psychiatric comorbidities. Another explanation is the fact that we did not quantify the number of tests performed, but asked the patients if they underwent a specific test at least once in the past. In addition, stigma may be an issue, as patients with anxiety or depression may not be evaluated adequately and may give up seeking a correct diagnosis. A finding that supports this hypothesis is that anxious patients in our study were less likely to undergo laboratory tests, although one would predict the opposite due to increased somatization and physical symptoms.

Non-pharmacological treatment was frequent; patients in all subgroups performed at least one modality. Interestingly, previous experience with psychotherapy was frequently a predictor of anxiety and depression in migraine patients. This could be explained by previous referrals from physicians or self-referrals to psychotherapy. More severe patients should have greater need for medication and non-pharmacological approaches, but in this case, we found only psychotherapy and, interestingly, reduced odds of undergoing physical therapy. The low probability of undergoing physical therapy could be due to kinesiophobia, a phenomenon related to the avoidance of physical therapy in the treatment of chronic pain, in patients with depression and anxiety (26, 27). Besides the overuse of health care services, anxiety and depression are both associated with significant psychological distress and poor health perception, whereas physical disability is only associated with depression and may corroborate the kinesiophobia (28).

We found no independent association between depression and a higher likelihood of using pharmacological treatment. One explanation for this lack of correlation may be the way we verified the use of medication. In our study, we did not quantify the number or duration of drugs previously tried, but evaluated these factors qualitatively (used or not used). However, we found a strong association between severe anxiety and acute medicine consumption. Higher anxiety levels could cause patients to seek more care and receive more preventive treatments, but patients may also use analgesics excessively due to cephalalgiaphobia, anticipatory anxiety, or compulsion (29). Severe anxiety patients used 10.7 times more acute medicines than non-severe anxiety patients. This is also in accordance with other studies' findings. Showed that analgesic consumption was greater in GAD patients with primary

headaches than in controls with primary headaches without GAD (11). Analgesics ingestion can occur prior to the onset of a headache due to anxiety, and evaluated the reasons for this behavior: 67% of patients reported difficulty coping with pain, 62% feared its emergence, and 45% consumed analgesics to reduce anxiety (30).

Our study has some limitations. First, it was an observational cross-sectional study based on medical charts and a retrospective self-reported questionnaire, so associations found may be not due to a cause–effect relationship. Second, patients were asked to remember all previously performed procedures, which can be influenced by reminder bias. Finally, we performed a single-center study. Thus, our study reflected a specific population, and selection bias may be have influenced our results.

## CONCLUSION

Anxiety and depression were common in migraine patients seen at a tertiary headache center, mostly in patients with chronic migraines. Depressed patients were often female, had more chronic migraines, and had undergone more psychotherapy than non-depressed patients, although they had a reduced chance of having previously undergone physiotherapy. Anxiety was also associated with female gender, chronic migraines, previous psychotherapy, and a risk of using acute pharmacological treatment that was 10.7 times higher than in other patient groups, which may lead to issues related to analgesic abuse. Anxiety and depression affect the journey of patients with migraines, probably beginning with primary care, and physicians, who routinely offer first-aid interventions, should be concerned with recognizing these mental disorders.

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# Application of thermal microcautery in migraine management

## Aplicação da microcauterização térmica no manejo da migrânea

Eleni Papageorgiou[1]
Konstantine Kovas[1]
Camillus Power[2]
Nikolaos Kostopoulos[3]

[1] Dept. of Neurology, General Hospital of Athens, G. Gennimatas, Greece.
[2] Dept. of Pain Medicine, Tallaght University Hospital, Dublin, Ireland.
[3] Holistic Health Centre, Athens, Greece

## ABSTRACT

Thermal microcautery is a novel minimally invasive intervention for migraine. We present a case series of twenty-one patients who underwent this technique. Nineteen patients reported improvement in migraine management. Of these four patients went on to complete remission and a further eleven patients reported over 50% improvement. In addition, the majority of patients noted reductions in intensity and duration of headache with a better response to medication. The efficacy of thermal microcautery generates a new hypothesis that attempts to explain how a neuromodulation technique may be helpful in the management of migraine.

**Keywords:** Thermal microcautery; Migraine; Neuromodulation.

## RESUMO

A microcauterização térmica é uma nova intervenção minimamente invasiva para enxaqueca. Apresentamos uma série de casos de vinte e um pacientes submetidos a essa técnica. Dezenove pacientes relataram melhora no tratamento da enxaqueca. Desses quatro pacientes, a remissão foi concluída e outros onze relataram mais de 50% de melhora. Além disso, a maioria dos pacientes observou reduções na intensidade e duração da dor de cabeça com uma melhor resposta à medicação aguda. A eficácia da microcauterização térmica gera uma nova hipótese que tenta explicar como uma técnica de neuromodulação pode ser útil no tratamento da enxaqueca.

**Descritores:** Microcauterização térmica, enxaqueca, neuromodulação.

***Correspondence**
Eleni Papageorgiou
E-mail: helenmorou@yahoo.gr

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## INTRODUCTION

Migraine is a highly disabling disease, with high financial and social impact (1). Migraine treatment can be both acute and preventive, several pharmacological classes can be effective, as also may non-pharmacological therapies (2,3). Nerve blocks, botulinum toxin type A, and neuromodulation may play an important role in the management of migraine (4).

A number of studies have come to light, showing that external stimulation of certain parts of the head, may contribute to the management of pain (5,6,7,8) Thermal microcautery have been used for the treatment of pain disorders, but limited information is available about its role in migraine treatment (9). We aimed in this study to present our experience in a case series of patients treated with thermal microcautery.

## METHODS

### Sample

Patients were selected from the Neurological Headache outpatient clinic of G.N.A. ''G. Gennimatas'', from November 2017 up to March 2019.

### Inclusion / exclusion criteria

The inclusion criteria were as follows –

1. Diagnosis of chronic migraine with or without aura and/or Medication Overuse Headache (MOH).
2. The failure of at least one preventive treatment.
3. Patients were not allowed to undergo Botox injections (10,11) Acupuncture and Transcutaneous Electrical Nerve Stimulation for at least 3 months.

### Technique description

In this technique we applied instantly intense heat (600° C) to an area of localized pain (2) identified by clinical examination before the procedure. The heat was applied by a low temperature cautery disposable fine tip pen, Fiab Disposable electrocautery pensF7255 (28 mm) which is routinely used in dermatology for microsurgery.

Thermal microcautery was performed on bilateral cervical, occipital, supraorbital and temporal areas, (12) depending on what patients referred to as the most painful points during the attack of migraine and also between acute attacks.

Post procedure a cooling cream was applied (1gr., Pistacia Lentiscus, Shorea robusta)

It was planned that each patient would undergo 4 sessions, every 7-10 days. Each patient had a recording of the frequency, duration, intensity of episodes of headache, medication use and response. We recorded the VAS pain score in each session.

The protocol of the study had been submitted to the Hospital's Ethical Committee and had been approved. All patients were fully informed about the aim of the study, the procedure and the complications and had filled out a consent form.

## RESULTS

Twenty-one patients have completed the study over a two-month period with follow-up on all patients for six months (twenty female patients – one male). The age ranged from 37 to 68 years old (average 51.1 years old). All of them had received at least one preventive therapy: six patients used propranolol, twelve topiramate, three valproic acid, five flunarizine, four amitriptyline, thirteen SSRIs-SNRIs, five botulinum-A. Additional, five patients had undergone Acupuncture and two used cannabis oil on a daily basis. None of them had undergone any invasive therapy or used anti-CGRP antibodies.

Fourteen patients used triptans at the acute phase of the episode, all of them paracetamol and/or NSAIDs and two Cephaly.

Fifteen of twenty-one patients had a combined diagnosis of migraine and MOH.

Nineteen of twenty-one patients reported overall improvement of their symptoms.

Four patients reported complete remission of their migraine which has persisted for six months.

Eleven patients reported over 50% improvement (reduction in the frequency, intensity and/or duration of headaches) and four patients reported a 30% improvement.

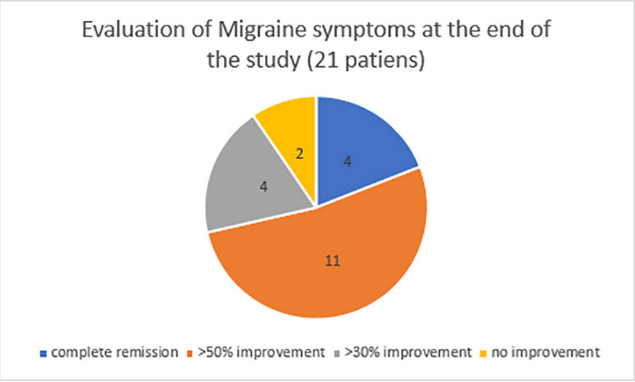


**Figure 1.** Pie graph of evaluation of Migraine symptoms at the end of the study (21 patients)

15 patients out 19 who reported improvement, recorded a reduction in the frequency of episodes, 16 a reduction in the intensity of the pain, 9 a reduction in the duration of each episode.

15 patients noted a better response to the drugs administered at the acute phase of pain,

Five patients were able to stop their preventive treatment in six months.

