Original Article

Accommodative functions in opium users and non-users

Tahereh Sadat Khoshnazar [1], Mehdi Sharifzadeh Kermani [2], Monireh Mahjoob [3] and Masoud Sadeghi [4]

[1] *Student Research Committee, Department of Optometry, Faculty of Rehabilitation, Shahid Beheshti University of Medical Sciences, Tehran, Iran*
[2] *Clinical Research Development Unit, Shafa Hospital, Kerman University of Medical Sciences, Kerman, Iran*
[3] *Health Promotion Research Center, Department of Optometry, School of Rehabilitation Sciences, Zahedan University of Medical Sciences, Zahedan, Iran*
[4] *Department of Optometry, School of Rehabilitation, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

ABSTRACT

Background: Emerging evidence highlights a concerning prevalence of accommodative and convergence anomalies in individuals with opioid use disorder. However, there remains a significant scarcity of data comparing accommodative functions of opium users and non-users. Hence, we investigated potential changes in accommodative functions of opium users compared to that of non-users. Furthermore, we evaluated changes in these parameters after administering 5% phenylephrine eye drops, both within and between the two groups.

Methods: This cross-sectional case-control study recruited opium users and non-users. The binocular amplitude of accommodation (AA), monocular estimate method (MEM), negative and positive relative accommodation (NRA and PRA, respectively), and monocular and binocular accommodative facility (AF) were assessed and documented. All measurements were repeated 30 min after instillation of one drop of 5% phenylephrine hydrochloride eye drops.

Results: We recruited 103 opium users and 107 non-users, with comparable mean ages ($P > 0.05$) but significantly different sex ratios ($P < 0.05$), with men outnumbering women among the opium users. All accommodative functions measured before and after the instillation of 5% phenylephrine, along with the differences in their values between the two time points, were comparable between the two groups (all $P > 0.05$), with the exception of the right-eye AF, which was significantly higher in non-users than in opium users after instillation ($P < 0.05$). Within the opium user group, all accommodative functions exhibited significant differences between pre- and post-instillation measurements (all $P < 0.05$), except for NRA, which did not change ($P > 0.05$). In contrast, the non-user group showed no significant differences between pre- and post-instillation measurements for all accommodative functions (all $P > 0.05$), except in the AA and the right-eye MEM (both $P < 0.05$).

Conclusions: We observed small but significant changes in most baseline accommodative functions after the application of 5% phenylephrine eye drops in opium users. In contrast, most parameters remained unchanged in healthy non-users. When comparing the results between the two groups pre- and post-application of phenylephrine, we found similar accommodative functions overall. However, non-users had a significantly higher value for the right-eye AF following the instillation. To better understand potential binocular anomalies in opium users, further longitudinal studies that are matched for age and sex should be conducted, focusing on additional aspects of binocular vision and ocular motility.

KEYWORDS

opium use, opium addiction, phenylephrine hydrochloride, binocular vision, ocular accommodation

Correspondences: Masoud Sadeghi, Department of Optometry, School of Rehabilitation, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Email: jaamejamoptometry@gmail.com. ORCID iD: https://orcid.org/0000-0002-8353-2904.

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INTRODUCTION

Opiates encompass a variety of substances, including naturally occurring morphine, semisynthetic heroin, and synthetic derivatives such as meperidine and methadone. Prescription opioids, such as hydrocodone, oxycodone, pentazocine, and fentanyl, also belong to this category [1]. Additionally, the sap of the poppy plant (Papaver somniferum)—known as opium, or Theriac—is included among the opiates [2].

The effects of opiates on the eyes and visual system can vary significantly [1]. These include oculomotor symptoms such as acute-onset esotropia with diplopia [3], downbeat nystagmus, saccadic intrusions and oscillations such as square wave jerks and saccadic pulses, decreased gain of sinusoidal vestibulo-ocular reflex and smooth pursuit [4], accommodative and convergence anomalies [5], and intermittent or constant exotropia [6, 7]; increased likelihood of developing cataracts [8]; and severe complications such as diffuse retinal ischemia [9].

Accommodative and non-strabismic binocular dysfunctions represent a diverse group of visual disorders that often accompany various asthenopic symptoms. These symptoms can be particularly bothersome during close work and may significantly impair daily activities, ultimately reducing the quality of life [10-12]. Although there are reports of a high prevalence of accommodative and convergence anomalies—such as accommodative insufficiency, accommodative infacility, and convergence insufficiency—in individuals with opioid use disorder [5], there is scarcity of data comparing accommodative functions between opium users and non-users.

Thus, we aimed to compare accommodation and binocular vision performance between opium users and non-users by measuring accommodative functions. Additionally, we evaluated any changes in these parameters after administrating 5% phenylephrine eye drops, both within and between groups.

