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Research Article

Association between pain intensity and cognitive function in primary headache

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Abstract

Background: Patients suffering from primary headaches such as migraine, tension-type headache, and cluster headache frequently report cognitive problems, particularly with attention and memory. The aim of this study was to see if there was a link between pain intensity and cognitive function in people who had primary headaches.

Methods: This cross-sectional study included 69 primary headache patients (37 migraines, 27 tension-type headaches and 5 cluster headaches; age range 18–80 year). Migraine, tension-type headache and cluster headache diagnosis were determined according to the International Classification of Headache Disorders 3rd edition beta version (ICHD-3 beta) diagnostic criteria. All eligible subjects underwent cognitive function examination using Montreal Cognitive Assessment Indonesian version (MoCA-INA), Trail Making test A (TMT-A), Trail Making test B (TMT-B), Trail Making test C (TMT-C), Forward Digit Span and Backward Digit Span. The intensity of pain was assessed using Numeric Rating Scale (NRS).

Results: There were 69 primary headache patients included in this study, 52 (75.4%) patients had abnormal MoCA-INA, 52(75.4%) patients had abnormal Forward Digit Span and 48(69.6%) patients had abnormal Backward Digit Span. There was significant correlation between pain intensity and cognitive function in migraine, TTH and cluster headaches patients. The MoCA-INA, Forward Digit Span and Backward Digit Span had negative correlations with pain intensity, whereas TMT A-time, TMT A-error, TMT B-time and TMT B-error had positive correlation.

Conclusion: There were significant associations between pain intensity of and cognitive function in primary headaches with $p<0.05$. It is suggested that the more severe pain intensity, the more impair of cognitive function.

Keywords

Primary headache, cognitive function, MoCA-INA, Digit Span, trail making test

Introduction

Primary headaches are headaches that are not associated with another pathology or disorder that causes them. “Primary” refers to a lack of clear underlying causative pathology, trauma, or systemic disease. Migraine and tension-type headache (TTH) are the most dominant headaches. Migraines are more disruptive to activity and require more medication than TTH. The male-to-female ratio is 1:3 for migraine and 4:5 for TTH after 12 years of age (Hashel et al. 2019). Tension-type headache is the most common type of primary headache, characterized by bilateral, non-throbbing, mild to moderate intensity. It is generally precipitated by stress and mental tension but does not worsen with routine physical activity (Yang et al. 2016). Although, TTH is generally not as intense as migraine, it has a significantly higher prevalence in the general population (lifelong prevalence up to 78%). Despite the diagnostic criteria for TTH have been defined, it is still difficult to distinguish tension-type headache from migraine because of overlapping symptoms. Some evidence suggests that stress, fatigue, alcohol consumption, and menstruation are some of the triggering factors for TTH and migraine (Waldie et al. 2015).

The recent global annual prevalence of TTH was estimated at 32% (30% for episodic TTH, 2.4% for chronic TTH). Episodic TTH rates ranged from 10.8%–37.3% and chronic TTH rates ranged from 0.6%–3.3%. Average annual TTH prevalence was greater in European countries (53%) followed by South America (31.5%), North America (30%), Asia (18.5%), Middle East (10.3%), and Africa (7%) (Waldie et al. 2015). In the Asia Pacific region, the median (range) prevalence of primary headache disorders over 1 year was 9.1% (1.5–22.8%) for migraine, 16.2% (10.8–33.8%) for TTH, and 2.9% (1.0–3.9)% for cluster headache. According to the United Nations, the estimated population in the Asia Pacific region was 3.85 billion in 2010, equal to 350 million migraine headaches, 624 million with TTH, and 112 million with cluster headaches (Song et al. 2016). Research in Korea has shown the prevalence of TTH to be as high as 21.2%. In Asian countries, the 1- year prevalence of TTH varies between 10.8% and 33.3%, this figure is lower than in European and North American countries (Peng and Wang 2014).

Tension-type headache causes significant disability with 60% of sufferers reporting decreased work effectiveness, increased absenteeism, and reduced social involvement. A randomized study based on the general Danish population revealed that 59% of participants with TTH had moderate to severe impairment of daily activities due to headache, but another 41% had no disturbance in their daily activities (Waldie et al. 2015; Smith 2016).