Patients tolerated the procedure well including application of the cooling cream. Five patients

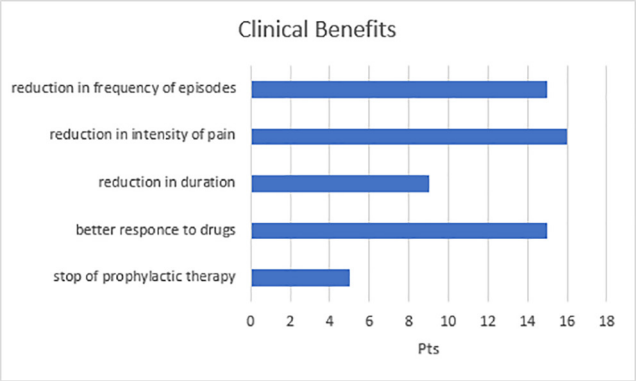


**Figure 2.** Bar graph of the clinical benefits of treatment.

experienced relief of migraine immediately following the procedure.

The mild burn after the application of cauterization was healed in 2-3 days, leaving no aesthetic marks. No skin reactions appeared.

## DISCUSSION

The present study shows promising results with thermal microcautery in migraine preventive treatment, due to its efficacy and tolerability (13).

Explanations for our findings may include the theory of the distorted communication within the trigeminocervical complex. A possible pathophysiological mechanism of action is the modification of the perception of pain through peripheral stimulation (1,14) in the regions of distribution of trigeminal and occipital nerves (12,15). Through the anatomical and functional convergence of these nerve endings, a wider distribution of the stimulus is supposed to trigger centrifugal pathways that regulate pain (16). It is known that stimulation of the occipital nerves regulates the activity of sensory neurons in the trigeminocervical complex; so, stimulation of the trigeminal nerve as well, is supposed to have the same effect. Its branches in the trigeminal divisions and C1 and C2 dermatomes (9) converge with sensory fibers of the dura mater and share the same receptive field. Thus, it is possible that an extracranial stimulation such as thermal microcautery can also modify the activity of the sensory fibers of the dura.

Migraine originates in a distorted communication within a complex neural network which leads to the well described neuro-vascular cascade of events (17). We hypothesize that a thermal microcautery stimulus resets this network restoring its natural homeostasis.

The study has several limitations, first it is not controlled by a sham procedure or other treatment as a comparator. A baseline phase before the treatment performed has not been performed, so a possible recall bias may affect our results.

Conclusion

Thermal microcautery is a promising therapy for migraine, further randomized clinical studies are necessary to confirm its efficacy

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# Cefaleia Dialítica Associada à Cefaleia por Privação de Cafeína em Pacientes Submetidos à Hemodiálise

## Dialysis Headache Associated with Caffeine-Withdrawal Headache in Patients Undergoing Hemodialysis

Edarlan Barbosa dos-Santos [1]
Kattiucy Gabrielle da Silva Brito [1]
Bernardo Afonso Ribeiro Pinto [2]
Tatiane Fernandes da Fonseca Gaban [2]
Antonio Marcos da Silva Catharino [1,3,4]

[1] Universidade Iguaçu, Programa de iniciação científica - Nova Iguaçu - Rio de Janeiro - Brasil
[2] Hospital Geral de Nova Iguaçu, Nefrologia - Nova Iguaçu - Rio de Janeiro - Brasil
[3] Hospital Geral de Nova Iguaçu, Neurologia - Nova Iguaçu - Rio de Janeiro - Brasil
[4] Universidade Iguaçu, Semiologia Médica \ Neurologia - Nova Iguaçu - Rio de Janeiro - Brasil

***Correspondence**
Antonio Marcos da Silva Catharino
E-mail: neurocurso@globo.com

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## ABSTRACT

Headaches are particularly relevant as a complication of hemodialysis, given that this condition increases the discomfort felt by patients undergoing this therapy. The objective of the present study was to evaluate the prevalence of headache in patients undergoing hemodialysis sessions, particularly considering dialysis headaches due to caffeine-withdrawal. This was a cross-sectional, observational, quantitative and qualitative study with questionnaires and interviews. The questionnaire addressed biopsychosocial aspects, clinical aspects and criteria for the classification of headaches according to the International Headache Society. A hundred and sixty patients with stage-V chronic kidney disease responded to the questionnaire during hemodialysis sessions. Headache prevalence was 90% and over the period studied 53.1% of patients presented the symptom. Among these patients with headaches, over half (55.3%) presented criteria for concomitant caffeine-withdrawal headaches and dialysis headaches. The beginning of headaches varied between one month and more than five years, with most occurring for more than five years. Frequency varied from sporadic crises to more than one crisis a day, though more than one crisis a day predominated. The interval between crises was of a few days, with mean duration of less than one hour, which ceased with the use of self-medicated analgesics, with no worsening factor. This condition is a challenge for neurologists and headache experts. More studies are needed to decrease this prevalence, to decrease the abusive use of analgesics and improve the quality of life of these patients.

**Keywords:** Headache; Renal Dialysis; Headache Disorders.

## RESUMO

A cefaleia como complicação da hemodiálise merece um lugar de destaque, uma vez que aumenta ainda mais o incômodo sofrido pelo paciente submetido a essa terapia. O objetivo deste trabalho é estudar a prevalência de cefaleia em pacientes submetidos a sessões de hemodiálise, com ênfase na cefaleia dialítica e na cefaleia por privação de cafeína. Este foi um estudo transversal, observacional, quantitativo e qualitativo utilizando questionários e entrevistas. O questionário abordou aspectos biopsicossociais, aspectos clínicos e critérios para classificação da cefaleia de acordo com a Sociedade Internacional de Cefaleia. Cento e sessenta pacientes com IRC em estágio V responderam ao questionário durante as sessões de hemodiálise. A prevalência da cefaleia foi de 90% e no período da pesquisa 53,1% dos pacientes apresentavam o sintoma. Dentre os pacientes com cefaleia, mais da metade (55,3%) apresentavam critérios para cefaleia por privação de cafeína e cefaleia dialítica concomitantemente. O início da cefaleia variou de um mês a mais de cinco anos, sendo a maioria há mais de cinco anos. A frequência variou de crises esporádicas a mais de uma crise por dia, predominando mais de uma crise por semana. O intervalo entre as crises foi de dias, com duração média de menos de uma hora, sendo cessada com uso de analgésicos, automedicados, sem fator agravante. Essa condição é considerada um desafio entre os neurologistas e especialistas em cefaleia. São necessários mais estudos para diminuir essa prevalência, diminuir o uso abusivo de analgésicos e melhorar a qualidade de vida desses pacientes.

**Descritores:** Cefaleia; Diálise Renal; Transtornos da Cefaleia.

## INTRODUCTION

Headaches are classified as either primary or secondary, based on the absence or not of underlying structural or metabolic disruptions causing the condition. This is a very frequent symptom in patients with renal failure undergoing hemodialysis.[1]

Headaches are triggered by several factors, which are either intrinsic or extrinsic, since individuals with migraines have lower thresholds to certain exposures, leading to a series of events and culminating in pain.[2]

Headaches are particularly relevant as a complication of hemodialysis, given that this condition increases the discomfort felt by patients undergoing this therapy. Moreover, there is an increasing number of patients that rely on this procedure. The relationship between hemodialysis and headaches can be observed at the beginning of the dialysis treatment, which can be followed by nausea, vomiting, muscle spasms, disorientation, systemic hypertension and convulsions.[3,4]

The most frequent triggering factors for dialysis headache, either mentioned by patients or by the medical team, were arterial hypertension (38%), followed by no identified factor (26%), arterial hypotension (12%) and changes to body weight (6%). Another factor mentioned as a trigger for headaches during hemodialysis were electrolyte disorders.[5]

Dialysis headache frequency was first described in 1972, with 70% of hemodialysis patients suffering from headaches. Over the years, this frequency decreased, as shown in a recent study where this proportion was of 48%.[6]

During hemodialysis, several substances are depurated. The International Headache Society (IHS) emphasizes the decrease of serum caffeine as being responsible for headache crises during dialysis sessions. The main symptom of cessation of caffeine is headache.[7] The study of Maia and cols. reports the benefits of using caffeine before hemodialysis sessions as a prophylactic measure for headaches.[8]

The objective of the present study was to evaluate the prevalence of headache in patients undergoing hemodialysis sessions, particularly considering dialysis headaches due to caffeine-withdrawal.

## MATERIAL AND METHODS

This was a cross-sectional, observational, quantitative and qualitative study conducted at a treatment center for patients with renal failure who were undergoing hemodialysis. The study comprised questionnaires and interviews with these patients.

The questionnaire was developed by the authors and addressed biopsychosocial aspects (age, gender, housing, life habits, previous pathological history, professional activities, among others), in addition to clinical aspects regarding the presence of headaches (family history, time of disease, frequency, duration, location, intensity, quality of pain, associated symptoms, triggering factors, worsening factors and relief factors during a crisis) and criteria for the classification of headaches according to the IHS.

The Google Docs software was used to manage the database of this research. All patients were consulted in advance and manifested their interest in taking part of this investigation by signing a free and informed consent statement. Thus, patients answered the questionnaire voluntarily after agreeing to participate in the research.

This project was approved by the ethics in research committee of the educational institution - UNIG, CAAE: 68978517.4.0000.8044, registry number: 2.416.322.

## RESULTS

Questionnaires were applied to 160 patients, with stage-V chronic kidney disease, during hemodialysis sessions. Most patients were in their 70s (25%), followed by patients in their 50s (21.2%). Moreover, most patients were male (61.9%). Regarding marital status, most patients were married, and more than half lived with their spouse and/or children. Over 60% considered themselves stressed and mentioned hemodialysis and one of the causes. Only 9% were smokers and 10% reported drinking alcoholic beverages for more than 10 years. Only 18% carried out physical or cultural activities regularly. All patients reported not having a professional occupation because of the disease and 70% reported feeling difficulty in their everyday life. Nearly 87% of patients presented associated arterial hypertension.