METHODS

This cross-sectional case-control study recruited opium users and non-users through convenience sampling from individuals visiting the ophthalmology outpatient clinic at Shafa Hospital in Kerman, Iran, between 01 November 2023 and 01 November 2024. The study protocol received approval from the ethics committee of Shahid Beheshti University of Medical Sciences and adhered to the ethical standards outlined in the Declaration of Helsinki. After a thorough briefing about the study, all participants provided written informed consent prior to their involvement.

The inclusion criteria for opium users were as follows: age of 20 – 60 years; opium use (only Theriac) [2] for at least 5 years; no systemic or ocular comorbidities such as diabetes mellitus, hypertension, central nervous system disorders, cataracts, glaucoma, or accommodation disorders; no history of refractive or intraocular surgeries; and no use of medications with effects similar to those of opium. The study excluded individuals who had not used opium for 2 – 4 weeks; who used any systemic psychotropic drugs, alcohol, hashish, or other illicit drugs; and those who underwent treatment for opioid use disorder. Non–drug-abusing healthy controls of both sexes were recruited from individuals in the same age range.

Comprehensive orthoptic assessments were performed [13], and detailed ocular examinations of the anterior and posterior segments [14, 15] were conducted using a slit-lamp microscope (Topcon, Tokyo, Japan). Objective manifest refraction was assessed using a Topcon KR 8900 auto-refracto-keratometer (Topcon Inc., Tokyo, Japan) and subjectively refined using a streak retinoscope (Heine Beta 200 Retinoscope; Heine Optotechnik, Herrsching, Germany). Best-corrected distance visual acuity was determined through full-distance sphere-cylindrical refraction using a trial frame and trial lenses, with visual acuity assessed by Snellen chart. Near visual acuity was recorded using a reduced Snellen near vision card. For participants with presbyopia, near-vision spectacles were prescribed as needed.

The accommodative and binocular tests were performed by the same examiner [16], applying standard methods as detailed elsewhere [5, 17-21], during the same daytime interval to avoid the effect of diurnal variation in accommodation values [22, 23]. The horizontal and vertical phoria for near and distance was determined using a prism bar and alternate cover test. The near point of convergence was measured and recorded in centimeters [17]. Pupil diameter was measured and recorded in millimeters using a standard pupil gauge printed on a near-vision reading card [18]. Final assessments included the near point of accommodation [17] for calculating binocular amplitude of accommodation (AA) [21] in diopters (D), monocular estimate method (MEM) findings in D [19], negative and positive relative accommodation in D (NRA and PRA, respectively) [20], and monocular and binocular accommodative facility (AF) in cycles per minute (CPM) [5]. Measurement of best-corrected distance and near visual acuities with all accommodative and binocular tests were repeated 30 min after instillation of one drop of 5% phenylephrine hydrochloride eye drops (Neophrin® 5, Sina Daru Co., Tehran, Iran) [24] in both eyes of each individual.

Data were entered into IBM SPSS Statistics for Windows (version 24.0; IBM Corp., Armonk, NY, USA). The Kolmogorov – Smirnov and Shapiro – Wilk tests were employed to assess the normality of data distribution. Quantitative data are presented as mean (standard deviation [SD]) for normally distributed data and as median (interquartile range [IQR]) for non-normally distributed data. Qualitative data are expressed as numbers (percentages). Means were compared using either the Student's *t*-test or the paired *t*-test, while medians were compared using the Mann – Whitney U test or the Wilcoxon signed-rank test, as appropriate. Categorical variables were analyzed using the chi-square test. To minimize type I error resulting from multiple testing, the Bonferroni correction method was employed, as explained elsewhere [25]. A significance level of $P < 0.05$ was established for all tests.

RESULTS

We recruited 210 individuals, 103 opium users and 107 non-users, with comparable mean ages ($P > 0.05$) and significantly different sex ratios ($P < 0.05$), with men outnumbering women among opium users (Table 1).

All accommodative functions measured at pre- and post-instillation of phenylephrine (Table 2), along with the differences in their values between the two time points (Table 3), were comparable between groups (all $P > 0.05$), except for the right-eye AF, which was significantly higher in non-users than in opium users at the post-instillation time point (mean [SD] values for non-users and opium users were 7.93 [5.08] and 6.65 [4.88] CPM, respectively; $P < 0.05$) (Table 2).

Within-group comparisons among the opium users uncovered a significant decrease in mean values of all accommodative functions between the pre- and post-instillation time points (all $P < 0.05$), except for the right-eye MEM, which increased significantly ($P < 0.05$), and the NRA, which was unchanged (mean [SD] values for pre- and post-instillation were + 1.71 [0.44] and + 1.70 [0.43] D, respectively; $P > 0.05$) (Table 2). At the pre- and post-instillation time points, the calculated mean (SD) values for AA, right-eye AF, left-eye AF, both-eyes AF, PRA, right-eye MEM, and left-eye MEM were 5.16 (3.15) and 5.13 (3.15) D, 6.73 (4.85) and 6.65 (4.88) CPM, 6.74 (4.61) and 6.68 (4.61) CPM, 4.91 (3.68) and 4.85 (3.68) CPM, - 0.89 (0.53) and - 0.88 (0.54) D, 0.92 (0.35) and 1.00 (0.40) D, and 1.01 (0.40) and 0.94 (0.35) D, respectively.