A significant indicator of functional capacity and the need for care as people age is cognitive impairment. When a disturbance in one or more cognitive domains is identified but does not match the criteria for a dementia diagnosis, mild cognitive impairment (MCI) is diagnosed. According to statistics, 16% of older persons have MCI, which is more common in adult males than females and does not lead to dementia. Evidence from longitudinal and cross- sectional research indicates that older persons with MCI may experience a decline in overall functional capacity (World Health Organization (WHO) 2017).

Cognitive impairment is one of the most common health problems for older people. It is estimated that the prevalence of cognitive impairment is > 40% among elderly people > 80 years. Cognitive impairment includes mild cognitive impairment and various types of dementia, and is associated with an increased risk of disability and death. The findings of previous studies showed that approximately 30% of participants aged 80 years and over were diagnosed with cognitive impairment, with a prevalence of 19% among men and 39% among women (Ren et al. 2018).

According to Indonesian research, the prevalence of cognitive disorders is 6.8%, which is slightly lower than the American Health and Retirement Study (8.8%) from 2012 (Pengpid et al. 2019). Smith (2016) reported that the logical reasoning and semantic processing tasks, and also that those with a TTH had greater psychomotor slowing and were more easily distracted (Smith 2016).

Migraine is a common headache disorder with an average prevalence of 20.2% in women and 9.4% in men. Migraine had a moderate to significant effect on processing speed and visuomotor scanning speed, whereas basic attention and verbal memory delay were only slightly affected, and speed of more complex psychomotor processing was not significantly affected.

Cluster headaches are more common in men and account for only one-tenth of the incidence of migraines, but cause disability comparable to migraines. There are few studies on cognitive performance in cluster headache. Although the patients displayed reversible cognitive decline during cluster attacks, their cognitive performance was detected as normal between attacks (Vuralli et al. 2018). The rate of deterioration in quality of life scores in cluster headache has been reported to be similar to the outcomes documented in migraine patients. Meanwhile, disability due to headache has been reported to be higher in patients with cluster headache than in migraine sufferers (Torkamani et al. 2015).

The MoCA-INA is a sensitive instrument in the screening for Mild Cognitive Impairment (MCI) that is based on the original Canadian version and includes cultural differentiation to Indonesia. The MoCA-INA assessment is more accurate in assessing cognitive impairment than the original version or other types of assessment. MoCA-INA assessment is used to detect mild cognitive dysfunction in any condition (Akbar et al. 2019).

Pain screening tools have become commonplace in a variety of health-care settings as part of routine care. The numeric rating scale (NRS) is a pain screening tool that is commonly used to assess current pain levels on a 0–10 scale, with 0 representing „no pain“ and 10 representing the worst possible level of pain. In outpatient care, the NRS is frequently used in clinical settings to assess pain.

The purpose of this study was to determine whether those are any association between pain intensity and cognitive function in patients with primary headaches comprised migraine, tension-type headache and cluster headache, in which the pain intensity was assessed using NRS scores.

Methods

We studied 69 subjects (Table 1) suffering from primary headache comprised 37 migraine, 27 TTH and 5 cluster headaches according to the International Classification of Headache Disorders, 3rd edition beta version (ICHD-3 beta) criteria (Headache Classification Committee of the International Headache Society (IHS) 2013). All patients were recruited among those attended during March and October 2020, the outpatient clinic of the Adam Malik General Hospital Medan and Universitas Sumatera Utara Hospital Medan. We included both male and female patients between 18 and 80 years old. We excluded patients with psychiatric or

Table 1. Characteristics of Primary headache patients.