Headache prevalence was 90% and over the period studied 53.1% of patients presented the symptom. Among these patients with headaches, over half (55.3%) presented criteria for concomitant caffeine-withdrawal headaches and dialysis headaches. In turn, 14.1% only presented criteria for dialysis headaches, according to the IHS.

The beginning of headaches varied between one month and more than five years, with most occurring for more than five years. Frequency varied from sporadic crises to more than one crisis a day, though more than one crisis a day predominated, which was compatible with hemodialysis sessions three times a week. The interval between crises was of a few days, with mean duration of less than one hour, which ceased with the use of self-medicated analgesics, with no worsening factor. The prevailing location of the pain was the front bilateral region, followed by the occipital and temporal regions, characterized as pulsating, with no aura, frequently associated with other symptoms such as scintillating scotomas, nausea, vomiting and photophobia. When asked about colors, most patients associated intensity of pain with the color red, followed by black.

## CONCLUSION AND DISCUSSION

A high prevalence of dialysis headache was observed, a frequent complication of hemodialysis that worsens the quality of life of patients that already present a debilitating disease. This condition is a challenge for neurologists and headache experts. The association between dialysis headache and headache by caffeine-withdrawal was observed in more than half of the patients with any kind of headache. More studies are needed to decrease this prevalence, to decrease the

abusive use of analgesics and improve the quality of life of these patients.

All patients reported that their headaches only improved with the use of analgesics. However, there are no controlled studies on prophylactic treatment or abortive treatment of dialysis headache.[9]

Frontal bilateral pain, characterized as pulsatile, with no aura, frequently associated with other symptoms such as scintillating scotomas, nausea, vomiting and photophobia is compatible with the literature found.

Despite their high prevalence, dialysis headaches remain scarcely studied.

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# Prevalence of thunderclap headache in patients with ruptured intracranial aneurysms: series of 60 cases

## Prevalência de cefaleia thunderclap em pacientes com aneurisma intracraniano roto: série de 60

Bruno Bertoli Esmanhotto [1]
Elcio Juliato Piovesan [2]
Marcos Christiano Lange [2]

[1] Faculdades Pequeno Príncipe, Curso de Medicina - Curitiba - PARANA - Brasil.
[2] Hospital de Clínicas - Universidade Federal do Paraná, Departamento de Neurologia - Curitiba.

## ABSTRACT

Thunderclap headache (TCH) is a head pain that begins suddenly and is severe at onset. TCH might be the first sign of subarachnoid hemorrhage. This study was conducted to evaluate the presence of thunderclap headache (TCH) in patients with ruptured intracranial aneurysm (RIA) and endovascular treatment (EVT). We evaluated the pattern of headache in 60 patients who suffered a RIA and EVT at time of admission and prospectively evaluated the characteristics of previous headache within one year before the rupture. Thirty-one patients (51,7 %) had TCH related to the rupture. Aneurysm size does not affect the occurrence of thunderclap headache (p=0,08). The vascular aneurysm territory is not related to presence of TCH (p=0,527). The prevalence of TCH in this cohort was similar to previous studies. All patients with acute thunderclap headache should be evaluated for subarachnoid hemorrhage.

**Keywords:** Ruptured Aneurysm; Subarachnoid Hemorrhage; Vascular Headache.

## RESUMO

Cefaleia thunderclap (CT) é uma dor de cabeça de início súbito e muito intensa. Pode ser o primeiro sinal de uma hemorragia subaracnoídea (HAS). Este estudo foi realizado para avaliar a prevalência de cefaleia thunderclap em pacientes que sofreram ruptura de aneurisma intracraniano (RIA) e submetidos a tratamento endovascular.(TEV) Foram avaliados 60 participantes com quadro de RIA e TEV no momento da admissão hospitalar, e foi questionado sobre as características da dor de cabeça prévia por um ano antes da ruptura. Trinta e um (51,7%) dos participantes relataram CT no momento da ruptura. O tamanho do aneurisma não teve relação com a ocorrência da CT (p=0.08). O território vascular também não teve relação com a presença de CT (p=0,527). A prevalência de CT neste estudo foi semelhante ao relatado em estudos prévios. Todos os pacientes com CT devem ser investigados para hemorragia subaracnoídea.

**Descritores:** Aneurisma Roto. Cefaleias Vasculares. Hemorragia Subaracnóidea.

***Correspondence**
Bruno Bertoli Esmanhotto
E-mail: bbesmanhotto@hotmail.com

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## INTRODUCTION

One of the main symptoms in patients with an intracranial aneurysm is headache, which is observed in all stages of the disease, i.e., prior to, during and after rupture of the aneurysm. Headache may be the only presenting symptom in up to 40% of patients[1]. Multicenter studies have shown that in the period before rupture headache is present in up to 36% of cases[2]. The character of the headache is not very specific, and there is no single pain characteristic that allows a diagnosis of aneurysm[3] to be suspected other than the presence of thunderclap headache (TCH), which requires investigation for subarachnoid hemorrhage[4].

Subarachnoid hemorrhage is most commonly due to rupture of an intracranial aneurysm. Ruptured aneurysms account for 85% of cases, non-aneurysmal peri mesencephalic hemorrhage (with excellent prognosis) account for 10%, and various rare disorders (transmural arterial dissection, cerebral arteriovenous malformation, dural arteriovenous fistula, mycotic aneurysm, and cocaine abuse) account for the rest[5].

"Thunderclap headache" refers to a headache that is very severe and has abrupt onset, reaching maximum intensity in less than 1 minute. A thunderclap headache is typically described by patients as an apoplectic event, one that clearly stands out from other types of headaches they may have previously experienced. Patients with thunderclap headache often liken the sensation to an explosion in their head or being struck in the head[6]. Primary TCH is diagnosed when all other potential underlying causes have been eliminated by diagnostic. Secondary TCH have multiple causes (Table 1)[6], and Subarachnoid Hemorrhage is the most common cause.[7] It is important to recall that the headache, although almost always present, is sometimes overshadowed by other symptoms and this results in misdiagnosis. Prior migraine, may lead to migraine as an incorrect diagnosis and not working up patients because their headache has responded to various analgesics, including triptans, is another reason for misdiagnosis.[8]

**Table 1.** Causes of Thunderclap Headache *

| |
|---|
| **Most Common Causes of Thunderclap Headache** |
| Reversible cerebral vasoconstriction syndrome |
| Subarachnoid hemorrhage |
| **Less Common Causes of Thunderclap Headache** |
| Cerebral infection |
| Cerebral venous sinus thrombosis |
| Cervical artery dissection |
| Complicated sinusitis |
| Hypertensive crisis |
| Intracerebral hemorrhage |
| Ischemic stroke |
| Spontaneous intracranial hypotension |
| Subdural hematoma |
| **Uncommon Causes of Thunderclap Headache** |
| Aqueductal stenosis |
| Brain tumor |
| Cardiac cephalgia |
| Giant cell arteritis |
| Pituitary apoplexy |
| Pheochromocytoma |
| Retroclival hematoma |
| Spontaneous spinal epidural hematoma |
| Third ventricle colloid cyst |

*Although the exact incidence of each cause of thunderclap headache is not well-defined, certain causes of thunderclap headache are more common than others based upon how often they present with thunderclap headache and the incidence of the condition itself. For example, although pituitary apoplexy might commonly present with thunderclap headache, as pituitary apoplexy is an uncommon condition, it is an unlikely cause of a patient's thunderclap headache.

## METHODS

We performed a prospective cohort study of consecutive patients with subarachnoid hemorrhage secondary to rupture of an aneurysm who had received EVT. The study was approved by the Hospital de Clínicas Committee for Ethics in Human Research, and all participants signed a voluntary informed-consent form. The exclusion criteria were patients over 18 years of age with the signs and symptoms of subarachnoid hemorrhage secondary to rupture of an aneurysm who had received EVT between June 1st, 2013, and June 1st 2014. The exclusion criteria were patients in coma, confused or unable to complete the questionnaire properly because of neurological disabilities, submitted to neurosurgery, presence of non-saccular aneurysms and loss of follow-up.

After embolization, these patients were interviewed about a history of headache using a purpose-built questionnaire by a neurologist. A questionnaire about the presence of headache based on the ICHD (International Classification of Headache Disorder) 3rd edition[4] criteria in the 12 months prior to rupture was applied after EVT. Depending on the characteristics of their headache at the first assessment, patients were classified as having migraine with aura, migraine without aura or tension-type headache.[4]

The diagnosis of subarachnoid hemorrhage was based on computed axial tomography (CAT), when this failed to confirm the diagnosis, an analysis of cerebrospinal fluid following lumbar puncture was done to confirm the hemorrhage. After the diagnosis, patients underwent digital subtraction angiography (DSA) to confirm the presence of and the site of the aneurysm, allowing the EVT. Two experienced Interventional Neuroradiologists, using remodeling technique, performed the coiling. Patients were treated with Gugliemli Detachable Coils (GDC, Stryker Neurovascular, Freemont, California, USA) and Hyperform Occlusion Balloon System (Covidien, Irvine, California, USA).

## Statistical Analysis

The non-parametric Mann-Whitney test was used to correlate the aneurysm size with its localization. The Fisher exact test was used to investigate the association between qualitative variables, and the Jarque-Bera test was used to test the variables for normality. P values of less than 0.05 were considered significant.

