Research Article

INTERNATIONAL RESEARCH JOURNAL OF PHARMACY

www.irjponline.com

ISSN 2230-8407 [LINKING]

COMPARATIVE ASSESSMENT OF SIZE OF THE PUPIL IN SUBJECTS WITH MIGRAINE AND PHOTOPHOBIA TO NORMAL SUBJECTS AND CORRELATION OF SEVERITY OF HEADACHE TO PUPIL SIZE

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How to cite: Bhojane VR, Mahajan MA, Kadam KN, Sathe SP. Comparative assessment of size of the pupil in subjects with migraine and photophobia to normal subjects and correlation of severity of headache to pupil size. International Research Journal of Pharmacy, 2025,16:4:24-27.

DOI:10.7897/2230-8407.110515

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ABSTRACT

Background: Abnormalities in the size of the pupil are a reason for migraine in photophobia in subjects. However, existing literature data is scarce concerning the grade of severity of migraine and the relation of pupil size in affected subjects.

Aim: The present study aimed to comparatively assess the size of the pupil in subjects with migraine and photophobia to normal subjects and the correlation of the severity of headache to pupil size.

Methods: The present study assessed 100 subjects having migraine with photophobia and were compared to 100 control subjects that had no history of headaches and were gender and age-matched. The size of the pupil was assessed using IOL Master 700 in all the subjects. The severity of the headache was assessed using the MIDAS (Migraine disability assessment) test questionnaire and MIDAS grades from 1 to 4 depicting minimal disability to severe disability in all the subjects. Pupil size was compared in all the grades.

Results: The mean pupil size was significantly higher in subjects with migraine with 4.87±0.7 mm compared to 3.6±0.47 mm in control subjects with $p<0.001$. In 100 subjects assessed with migraine, following MIDAS grades, 40 subjects showed severe disability with Grade 4, 30 subjects showed moderate disability of Grade 3, 20 subjects showed mild disability of Grade 2, and 10 subjects showed minimal disability with Grade 1. Pupil size was largest in the Grade 4 category with a mean value of 5.4±0.77mm.

Conclusion: The present study concludes that pupil size in subjects with migraine and photophobia was larger compared to control subjects and can lead to triggering of the migraine attack. More severe migraine disability was seen in subjects with larger pupil size.

Keywords: MIDAS, migraine with photophobia, pupil, pupil size, photophobia

INTRODUCTION

Migraine is the third most common disorder prevalent globally and presents an estimated Worldwide prevalence of approximately 14.7% affecting one subject among every seven individuals. Migraine attacks comprise a core component of

light sensitivity known as photophobia in nearly 80% of the subjects. In one-third of the subjects having migraine, the triggering factor for the migraine attack is contributed to the bright light.[1]

Presently, the diagnosis of migraine is based on the clinical criteria including the throbbing pain which is mostly unilateral, gets worse by the activity, and is associated with sensitivity to light/photophobia, nausea, and/or sensitivity to sound (phonophobia). Among all the peculiar features associated with migraine, photophobia is the most common feature and often comprises the disabling component of a migraine attack that serves as a criterion for diagnosis. Photophobia represents exacerbation and/or triggering factor of headache by light. However, light sensitivity can also be seen between migraine attacks and is supported by findings of the threshold for lower interictal light sensitivity in migraineurs compared to control subjects without headaches.[2,3]

The reason for photophobia in migraine subjects is not known completely, however, various neural circuits suggest cortical hypersensitivity to light, changes in ocular parasympathetic outflow, and intrinsically photosensitive retinal ganglion cell pathways posing action on dura-sensitive thalamocortical neurons which can affect the adaptation of the pupillary responses to light. Unilateral and transient mydriasis was previously reported in subjects having a medical history of migraine and it has been considered as Adie 's-like tonic pupil which is considered to be caused by migraine. The majority of existing literature data shows Adie's pupil as secondary to migraine attack owing to prolonged vasospasm leading to damage in the parasympathetic pathway.[4]

Abnormalities in the pupil are the reason for migraine associated with photophobia and the association of the grade of severity of migraine to the pupil size has not been extensively researched. The use of blue light filters and tinted glass has been reported as treatment options in subjects with migraine as some wavelengths of light have been shown to trigger migraine attacks which are not widely assessed.[5] Hence, the present study aimed to comparatively assess the size of the pupil in subjects with migraine and photophobia to normal subjects and the correlation of severity of headache to pupil size.

MATERIALS AND METHODS

The present case-control prospective clinical study was aimed to comparatively assess the size of the pupil in subjects with migraine and photophobia to normal subjects and the correlation of severity of headache to pupil size. The study was done at Department of Ophthalmology, SMBT Institute of Medical Sciences and Research Centre, Dhamangaon, Nashik, Maharashtra. Verbal and written informed consent were taken from all the subjects before study participation.

The study included 200 eyes in 100 subjects having migraine with photophobia in subjects aged 20-30 years and male: female ratio of 40:60. The study also assessed gender and age-matched subjects that comprised the control group. The inclusion criteria for the study were subjects, cases, and controls with no significant refractive error and visual acuity of 6/6. The exclusion criteria for the study were subjects who did not give consent for study participation and subjects having significant refractive error.