Characteristics	N = 69	%
Gender		
Male	28	40.6
Female	41	59.4
Age		
<25 years	25	36.2
25–45 years	12	17.4
46–65 years	30	43.5
>65 years	2	2.9
Education		
Primary school	0	0
Junior High school	5	7.2
Senior High School	36	52.2
University	28	40.6
Ocupation		
Housewifes	14	20.3
Enterpreneurs	9	13.0
Civil servants	6	8.7
Students	23	33.3
Farmers	8	11.6
Private pensioners	4	5.8
Private employees	5	7.2
Type of headache		
Migraine	37	53.6
TTH	27	39.1
Cluster headache	5	7.2
Duration of headache		
< 30 minutes	7	10.1
30 minutes – 2 hours	13	18.8
24–72 hours	27	39.1
> 72 hours	22	31.9
Skor MoCA-INA		
Abnormal	52	75.4
Normal	17	24.6
Forward Digit Span		
Abnormal	52	75.4
Normal	17	24.6
Backward Digit Span		
Abnormal	48	69.6
Normal	21	30.4

N = number of subjects; MoCA-INA = Montreal Cognitive Assessment Indonesian Version.

neurological disease, who are currently taking headache medication, patients with chronic diseases, patients with neurological deficits related to his/her headache, depression, extrapyramidal disorders, chronic obstructive pulmonary disease (COPD), bronchial asthma, heart failure, diabetes mellitus, cardiovascular disease and malignancy.

Written informed consent, following a detailed explanation of the study procedures and purposes, was obtained from each subject. The study was approved by Health Research Ethics Committee, Faculty of Medicine, Universitas Sumatera Utara (ethical code No: 230/TGL/KEPK FK USU-RSUP HAM/2020).

Through medical examination, the characteristics of the patients were noted, and the Numeric Rating Scale for Pain (NRS) scores was used to assess the severity of the headaches. The NRS scores are divided into 4 degrees of pain perception (0 = no pain, 1–3 = mild pain, 4–7 = moderate pain, and 8–10 = severe pain).

Results

There were 69 primary headache patients who met the inclusion and exclusion criteria and were enrolled in the study out of all primary headache patients who visited the Neurology Polyclinic Adam Malik General Hospital and Universitas Sumatera Utara Hospital in March 2020. Based on gender, it was found that 59.4% were female and 40.6% were male. Meanwhile, when assessed from the age range, 43.5% were aged 46–65 years, 36.2% were aged <25 years, 17.4% were aged 25–45 years and only 2.9% were aged > 65 years. When the sample was divided by education level, 52.2% were high school graduates, 40.6% were university graduates, and 7.2% were junior high school graduates. The majority of the samples 33.3% were students, 20.3% housewives, 13% entrepreneur, 11.6% farmers, 8.7% civil servants, 7.2% private employees, and only 5.8% were private pensioner.

From this study we found most of the subjects were migraine (53.6%) followed by tension-type headache (39.1%) and cluster headache (7.2%). Regarding duration of headache, 39.1% for 24–72 hours, 31.9% for >72 hours, 18.8% for 30 minutes – 2 hours, 10.1% for <30 minutes. If assessed based on the MoCA-INA score, it appears that 75.4% are abnormal and only 24.6% are normal. Same with the assessment based on Forward Digit Span, 75.4% were found to be abnormal and only 24.6% normal. Assessment with Backward Digit Span showed that 69.6% were found to be abnormal and 30.4% were found to be normal. Table 1 shows the characteristics of research subjects.

The descriptive analysis was assessed based on several variables consisting of age (Median 45; Min-Max 20–72), headache intensity (Median 6; Min–Max 4–8), MoCA-INA score (Median 23; Min–Max 14–29).), Trail Making Test A – time (Median 187; Min-Max 97–199), Trail Making Test A – error (Median 5; Min–Max 0–12), Trail Making Test B – time (Median 335; Min–Max 113–399), Trail Making Test A – error (Median 3; Min–Max 0–9), Forward Digit Span (Median 3; Min–Max 1–8), and Backward Digit Span (Median 3; Min–Max 1–5). Table 2 shows the descriptive analysis of age, NRS scores and cognitive function features of the subjects.

To determine the correlation of pain intensity that assessed by NRS scores with cognitive function based on sever-

Table 2. Descriptive analysis of age, NRS scores and cognitive function.