## RESULTS

In total, we recruited 60 patients with RIA, 48 (80%) were women and 12 men (20%), with a mean age of 49.5 3 12.9 years. Thirty-seven (61.7%) had a history of headache in the 12 months prior to rupture of the aneurysm and were distributed as follows: 16 (43.2%) with tension-type headache; 11 (29.7%) with migraine without aura; nine (24.3%) with migraine with aura; and one (2.7%) with non-specific characteristics. (Table 2). From 60 cases, 31 (51.7%) had TCH as clinical presentation of SAH. Arterial Hypertension and tabagism were present in 18 (58%) patients and 10 (32%) participants with TCH, respectively. In 23 (74%) participants with TCH the aneurysm size were less than 10 mm, and in 8 (26%) were larger than 10 mm. The aneurysm size was not statistically significant in occurrence of TCH (p=0.08) In 48 patients (80%) the aneurysms were localized in anterior circulation and 12 (20%) in posterior circulation, but no difference in prevalence of TCH in this 2 subsets was shown. (p=0.527)(Table 3).

**Table 3.** Presence of TCH according vascular territory

| Thunderclap Headache | Aneurysm Localization | | | |
|---|---|---|---|---|
| | Anterior Circulation | | Posterior Circulation | |
| | n | % | n | % |
| No | 22 | 45,8% | 7 | 58,3% |
| Yes | 26 | 54,2% | 5 | 41,7% |
| Total | 48 | 100,0% | 12 | 100,0% |

p= 0,527

## DISCUSSION

Epidemiological studies in the Brazilian population have shown the prevalence of migraine and tension-type headache to be 15.2% and 13%, respectively[9,10]. In the present study, the prevalence of both types of headache in patients with an intracranial aneurysm was twice as high: 33.4% for migraine (15% with aura and 18.4% without aura) and 26.7% for tension-type headache.

Subarachnoid haemorrhage is the most common cause of secondary TCH and should be the focus of the initial assessment given the significant associated morbidity and mortality. Initial misdiagnosis and subsequent rebleeding corresponds with a worsening prognosis. Historically, the diagnosis of SAH was missed on initial presentation in 11% to 25%25% of patients presenting with TCH.[8,11,12]

A study performed in 364 patients, with intracranial aneurysms confirmed by angiography, evaluated presence of warning signs (moderate or severe headache, dizziness, nausea/vomiting, transitory sensitivity and/or motor deficit, loss of consciousness, visual or oculomotor disturbances) preceding major hemorrhage.

Two specific groups are considered: 1) 78 patients with SAH at admission (Group A). This group of patients with referral and correct diagnosis at the first episode of non-catastrophic SAH is considered a "recognized" minor leak; 2) 74 patients with SAH and history of premonitory warning signs (Group B). These patients had not identified minor leak and were referred and diagnosed only at a second episode of SAH. Headache described by the patients as sudden, severe and unusual was the main symptom in Groups A and B; in 82.5% of cases it was localized. Thunderclap headache was an isolated symptom in 14.1 % of patients in Group A and in 32.4% in Group B and in respectively 37.2% and 28.4% of cases it was associated with nausea or vomiting. [13] The present study has shown the prevalence of TCH was 51,7 %. And TCH associated with nausea and vomiting was 75 %.

**Table 2.** Clinical characteristics of patients with primary headache and intracranial aneurysms before their rupture (n=37).

| Characteristics | Migraine with aura | Migraine without aura | TTH | All types* |
|---|---|---|---|---|
| | (n = 9) | (n = 11) | (n = 16) | (n = 37) |
| Mean Age (years) | 47 | 42,4 | 48,3 | 46,3 |
| Thunderclap headache | 6 (16,2%) | 4 (10,8%) | 10 (27%) | 21 (56,8%) |
| Female | 9 (24,3%) | 8 (21,6%) | 12 (32,4%) | 30 (81%) |
| Male | 0 | 3 (8,1%) | 4 (10,9%) | 7 (19%) |
| Arterial Hypertension | 5 (13,5%) | 5 (13,5%) | 7 (19%) | 18 (48,7%) |
| Smoker | 5 (13,5%) | 3 (8,1%) | 4 (10,9%) | 13 (35,1%) |
| **Aneurysm size** | | | | |
| <10 mm | 5 (13,5%) | 7 (19%) | 14 (37,8%) | 27 (73%) |
| 10 - 24 mm | 3 (8,1%) | 1 (2,7%) | 2 (5,4%) | 8 (21,6%) |
| >24 mm | 0 | 2 (5,4%) | 0 | 2 (5,4%) |

*Including nonspecific headache

In addition, a recent study identified the presence of migraine as independent risk factor for rupture of an intracranial aneurysm[5].

The present study has limitations. Firstly, the patients may have overlooked episodes of mild headache or forgotten details of the pain in the 12 months prior to treatment. Secondly, the number of participants was small.

## CONCLUSION

In summary, we conclude that nearly half of patients with ruptured intracranial aneurysms presented thunderclap headache and there is no relation with size aneurysm and vascular territory.

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# Clinical characteristics of headaches attributed to diagnostic and therapeutic procedures

## Características clínicas das cefaleias atribuídas a procedimentos diagnósticos e terapëuticos

Raimundo Pereira Silva-Néto [1]

[1] Federal University of the Parnaíba Delta, Brazil.

## ABSTRACT

Headaches may appear after performing diagnostic and / or therapeutic procedures with close temporal relationship to these events. The objective of this research was to know the clinical characteristics of headache secondary to diagnostic and / or therapeutic procedures. We reviewed secondary headaches according to ICHD-3, and searched for those that arose after performing a diagnostic and / or therapeutic procedure. A total of 11 different diagnoses of headache attributed to diagnostic and / or therapeutic procedures were found. Some secondary headaches are due to diagnostic and / or therapeutic procedures.

**Keywords:** Secondary headaches; Diagnostic procedures; Therapeutic procedures.

## RESUMO

Cefaleias podem surgir após realização de procedimentos diagnósticos e/ou terapêuticos com estreita relação temporal com esses eventos. O objetivo desta pesquisa foi conhecer as características clínicas das cefaleias secundárias a procedimentos diagnósticos e/ou terapêuticos. Nós revisamos as cefaleias secundárias, de acordo com a ICHD-3, e buscamos aquelas que surgiram após a realização de um procedimento diagnóstico e / ou terapêutico. Foram encontrados 11 diagnósticos diferentes de cefaleias atribuídas a procedimentos diagnósticos e / ou terapêuticos. Algumas cefaleias secundárias são decorrentes de procedimentos diagnósticos e/ou terapêuticos.

**Descritores:** Cefaleias secundárias; Procedimentos diagnósticos; Procedimentos terapêuticos

## INTRODUCTION

Secondary headache is defined when a new headache occurs for the first time in close temporal relationship to an intracranial disorder[1]. The clinical presentation of all these disorders can be diverse and often mimics the characteristics of primary headaches, which may delay the diagnosis[2].

Headache may appear as a side effect due to the performance of some diagnostic and / or therapeutic procedures, such as neurosurgery, endovascular treatments, puncture of the dura mater for cerebrospinal fluid (CSF) removal or injection of some substance, among others[1].

Knowledge of the clinical characteristics of these headaches is important to improve diagnostic accuracy and therapeutic management, as well as the development of prophylactic measures.

## METHODS

In this review, we examined the diagnosis of all secondary headaches, according to International Classification of Headache Disorders, Third Edition (ICHD-3)[1]. The headaches that appeared after performing a diagnostic and / or therapeutic procedure were selected. In addition, we seek articles related to these headaches in the main databases to better characterize them.

## RESULTS

A total of 11 different diagnoses of headache attributed to diagnostic and / or therapeutic procedures were found (Table 1).

***Correspondence**
Raimundo Pereira Silva-Néto
Universidade Federal do Delta do Parnaíba, Avenida São Sebastião, 2819, Fátima, Parnaíba, PI
64001-020, Brasil. Tel. + 55 3237-2104.
E-mail: neurocefaleia@terra.com.br

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**Table 1.** Headaches attributed to diagnostic and / or therapeutic procedures, according to ICHD-3

| |
|---|
| Acute or persistent headache attributed to craniotomy |
| Post-endarterectomy headache |
| Headache attributed to carotid or vertebral angioplasty or stenting |
| Headache attributed to cranial venous sinus stenting |
| Headache attributed to an intracranial endarterial procedure |
| Angiography headache |
| Post-dural puncture headache |
| Headache attributed to intrathecal injection |
| Dialysis headache |
| Headache attributed to radiosurgery of the brain |
| Post-electroconvulsive therapy headache |

## DISCUSSION

According to ICHD-3[1], some diagnostic and / or therapeutic procedures may cause headache. In the following, these headaches that are considered secondary will be described.

### Acute or persistent headache attributed to craniotomy

A craniotomy is a neurosurgical technique, whereby part of the skull is opened or removed for access to treat conditions such as brain tumors, aneurysms, and arteriovenous malformations[3].

Retrospective studies have shown that more than 30% of the patients submitted to this surgical procedure had headache attributed to craniotomy as an adverse event[4-6].

However, when headache occurs after head injury surgery, it will be coded as acute headache attributed to moderate or severe traumatic head injury.

According to ICHD-3, this headache must have occurred within seven days after craniotomy, after the patient has regained consciousness or after discontinuation of medications that impair the ability to feel or report headache. In addition, headache should be resolved within three months of its initiation[1].