The study assessed all the subjects with anterior and posterior segment evaluation as normal. The present study utilized the criteria by ICHD-3 (International Classification of Headache Disorders) for the classification of migraine in the study subjects. MIDAS (migraine disability assessment) test questionnaire was filled out for all the subjects that had migraine with photophobia which gathered necessary data and the side of headache was also assessed in all the subjects.

The size of the pupil was measured with the pupil in the non-dilated state in all the subjects using the IOL Master 700. The photopic pupil size was measured using the normal bright light surroundings. All the measurements were done by a single examiner expert in the field for controls as well as cases under identical lighting conditions. No subject used any medication or eye drops before the study. In all the subjects, a neurological examination was done before the study which showed normal results.

The data gathered were analyzed statistically using SPSS (Statistical Package for the Social Sciences) software version 24.0 (IBM Corp., Armonk. NY, USA) for assessment of descriptive measures, one-way ANOVA (analysis of variance), and chi-square test. The results were expressed as mean and standard deviation and frequency and percentages. The p-value of <0.05 was considered statistically significant.

RESULTS

The present case-control prospective clinical study was aimed to comparatively assess the size of the pupil in subjects with migraine and photophobia to normal subjects and the correlation of severity of headache to pupil size. The present study

assessed 100 subjects having migraine with photophobia and were compared to 100 control subjects who had no history of headaches and were gender and age-matched. The size of the pupil was assessed using IOL Master 700 in all the subjects.

On assessing the mean pupil size, it was seen that the mean size of the pupil was 4.87±0.89 mm in subjects having migraine with photophobia, whereas, the mean pupil size was 3.6±0.47 mm in healthy control subjects with no migraine and photophobia. This difference in pupil size in the two study groups was highly statistically significant with a p-value of <0.0001 (Table 1).

Among 100 assessed study subjects with migraine, following the MIDAS grades, it was seen that 40 subjects showed severe disability with Grade 4, 30 subjects showed moderate disability with MIDAS grade 3, 20 subjects showed mild disability with Grade 2, and 10 subjects had minimal disability with Grade 1. The largest pupil size was seen in subjects with Grade 4 disability with a mean pupil size of 5.4±0.77mm. In Grade 3 severity, the mean pupil size was 4.4±0.66mm. Grade 2 severity showed a mean pupil size of 4.24±0.42mm, and Grade 1 category subjects showed a mean pupil size of 3.93±0.56mm. The largest pupil size was seen in subjects with the Grade 4 category among all grades of disability.

The study results showed that in 80% of the subjects, larger pupil size was seen on the side which was frequently associated with the attack of the migraine, and in the other 20% of subjects, both sides depicted similar frequency of the migraine attack. The time of pupil reaction to the light increased with the larger pupil sizes, however, it has not been quantified in the study. Near vision, however, was normal in these subjects and no subject particularly complained about the difficulties in the near vision. The largest diameter of the pupil in the present study was 7.0 and 6.6 mm in a study subject that reported severe migraine attacks and photophobia whenever the subject was exposed to sunlight owing to which subject preferred to stay indoors the majority of the time.

DISCUSSION

The present study assessed 100 subjects having migraine with photophobia and were compared to 100 control subjects who had no history of headaches and were gender and age-matched. The size of the pupil was assessed using IOL Master 700 in all the subjects. The study design of the present study was similar to the studies of Ryu HK et al[6] in 2021 and Mahroo OA et al[7] in 2017 where authors adopted a study protocol similar to the present study in their respective studies on migraine subjects.

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It was also seen that in 80% of the subjects, larger pupil size was seen on the side which was frequently associated with the attack of the migraine, and in the other 20% of subjects, both sides depicted similar frequency of the migraine attack. The time of pupil reaction to the light increased with the larger pupil sizes, however, it has not been quantified in the study. Near vision, however, was normal in these subjects and no subject particularly complained about the difficulties in the near vision. The largest diameter of the pupil in the present study was 7.0 and 6.6 mm in a study subject that reported severe migraine attacks and photophobia whenever the subject was exposed to sunlight owing to which subject preferred to stay indoors the majority of the time. These results were in line with the findings of Amiri P et al[12] in 2022 and Tafakhori A et al[13] in 2011 where authors reported larger pupil size was seen on the side which was frequently associated with the attack of migraine which was similar to the present study.

CONCLUSIONS

The present study, within its limitations, concludes that pupil size in subjects with migraine and photophobia was larger compared to control subjects and can lead to triggering the migraine attack. More severe migraine disability was seen in subjects with larger pupil size. In the future, prospective studies with subjects from different geographical areas and sun conditions will be needed to assess the effect of photophobia on migraine and pupil sizes in affected subjects.

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	No headache	**Migraine with photophobia**	**p-value**
Mean photopic pupil size (mm)	3.6±0.47	4.87±0.89	**<0.0001**

Table 1: Mean in pupil size in controls and subjects with migraine

Mean photopic pupil size (mm)	**MIDAS grades of migraine severity**
Grade 1	3.93±0.56
Grade 2	4.24±0.42
Grade 3	4.4±0.66
Grade 4	5.4±0.77

Table 2: Mean pupil size in subjects with migraine to different grades of severity