Variables	Median	Min – Max
Age	45	20–72
Pain intensity (NRS scores)	6	4–8
MoCA-INA scores	23	14–29
Trail Making Test A – time	187	97–199
Trail Making Test A – error	5	0–12
Trail Making Test B – time	335	113–399
Trail Making Test B – error	3	0–9
Forward Digit Span	3	1–8
Backward Digit Span	3	1–5

MoCA-INA, Montreal Cognitive Assessment Indonesian Version; NRS, Numeric rating scale; Min, Minimum; Max, Maximum.

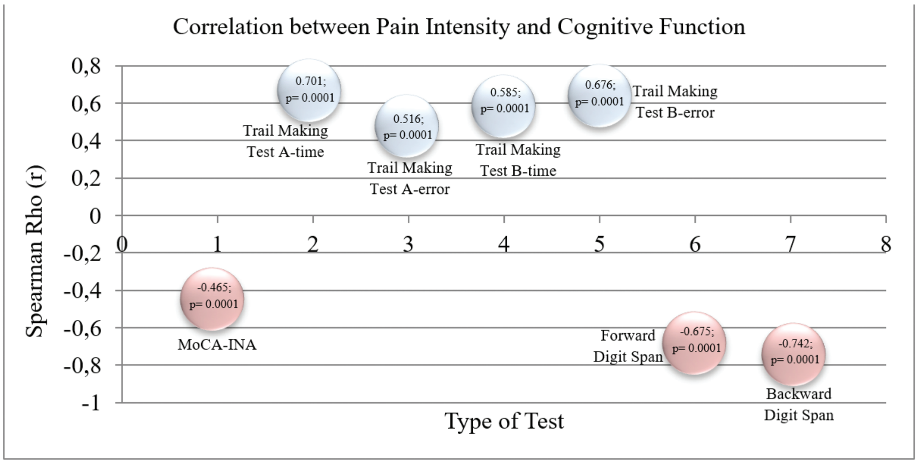

Figure 1. Correlation of each cognitive function test with pain intensity assessed by NRS scores. Values within balls represent correlation coefficients and p values. Blue balls indicate positive correlation and red balls indicate negative correlations; significant correlations p < 0.05.

al variables, Spearman's correlation test was carried out and showed the MoCA-INA score (r = -0.465; p value 0.0001), Trail Making Test A – time (r = 0.701 p value 0.0001), Trail Making Test A – error (r = 0.516; p value 0.0001), Trail Making Test B – time (r = 0.585; p value 0.0001), Trail Making Test B – error (r = 0.676; p value 0.0001), Forward Digit Span (r = -0.675 ; p value 0.0001), Backward Digit Span (r = -0.742; p value 0.0001). P < 0.05 indicates a significant correlation between pain intensity and cognitive function. The MoCA-INA, Forward Digit Span and Backward Digit Span had negative correlations with pain intensity, whereas TMT A-time, TMT A-error, TMT B-time and TMT B-error had positive correlation. Fig. 1 shows the correlation between pain intensity and cognitive function.

Discussion

According to the findings of this study, 59.4% were female, with 43.5% being between the ages of 46 and 65. In terms of headache type, 53.6% had migraine, 39.1% had tension-type headache, and 7.2% had cluster headache, with 39.1% experiencing pain for 24 to 72 hours. According to the MoCA-INA score, 75.4% are abnormal, while just 24.6% are normal. Similar to the Forward Digit Span evaluation, 75.4% were determined to be abnormal and only 24.6% normal. Backward Digit Span testing revealed that 69.6% were abnormal, whereas 30.4% were normal. The median age in this study was 45 years (min 20–max 72), and the median MoCA- INA was 23 (min 14–max 29). The findings of a study conducted by Huang et al. (2017) on 34 migraine patients revealed that 28 samples were female and 6 were male with the average of age was 36.065 ± 10,046 years old, and the headache lasted 23.4 ± 24,197 hours. They found that sample with migraines performed considerably worse (p = 0.007) than healthy subjects in language (p = 0.005), memory (p = 0.006), executive function (p = 0.042), calculation (p = 0.018), and orientation (p = 0.012) on the Montreal Cognitive Assessment (MoCA-INA). In the migraine sample, the mean MoCA-INA score was 25.677 ± 0.604 (Huang et al. 2017).