Headache attributed to craniotomy is more common after surgery of the skull base compared to other locations. Usually, it is felt at the site of the craniotomy, but may be more diffuse and resemble tension-type headache or migraine[1].

If headache resolved within three months after its onset, it will be classified as acute, but if it persists for more than three months, it will be called chronic. When headache following craniotomy becomes persistent, the possibility of medication-overuse headache needs to be considered[1].

In the abortive treatment of this headache, several drugs have been tried, such as infiltration of the scar with local anesthesia[7], opioids, especially codeine and morphine, acetaminophen, non-hormonal anti-inflammatories[8], and sumatriptan[9]. There are few studies on prophylactic treatment of headache attributed to craniotomy[10]. The best therapeutic responses were with verapamil[11] and divalproex sodium[12].

### Post-endarterectomy headache

This headache is caused by the surgical procedure of carotid endarterectomy. It develops within one week after of the carotid endarterectomy, but it is resolved within the first 30 days. Headache can occur without any other associated symptom or be a warning symptom preceding the focal deficits of (mostly hemorrhagic) stroke[1].

Headache is unilateral, on the side of carotid endarterectomy, and may involve the neck and face. The headache has a pulsating character and a mild intensity. It manifests as cluster headache-like pain occurring once or twice a day in attacks lasting two to three hours[1].

There are three subforms of post-endarterectomy headache, but they are not coded separately. The first is the most frequent (up to 60% of cases), a diffuse, mild and isolated headache, which occurs in the first days after surgery and is a benign, self-limiting condition; the second (up to 38% of cases), a unilateral cluster headache-like pain with attacks, lasting two to three hours, occurring once or twice a day and resolves in about two weeks; and the third, unilateral pulsating and severe pain occurring three days after surgery. This latter subform is part of the rare hyperperfusion syndrome, often preceding a rise in blood pressure and the onset of seizures or neurological deficits on or about the seventh day. Urgent treatment is required, since these symptoms can herald cerebral haemorrhage[1].

Some studies have shown that headache occurs in 38% to 62% of patients undergoing endarterectomy. Usually, the location of the pain is on the same side of the surgical procedure. It has a dull or pressure character and a moderate to severe intensity. In more than 50% of patients there is no need for treatment[13,14], but when it is part of the hyperfusion syndrome, treatment is an emergency as these symptoms may indicate a brain hemorrhage.

### Headache attributed to carotid or vertebral angioplasty or stenting

Carotid and vertebral angioplasty and/or stenting are performed to treat patients with cervical artery stenosis, but one-third of these patients develops headache. This headache is caused by the endovascular procedures of carotid or cervical angioplasty and / or stenting without arterial dissection. It develops within a week but resolves within a one month after angioplasty and / or stenting[1].

Headache attacks usually occur within 10 minutes in which these procedures are performed. They are localized to the frontotemporal region, ipsilateral to the procedure, in pressure, mild intensity, and lasting a maximum of 10 minutes.

Studies show that carotid percutaneous transluminal angioplasty may cause arterial dissection, often resulting

in cervical, facial or cranial pain. However, the relative risk of painful dilation depends on individual risk factors, such as a history of myocardial infarction. In addition, the radiation pattern of pain depends on which carotid segment is dilated[15].

Data on carotid angioplasty headache and diagnostic criteria are based on few studies. Despite the scarcity of data, this headache seems to be relatively frequent. In two studies, its occurrence ranged from 39% to 51%[15,16].

## Headache attributed to cranial venous sinus stenting

In recent years, lateral sinus stenosis stenting has been used in the treatment of idiopathic intracranial hypertension. Suppression of stenosis may reduce intracranial pressure by decreasing the pressure in the upper longitudinal sinus. However, unilateral headache may be caused by the stent and on the same side of the cranial venous sinus stent[17].

This headache devolops within one week after the jugular or cranial venous stent has been performed. Headache is ipsilateral to the stenting and it resolves within three months[1].

In one series of 21patients stented for idiopathic intracranial hypertension, 10 patients exhibited 'stent-headaches' differing from those experienced before treatment, located at the site of the stent, in the mastoid region, and lasting about three weeks. These "stent-headaches" disappeared after 3 months of stenting[17].

## Headache attributed to an intracranial endarterial procedure

Some studies have shown that balloon inflation in the intracranial arteries during therapeutic embolization of intracerebral arteriovenous malformations (AVMs) cause pain by distension of these vessels[18]. Probably, mechanical vessel distension activates the trigeminovascular nociceptive system in susceptible individuals[19].

It is a unilateral headache directly caused by intracranial endarterial procedure, ipsilateral to the procedure and lasting less than 24 hours. Pain was described as brief, sharp or localized pressure of mild to moderate intensity, felt ipsilaterally to the manipulated vessel. This headache develops within one week and resolves within one month after the procedure[1,19].

The occurrence of this headache during endovascular procedures is not yet well-defined. There is limited information to define its frequency, risk factors, pathogenesis and implications for future pain management[19]. In some evaluated procedures, the headache occurrence attributed to an intracranial endoarterial procedure ranged from 10.6% to 68.0%[18-21].

## Angiography headache

This headache is caused by intra-arterial carotid or vertebral angiography. It develops during contrast injection or within 24 hours after angiography, lasting less than one hour. It disappears within 72 hours after angiography[1].

The frequency of post angiography headache ranges from 30.2% to 39.1%[16,22,23]. Possibly a headache is due to irritation of the trigeminovascular system by contrast agents or mechanical stimuli, resulting in the release of vasoactive peptides[24].

## Post-dural puncture headache

Headache occurring within five days of a lumbar puncture, caused by CSF leakage through the dural puncture. It is usually accompanied by neck stiffness and / or subjective hearing symptoms and it gets worse when the individual takes the upright position. It remits spontaneously within two weeks, or after healing from the leak with autologous epidural lumbar patch[1].

Puncture of the dura-mater occurs during diagnostic or therapeutic procedures, spinal anesthesia or inadvertently during epidural anesthesia. After puncture, post-dural puncture headache may appear as a common complication in approximately 7.5% of the patients[25,26].

## Headache attributed to intrathecal injection

Some drugs that act on the central nervous system such as analgesics, anesthetics, and antineoplastics are injected directly into the subarachnoid space, thus avoiding the blood-brain barrier. This route of administration is known as the subarachnoid or intrathecal route.

After intrathecal injection, the most common adverse effects are headache and low back pain[27]. Headache develops within four days of intrathecal injection and significantly improves within 14 days after intrathecal injection. Signs of meningeal irritation are present. In addition, headache experienced in both upright and recumbent postures[1].

## Dialysis headache

Dialysis is a therapeutic procedure used by patients with kidney failure, where a machine replaces the diseased kidney and filters the blood, eliminating toxic substances such as sodium, potassium, urea and creatinine. Frequently, patients with chronic kidney disease experience headache during dialysis[28], whose pathophysiology is still unknown.

The prevalence of dialysis headache varies between 27% and 73%[28]. This headache is characterized by developing during a hemodialysis session and resolving within 72 hours after the end of the dialysis session. Headache episodes cease altogether after successful kidney transplantation and termination of haemodialysis[1].

Dialysis headache was described for the first time by Bana and Yap in 1972[29], but its clinical characterization has been detailed improvement in recent years. In most patients, headache is pulsatile, located in the frontal region, moderate to severe intensity, and may be accompanied by nausea and vomiting[30-33]. There are

no controlled studies on the prophylactic or abortive treatment of dialysis headache.

### Headache attributed to radiosurgery of the brain

Brain radiosurgery is used in the treatment of brain injuries, such as arteriovenous malformations[34] and intracranial tumors[35]. In some primary headaches, such as refractory cluster headache, brain radiosurgery may also be useful[36]. Cerebral edema is the most frequent complication of this procedure[37,38].

More rarely, headache may appear in a patient in whom radiosurgery of the brain has been performed. It develops within seven days, but it is resolved within three months after radiosurgery. There have been no validation studies of its diagnostic criteria. Currently, it is in the appendix of ICHD-3 (A5.7), but it is not better accounted for by another ICHD-3 diagnosis[1].

Studies on this new headache do not provided detailed descriptions of its clinical features. In some cases, the headache syndrome was short-lived, occurred more than a year after the procedure and resembled migraine or thunderclap headache[1].

### Post-electroconvulsive therapy headache

Electroconvulsive therapy (ECT) is commonly used in the treatment of various psychiatric disorders, such as severe depression, schizophrenia, and bipolar disorders. Headache is the main adverse effect resulting from this therapeutic procedure. Its incidence varies from 26% to 85% and makes it difficult for the patient to continue with this treatment[39].

This headache occurs when a course of electroconvulsive therapy (ECT) has been given in a headache-free patient to treat an epileptic seizure. It is necessary that headache has developed after ≥50% of ECT sessions; each headache has developed within four hours after ECT; and each headache has resolved within 72 hours after ECT. There have been no validation studies of its diagnostic criteria. Currently, it is in the appendix of ICHD-3 (A7.6.3), but it is not better accounted for by another ICHD-3 diagnosis[1].

Usually, post-ECT headache is treated with analgesics and / or non-steroidal anti-inflammatory drugs, but other optional treatments are being described. In some case reports, mirtazapine[39] and topiramate[40] were effective.

## CONCLUSION

Some secondary headaches are due to diagnostic and / or therapeutic procedures.

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# Telemedicine in the Management of Primary Headaches: A Critical Review

## Telemedicina no manejo das cefaleias primárias: uma revisão crítica

Renan Barros Domingues[1]
Cassio Batista Lacerda [1]
Paulo Diego Santos Silva, MD[1]

[1] Serviço de Cefaleia, Departamento de Neurologia, Irmandade da Santa Casa de Misericórdia de São Paulo.

## ABSTRACT

Telemedicine is a modality of health care services delivery with the use of communication technologies. Its use has grown in several medicine areas. Several studies evaluated the feasibility, acceptance, efficacy, cost-effectiveness, and safety of telemedicine in the diagnosis and management of primary headache disorders. Videoconsultations were shown to be effective, convenient, and safe for primary headache disorders and migraine follow up. Some mobile health devices were show to improve adherence favoring better outcomes. Handling health data is a major concern so that international compliance standards must be adopted in all telemedicine procedures. The impact in the health system and increased access to appropriate primary headache treatments with the use of these technologies has yet to be elucidated.

**Keywords:** Telemedicine, Primary Headache; Migraine; Videoconsultation; Mobile Health

## RESUMO

A telemedicina é uma modalidade de disponibilização de serviços médicos com o uso da tecnologia da informação. Seu uso tem crescido enormemente em várias áreas da medicina. Vários estudos avaliaram a viabilidade, aceitação, eficácia, custo-efetividade e segurança da telemedicina no diagnóstico e tratamento das cefaleias primárias. A vídeoconsulta mostrou-se uma forma eficaz, conveniente e segura no seguimento terapêutico das cefaleias primárias e da enxaqueca. Alguns aplicativos para dispositivos móveis mostraram aumento da aderência, favorecendo melhores resultados. A segurança de dados de saúde é uma preocupação, sendo imprescindível seguir rigorosamente os protocolos internacionais de conformidade. O impacto no sistema de saúde e o aumento do acesso a tratamentos adequados proporcionados por estas tecnologias ainda precisa ser melhor elucidado.

**Descritores:** Telemedicina; Cefaleias Primárias; Enxaqueca; Vídeoconsultas; Aplicativos de Saúde.

## INTRODUCTION

The definition of telemedicine according to the World Health Organization is "The delivery of health care services, where distance is a critical factor, by all health care professionals using information and communication technologies for the exchange of valid information for diagnosis, treatment and prevention of disease and injuries, research and evaluation, and for the continuing education of health care providers, all in the interests of advancing the health of individuals and their communities".[1,2] The history of telemedicine begins in the early 20th century with the transmission of eletrocardiographic using telephone wires. [3] Other technologies, such as closed circuit television, began to be used in the 1950s and 1960s. [4,5] In 1967, the Massachusetts General Hospital starts to provide remote health healthcare services to Boston Logan Airport, being the first structured telemedicine service. [6] With the introduction of World Wide Web (www) in 1990, the possibility of health information exchange is greatly expanded, by replacing analogue processes with digital ones, increasing enormously the capacity to store and transmit data. [7]

***Correspondence**
Renan Barros Domingues
Rua Vergueiro, 1421 cj 603 Torre Sul, Vila Mariana, São Paulo, SP, CEP 01504-000
E-mail: contato@renandomingues.med.br

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The delivery of telemedicine services can be made by four different ways: 1) synchronous – with live video between patient and provider or non-specialist with specialist, 2) store and forward - by acquiring medical data and further transmitting it to a provider or a specialist, 3) remote monitoring - with the use of wearables and biosensors, and 4) mobile health (mHealth) - which is the health practice supported by mobile devices. [8-10] The use of telemedicine in Neurology is growing due to the fact that neurological care is still poor around the world. Telestroke accounts for 65% stroke treatments "in the USA" - A determiner is probably missing here and Canada. Several studies have showed potential benefits of telemedicine in the management of Parkinson's Disease, Epilepsy, Multiple Sclerosis, Brain and Spinal injury, and Amytrophic Lateral Sclerosis. [11,12]

Primary headaches are associated with a significant impact. [13-15] However, the availability of headache medical services is poor worldwide and even higher in developing countries such as Brazil. [16-21] Considering the need to expand access to headache treatment and the high prevalence of these disorders, telemedicine seems to be an attractive alternative to provide care for these patients. In the present review we will critically discuss the current evidence about this topic.

## TELEMEDICINE AND HEADACHE IN THE LITERATURE

By searching with the words "Telemedicine" and "Headache" in the PubMed database 53 articles are found, including several article types, such as clinical trials, case reports, reviews, and opinion articles. Among them, twenty are clinical studies or case presentations evaluating specific telemedicine procedures in the treatment of headache or specific headache disorders. The first scientific paper about the use of communication technologies in headache care was published in 2004. Several studies about behavioral interventions on adherence and outcomes in headache treatment with the use of mHealth were published between 2004 and 2016, when the first well designed, prospective telemedicine and headache clinical trial article was published. [22-24] In this critical review we took into consideration the most important articles evaluating synchronous telemedicine and mobile health (mHealth).

### Synchronous telemedine (videoconsultations)

Müller et al. evaluated synchronous telemedicine and showed high levels of acceptability, feasibility, as well as cost effectiveness with videoconsutations when compared to conventional consultations. The study was carried out in Northern Norway and included adult patients referred to a neurologist for non-acute headache treatment by primary care physician. The patients were randomized for telemedicine consultations or conventional face-to-face appointments. Videoconsultations were performed using appropriate equipment in a telemedicine hospital room, with audio and video communication between the neurologist and the patient in the videoconference room. The same physician carried out the consultations of the telemedicine group and the conventional consultation group. Nearly 400 hundred subjects were randomized for telemedicine or conventional consultations and were followed for one year and telemedicine was shown to be feasible. [25] In another publication originated from the same clinical trial the authors compared efficacy of telemedicine and conventional treatment with visual analogue scale (VAS) and headache impact test (HIT-6), showing non-inferiority of telemedicine approach. [26] The satisfaction of patients with telemedicine was also evaluated by the same study group. Telemedicine patients did not express less satisfaction than those with traditional consultation. [27] The safety of using telemedicine was also assessed. The ability to identify secondary headaches over one year of follow up was not significantly different between telemedicine and conventional consultations. The percentage of neuroimaging exams indication, neuroimaging abnormalities, as well as the proportions of hospitalized patients during the follow up period was not significantly different between the two groups. It was estimated that over 20,000 telemedicine consultations are necessary to miss one secondary headache. [28]

The feasibility of telemedicine consultations was also evaluated in children with headache. Vierhile and cols. conducted a small open study in which children were evaluated in a spoke site with the presence of a nurse practitioner. The connection was established with a hub center with a specialist. Overall, the headache outcomes were comparable to outcomes with conventional in office consultations. Most of the parents liked not having to drive to the medical center and not having to cancel the activities of the children due to medical consultation. [29] Qubty et al. carried out a prospective pediatric headache telemedicine study and showed that telemedicine was convenient, cost-effective, and patient-centered for routine pediatric headache follow-up visits. Overall patients and family were satisfied with telemedicine. [30]

The efficacy of telemedicine has also been tested for the management of specific headache types. Bekkelung and Müller compared video consultations and traditional consultations in patients with Medication Overuse Headache (MOH). The group treated with telemedicine had non-inferior outcomes, including reduction in the number of headache days and reduction of analgesic consumption. [31] Friedman et al. conducted a prospective, randomized trial of telemedicine for migraine management. Patients were evaluated in an initial in-office visit and then randomized for follow-up with telemedicine consultations or in-office visits. Telemedicine consultations were conducted with specific software installed on a patient choice computer and were carried out by the same physician of the traditional consultations group. The follow-up time was one year. All the measured outcomes, including efficacy of treatment, headache impact, and safety, were similar between the two groups. Physician productivity was higher with

telemedicine group. The perception of convenience by the patients was higher in the telemedicine group. [32]

### Mobile health (mHealth)

The use of mHealth has potential advantages as an auxiliary tool in the management of headaches, particularly in patient education and life style modification that are important in the effective treatment of people with headache disorders. The mHealth devices may be a good way to record headache-related symptoms and information such as possible triggers.

Despite the availability of a growing number of smartphone apps, in particular electronic headache diaries, there is still little evidence about its efficacy and safety in handling patient data. Mosadeghi-Nik and cols. carried out a systematic review with smartphone headache diaries, which are presumably easier and more practical to use than paper-based diaries. One reported advantage is that electronic diaries can be filled in real time. Another advantage is that assistant physician can have access patient data through a web portal, also facilitating the database generation. However, the authors point that the evidence of effectiveness and safety of these mobile apps for headache disorders treatment is still limited. [33] In a recent narrative review, Stubberud and Linde sought for clinical evidence on mHealth based classical behavioral therapies, such as cognitive behavioral therapy, biofeedback, and relaxation in patients with migraine; however, evidence is still missing in this field. [34] In a systematic review, Hundert et all. also evaluated clinical evidence with the use of some available headache diary apps. The authors found 38 headache diary apps but only 18% were developed with headache expertise. Little evidence regarding its effectiveness was found. [35] Concern about privacy with headache diary smartphone apps was also reported by Minem et al. that examined 29 apps (14 diary apps and 15 relaxation apps). Only 11/14 headache diaries disclosed privacy policy and 6 stated that user data were used for targeted advertisements. Only 11/15 relaxation apps had disclosed privacy policies. [36]