Research by Gil-Gouveia et al. (2015) showed that the mean age of the sample whose experienced migraine was 31.8 ± 8.8 years with attacks ± 6.7 times for each sample and it was found that attack intensity and disability score correlated with intensity and disability of pain and worsening mental health (Gil-Gouveia et al. 2015). Zampieri et al. (2014) in his research that discussed headaches and psychological disorders, it showed that in patients with chronic headaches, 90% were women and 10% were men with an average age of 44 ± 14.1 years (Zampieri et al. 2014).

Cognitive dysfunction has recently emerged as a major issue among migraine sufferers. Despite the fact that all clinical studies reveal impaired cognitive performance during migraine attacks, the interictal data is contradictory. In the majority of clinic-based research, migraineurs have poor cognitive function. A difference in cognitive functions between migraineurs and controls was not found in population-based research. Information processing speed, fundamental attention, executive function, verbal and nonverbal memory, and language abilities are the specific cognitive areas involved. Studies on neurophysiology, imaging, and pharmacology lend support to the clinical signs of migraine-related cognitive impairment. Longitudinal studies have not shown progressive cognitive decline over time in migraine patients (Vuralli et al. 2018). Altered functional connectivity is found in cognitive brain networks, such as the executive control network, the default mode network, the visual network. It appears to be associated with disease duration, gender, and chronicity of migraine (Kotb et al. 2020).

The role of sex hormones is more often found in cases of migraine headaches. Entering the age of puberty, due to hormonal changes, the frequency of headaches is increasing with the incidence rate being 2–3 times more frequent in women than in men which proves that changes in hormonal status play a major role in the occurrence of migraines. Included in these hormonal changes are menarche, menstruation, pregnancy, menopause, and also the use of hormonal contraception, both oral and hormonal replacement therapy. Migraines strike women 3 times more often than men. Migraines appear more often 1–2 years before or after menarche, the tendency to suffer from migraines at the age of menarche will experience migraines in the future. The peak age for migraines in women after puberty is around 30 to 39 years. Changes in sex hormones, especially in women, trigger migraines. Female hormones, especially estrogen, fluctuate during a woman‘s life in accordance with the natural cycle of hormones, which can trigger migraines. Estrogen withdrawal acts as a migraine trigger and this was confirmed through a study on experimental animals which showed the female gonadotropin hormone increases the risk of migraine through estrogen-dependent electrophysiological effects, serotonergic tone, and also suspected of cortical spreading depression (Susanti 2020).

Women have a much greater number of active trigger points (TrPs) than men, especially in the sub-occipital, temporal, splenius muscles. The number of active TrPs is thought to be caused by differences in innate muscle structure between males and females In TTH patients, the number of active TrPs is likewise inversely correlated with anxiety levels. Muscle discomfort has been linked to anxiety levels in previous research. Stress really increases the likelihood that pain may manifest. There is evidence to suggest that women experience more anxiety than men (1.8:1) (Wang et al. 2014).

Smith (2016) reported that the tension-type headache (TTH) with cognitive impairment, the headache duration was >30 minutes and < 4 hours. The results of the study confirm a global increase in the effects of migraines when the person has TTH. The results confirmed impairments in logical reasoning and migraine processing tasks, and also demonstrated that the sample with TTH had greater psychomotor retardation and was more easily distracted. The effect does not continue after the headache is gone (Smith 2016).

The Significant associations between pain severity and cognitive performance were discovered in the current investigation. While MoCA-INA, Forward Digit Span, and Backward Digit Span had negative relationships with pain severity, Trail Making Test A-time, TMT A- error, TMT B-time, and TMT B-error had positive connections. This makes sense because stronger cognitive performance is indicated by higher values of MoCA-INA, TMT A-time, TMT A-error, TMT B-time, and TMT B-error, and vice versa. Meanwhile, the higher the values of the Forward Digit Span and the Backward Digit Span, the worse the cognitive function and vice versa. On the other hand, the higher the NRS value indicates the more severe the pain intensity.

Conclusion

According to some theories, patients with primary headaches may experience cognitive impairment in proportion to how intense their pain is, and vice versa. However, given the small sample size, our data should be regarded with caution.

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