One large and controlled study evaluated the efficacy of a mHealth device in headache management. The value of electronic monitoring and alerting system was assessed in the management of MOH in a controlled multicenter study. In this study, Tassorelli et cols. evaluated the Comoestas tool which is a diary with an alerting system that allows remote monitoring of key clinical data. The system has a headache diary allowing data collection to a web platform, generating high and low priority alerts. The system also facilitates electronic communication with smartphone, e-diary, and E-mail text messages as well as smartphone calls. A significantly higher percentage of patients were overuse-free, there was a lower rate of subjects lost to follow-up, and higher level of patients satisfaction were registered in the group treated with the aid of Comoestas. [37]

One study compared the use of paper-based diaries and electronic diaries. Bandarian-Babooch et al. compared two paper diaries (short and long) and four types of electronic diaries. The authors found more missing date and more errors in data filling in the long paper use than with short paper diary and electronic diaries. Long paper diaries were found more burdensome and significantly less easy to use than electronic diaries and short paper diaries. The authors concluded that electronic diary is a potentially useful tool in clinical trials as well as in the behavioral treatment of headaches. [38]

## DISCUSSION

The available evidence shows that telemedicine is effective, convenient, and cost-effective in the treatment of primary headaches. Concern about safety still exists but available published data shows that using appropriate screening tools or a first face-to-face consultation, the safety level is in identifying secondary headaches is similar between telemedicine and conventional consultations. Therefore, there is scientific evidence that telemedicine is viable for primary headache disorders follow-up, allowing higher physician productivity, and it is associated with high level of satisfaction by the patients or caregivers. There is also some evidence that the use of mHealth devices may contribute in monitoring headache, potentially contributing to better outcomes and easier interaction between patient and assistant physician.

The health system impact of using telemedicine in headache care still needs to be measured. Considering that telemedicine is a potentially useful tool in primary care, it can be used in this setting in the management of patients with primary headache disorders. [39] Potential advantages would be an earlier introduction of preventive treatments, better orientation for patients in the management of headache attacks, lifestyle change orientation, and analgesics overuse prevention. This would also facilitate the identification of patients requiring treatment at a specialized tertiary center. Despite these potential advantages, there is still need for studies evaluating the clinical and economic impact in health system and how it can facilitate the access of patients to adequate treatments.

The use of telemedicine brings concerns about data security and compliance with local legislations. Most of the available synchronous telemedicine studies cited in this review employed validated and safe telemedicine platforms that allow the storage and inviolability of data, as well as making it available to the patient or guardian upon request. There is still concern about some mHealth devices, particularly electronic diaries, since many of them do not disclose data security policy. Creating and maintaining large headache databases has potential enormous benefits, for example, in generating local and national headache registries that can help to guide public health policies. [40] Handling these databanks should be done according to all compliance rules to avoid targeted advertisements. Health Insurance Portability and Accountability Act (HIPAA) established security standards for protecting health information in its electronic form. [41,42] The procedures established by HIPAA must be adopted by every app or system dedicated to telemedicine. Regulatory and legal issues regarding telemedicine have specificities around world. [43] In Brazil, some general

rules were published in 2002; however, they do not address technological developments and telemedicine advances over the last 17 years. There is a new and more detailed regulation under discussion and it is expected that this regulation with more specific rules, detailing of technological requirements, and better specification procedures will be available until 2020.

In conclusion, the existing evidence favors telemedicine as an alternative in the treatment of primary headache disorders. This modality of delivering medical care may be an option for patients with difficulty in accessing in-office consultations. It is possible that, as in other areas of medicine, telemedicine may increase the access to available headache treatments. The current available treatments are not yet widely available because, among other factors, there are no headache experts in many regions. The use of telemedicine within ethical and compliance parameters by qualified professionals may be incorporated into the treatment of primary headache disorders. Not as a new treatment, but as an agile and scalable way to deliver currently available headache treatments.

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# Intracranial lipoma manifesting with change in preexisting headache characteristics

## Lipoma intracraniano que se manifesta com mudança das características de cefaleia preexistente

Patrick Emanuell Mesquita Sousa Santos[1]
Ivan Rodrigues Silva[1,2]
Mário Fernando Prieto Peres[3]
Raimundo Pereira Silva-Néto[1]

[1] Federal University of Delta of Parnaíba, Brazil.
[2] Dirceu Arcoverde State Hospital, Parnaíba, Brazil.
[3] Education and Research Israelite Institute Albert Einstein, Brazil; Institute of Psychiatry, HCFMUSP, Brazil.

## ABSTRACT

Intracranial lipomas represent 0.1% to 0.5% of all intracranial tumors. Approximately half of the patients are asymptomatic. In symptomatic patients, headache is the most common symptom. We describe the case of a 71-year-old woman with history of generalized seizures and episodic migraine for about 30 years. In recent months, there has been a change in the characteristics of headache. She was admitted to the emergency room with muscle weakness in left hemibody and intense headache onset approximately four hours ago. Neuroimaging exams revealed a median frontal expansive lesion suggestive of intracranial lipoma.

**Keywords:** Migraine; Epilepsy; Intracranial lipoma.

## RESUMO

Lipomas intracranianos representam 0,1% a 0,5% de todos os tumores intracranianos. Cerca de metade dos pacientes portadores dessa rara formação são assintomáticos. Naqueles sintomáticos, a cefaleia é o principal sintoma. Nós descrevemos o caso de uma mulher de 71 anos com história de convulsões e migrânea episódica há cerca de 30 anos. Nos últimos meses, houve mudanças nas características da dor. Ela foi admitida na emergência com fraqueza muscular no hemicorpo esquerdo e intensa cefaleia, com início há cerca de quatro horas. Os exames de imagem revelaram uma lesão expansiva frontal mediana sugestiva de lipoma intracraniano.

**Descritores:** Migrânea; Epilepsia; Lipoma intracraniano.

***Correspondence**
R. P. Silva-Néto
Federal University of Delta of Parnaíba, Avenida São Sebastião, 2819, Fátima, Parnaíba, PI 64001-020, Brazil. E-mail: neurocefaleia@terra.com.br

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We describe the case of a 71-year-old woman with history of generalized seizures and episodic migraine for about 30 years. Headache presented pressure characteristics, worsening in the last two months. Before, she had three headache attacks a week, but in recent months, headache occurs daily. Headache attacks don't remit with simple analgesics. Recently, she was admitted to the emergency room with muscle weakness in left hemibody and intense headache onset approximately four hours ago. Her neurologic examination was normal. Diagnostic hypothesis of stroke was considered. She underwent a CT scan of the skull that showed an interhemispheric hypodense mass. MRI revealed a median frontal expansive lesion suggestive of intracranial lipoma (Figure 1).

Intracranial lipomas (IL) represent 0.1% to 0.5% of all intracranial tumors and are located mainly in the area of corpus callosum[1]. A retrospective study with 17 patients diagnosed with IL was conducted at a tertiary center. He showed that 47% of these patients complained of headache[2]. There is another study stating that half of the cases of IL was asymptomatic. In the other half, the main symptoms were seizures, headache and muscle weakness[3].

Surgical intervention is rarely required, because there may be vascular structures near or within the lipomas and complications may develop due to surgical excision[2]. Thus, the best therapeutic option for IL symptoms remains unclear.

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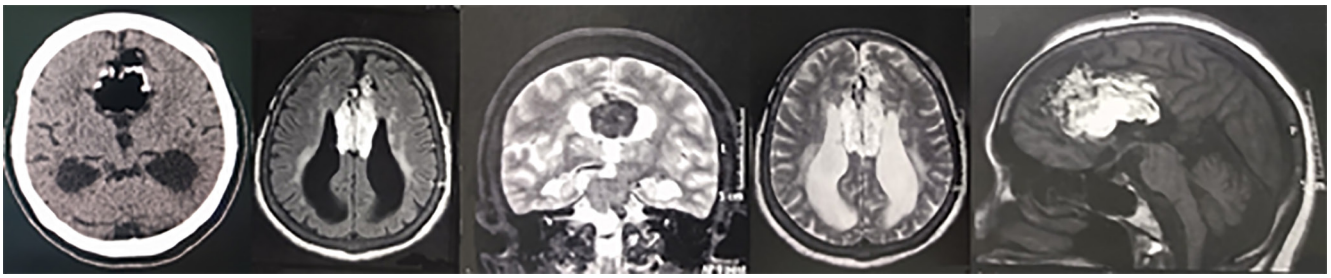

**Figure 1.** (A) CT. (B) Axial RNM T1W. (C) Coronal RNM T2W. (D) Axial RNM T2W. (E) Sagittal RNM T1W.Frontal median lesion of fat content measuring about 6.6 x 4.5 x 3.5 cm associated with signs of corpus callosum dysgenesis and colpocephalic aspect of the lateral ventricles.

# The neurologist's hammer

## O martelo do neurologista

Eduardo Nogueira [1]
Yara Dadalti Fragoso [1]

Neurologist's hammer [1]

## ABSTRACT

From the obscurity of 18th century wineries to the hands of the greatest neurologists in history, the percussion hammer has a fascinating history. The first famous percussion hammer was created in 1841 by the German physician Max Wintrich and was initially used for thoracic percussion. In 1875, Erb and Westphal both published simultaneous articles with the results from research that they had conducted separately, from which they confirmed that percussive objects were useful for stimulating deep tendon reflexes, especially patellar reflexes. The percussion hammer, however, was not yet ideal. It was designed to strike the thorax rather than the tendons, so it did not have the right weight or ideal length, and even its shape was not practical. New modified versions of the instrument subsequently emerged, and the hammer became the characteristic symbol of the neurologist.

**Keywords:** Hammer; Neurology; History; Reflexes.

## RESUMO

Da obscuridade das adegas do século XVIII às mãos dos maiores neurologistas da história, o martelo de percussão tem uma história fascinante. O primeiro martelo de percussão a ganhar notoriedade foi criado em 1841 pelo médico alemão Max Wintrich, sendo inicialmente usado para percussão torácica. Em 1875 Erb e Westphal publicaram em conjunto um artigo com os resultados de suas pesquisas, que foram realizadas separadamente, confirmando o uso dos objetos de percussão para o estímulo dos reflexos tendíneos profundos, em especial o patelar. O martelo de percussão, contudo, ainda não era o ideal. Por ter sido desenvolvido para percutir o tórax e não os tendões, ele não tinha o peso certo, o comprimento ideal e nem mesmo um formato prático. Novas versões modificadas do instrumento foram surgindo até que o martelo se tornasse o símbolo característico do médico neurologista.

**Descritores:** Martelo; Neurologia; História; Reflexos.

Headache is one of the neurological complaints that leads a patient to seek urgent care more often. Although it seems a common issue the patient should be submitted through a very careful and detailed physical examination (including neurological examination) so redflag symptoms and secondary causes of headache can be excluded.

For that matter the percussion hammer is an indispensable tool for the neurologist and general practitioner.

Percussion is an aid to medical diagnosis. The delicate percussion hammer neurologists use daily has its origins in the dark wine cellars of 18th century Austria, where young Leopold Auenbrugger routinely struck casks of wine in order to check the level of fluid [1]. As a music admirer, he had sensitive ears and wrote the axiom "the thorax of a healthy person sounds, when struck". Auenbrugger favored thumping his patients' chest directly with his own fingers, as most doctors still do today [1].

The first percussion hammer for medical use was created by Max Wintrich, in 1841. This German doctor presented the scientific world with his gadget made of steel and rubber, for use in thoracic percussion (Fig 1) [2]. However, it was only in 1875, when Carl Westphal was the Editor of Archiv für Psychiatrie

***Correspondence**
Yara Dadalti Fragoso
E-mail: yara@bsnet.com.br

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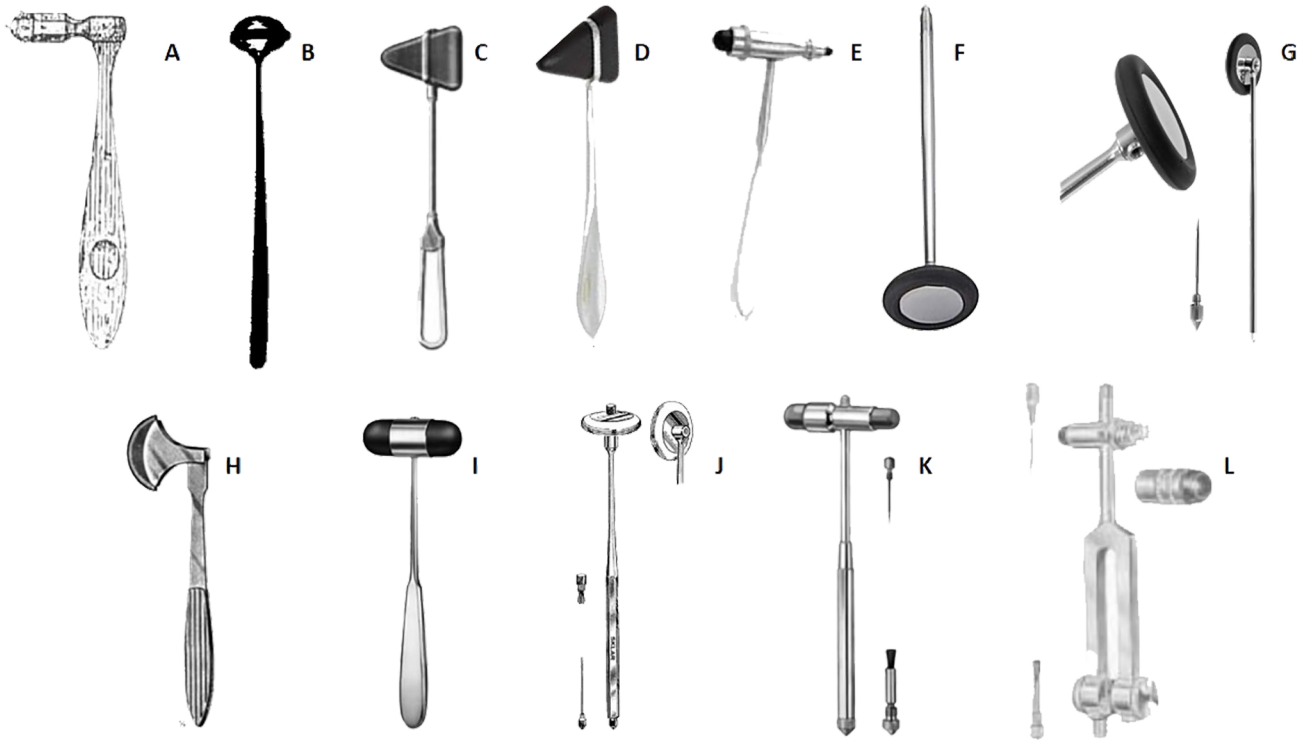


**Figure 1.** Drawings from different neurologist's hammers

und Nervenkrankheiten ("Archive for Psychiatry and Nerve Sickness"), that the hammer for eliciting reflexes was created. While reviewing a paper by his colleague Wilhelm Erb, Westphal was astonished to see that Erb had reached conclusions that were rather like his own. Separate articles from Erb and Westphal were published in the same issue of Archiv für Psychiatrie und Nervenkrankheiten [3, 4].

Erb wrote: "If one firmly holds and supports the leg to be examined, slightly bent at the hip and knee joint with all the muscles relaxed, and then lightly and elastically taps the region of the ligamentum patellae with the finger or with the percussion hammer [...] each tap is immediately followed by a slight but significant and evidently reflex contraction of the quadriceps; [...] and it is extremely difficult to suppress this reflex voluntarily". Westphal wrote that the idea of tendon percussion was given to him by one of his patients who said that when he sat on a chair and lightly tapped the area below the kneecap of the affected leg, it moved forwards with a sudden jerk. While Erb described in detail how to elicit the patellar reflex with a percussion hammer, Westphal described finger percussion, but mentioned that a precision hammer would be more effective in this maneuver [5].

Thus, Westphal and Erb started the history of the neurological percussion hammer. This history continued with the arrival of different models of this tool for neurological examinations. New modified versions of the instrument emerged over the course of the final years of the 19th century [6]. Schematic images of some percussion hammers are shown in 1.

Some of these hammers gained small gadgets like a needle with sharp and blunt points inserted into the handle, a small brush, or even a ruler or Wartenberg wheel. In 1888, John Taylor introduced the first reflex hammer with a triangular shaped head made of rubber circled by a metal band. It had a metal handle finishing in a loop and was manufactured to order by the Snowdon Brothers Instruments Company [7]. Around 1920, the loop was replaced by solid metal, giving this percussion hammer the shape that we all know so well.

In 1894, William Christopher Krauss devised a model that had two rounded pieces attached to a metal. The large piece was designed to be used for the knee jerk and the small one for the biceps jerk. The warm rubber handle, the cold metal head, the sharp and blunt pin heads and the brush would help in testing sensitivity [2]. Ernst LO Trömner introduced the metal handle tapering to a thin end, in order to test cutaneous reflexes as well. The Vernon hammer consisted of a rubber disk around a metal sphere.

The Queen Square Hospital and Babinski hammers followed, comprising a rubber disk around a flat metal disk [7]. The main difference between these lies in their ease of carrying, since Queen Square is rigid, while Babinski is smaller and telescopic, with a shorter handle. Even if some consider these to be similar, Queen Square is almost 150 grams heavier than Babinski [2]. The Queen Square Hospital hammer was developed by Miss Wintle, a nurse at the hospital.

The Rabiner hammer has a rubber disk that can be used in parallel with or perpendicular to the handle, as well as an inserted brush and needle for superficial reflexes

and sensitivity assessment. The history of the Rabiner hammer is quite peculiar. Babinski and Rabiner had an argument about the physiology behind the Babinski reflex. The argument occurred during a black-tie dinner in Vienna and the two neurologists became physical, pushing and shoving each other to the amazement of the dinner guests. The dispute was settled and, as a token of respect and apology, Babinski gave his own percussion hammer to Rabiner who returned to New York and modified its shape and appearance [2, 7].

With the rubber disk attached to the handle at 90 degrees, the Berliner hammer looks like a throwing axe. The Stookey hammer is collapsible and is accompanied by a camel hairbrush and two sharp pins for testing superficial sensitivity, including two-point discrimination. In addition, the Stookey hammer has a rough structure to test the plantar response [6, 8]. The five-in-one hammer includes a tuning fork and a Waterberg wheel. The Dejerine hammer features a hollow metal handle with inserted hick brush and needle, and a double rubber head. Imaginative improvements to this tool continue to be made. Neuropediatric wards nowadays have a variety of animal-shaped and colorful percussion hammers.

Although the hammer was initially developed for percussion of the thorax and abdomen in medical practice, it has now become the hallmark of the neurologist. Purists among the practitioners of the art of neurological examination will favor one hammer or another. The present authors have their favorite ones as well, but we do not feel like arguing about this. Use of a percussion hammer is a matter of personal taste and experience: one of these situations in which there is no right or wrong.

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