In contrast, within-group comparisons among non-users found no significant differences between pre- and post-instillation values of all accommodative functions (all $P > 0.05$), except for a significant decrease in AA (mean [SD] values for pre- and post-instillation were 5.80 [3.28] and 5.76 [3.25] D, respectively; $P < 0.05$) and increase in the right-eye MEM (mean [SD] values for pre- and post-instillation were 0.84 [0.36] and 0.92 [0.44] D, respectively; $P < 0.05$) (Table 2).

Table 1. Comparison of demographic characteristics of study groups

Variable	Opium users (n = 103)	Non-users (n = 107)	*P*-value
Age (y), Mean ± SD	41.6 ± 11.0	39.1 ± 10.5	0.093
Sex (Men / Women), n (%)	72 (69.9) / 31 (30.1)	47 (43.9) / 60 (56.1)	**< 0.001**

Abbreviations: n, number of participants; y, years; SD, standard deviation; %, percentage. Note: *P*-value < 0.05 is shown in bold.

Table 2. Between-group and within-group comparisons of accommodative functions before and after instillation of 5% phenylephrine

Variable		Time-point	Opium users, Median (IQR) (Range)	Non-users, Median (IQR) (Range)	[2] *P*-value
AA (D)		Pre	+ 5.00 (+ 4.50) (+ 0.5 to + 12.50)	+ 5.00 (+ 4.50) (+ 0.50 to + 16.00)	0.163
		Post	+ 5.00 (+ 4.50) (+ 0.5 to + 12.50)	+ 5.00 (+ 4.50) (+ 0.50 to + 16.00)	0.173
		[1] ***P*-value**	**0.014**	**0.020**	-
AF (CPM)	**OD**	Pre	5.00 (8.00) (1.00 to 19.00)	6.00 (9.00) (1.00 to 23.00)	0.057
		Post	5.00 (8.00) (1.00 to 19.00)	7.00 (9.00) (1.00 to 20.00)	**0.044**
		[1] ***P*-value**	**0.011**	0.329	-
	OS	Pre	5.00 (8.00) (1.00 to 18.00)	7.00 (9.00) (- 0.75 to 23.00)	0.093
		Post	5.00 (8.00) (1.00 to 18.00)	7.00 (9.00) (1.00 to 23.00)	0.056
		[1] ***P*-value**	**0.034**	0.160	-
	OU	Pre	4.00 (5.00) (1.00 to 15.00)	5.00 (8.00) (1.00 to 17.00)	0.108
		Post	4.00 (5.00) (1.00 to 15.00)	5.00 (8.00) (1.00 to 16.00)	0.093
		[1] ***P*-value**	**0.063**	0.059	-
PRA (D)		Pre	- 0.75 (+ 0.75) (- 2.25 to - 0.25)	- 0.75 (+ 1.00) (- 2.50 to + 1.50)	0.176
		Post	- 0.75 (+ 0.75) (- 2.25 to - 0.25)	- 0.75 (+ 1.00) (- 2.50 to + 2.00)	0.270
		[1] ***P*-value**	**0.046**	0.121	-
NRA (D)		Pre	+ 1.75 (+ 0.50) (+ 0.75 to + 2.50)	+ 1.75 (+ 0.50) (+ 0.75 to + 2.50)	0.274
		Post	+ 1.75 (+ 0.50) (+ 0.75 to + 2.50)	+ 1.75 (+ 0.50) (- 1.00 to + 2.50)	0.180
		[1] ***P*-value**	0.317	0.366	-
MEM (D)	**OD**	Pre	+ 1.00 (+ 0.50) (+ 0.25 to + 1.75)	+ 0.75 (+ 0.50) (- 0.50 to + 2.00)	0.091
		Post	+ 1.00 (+ 0.50) (+ 0.25 to + 1.75)	+ 0.75 (+ 0.75) (- 0.75 to + 2.00)	0.179
		[1] ***P*-value**	**0.001**	**0.001**	-
	OS	Pre	+ 1.00 (+ 0.50) (+ 0.25 to + 1.75)	+ 0.75 (+ 0.75) (- 0.75 to + 2.00)	0.060
		Post	+ 1.00 (+ 0.50) (+ 0.25 to + 1.75)	+ 0.75 (+ 0.75) (- 0.25 to + 2.00)	0.176
		[1] ***P*-value**	**0.005**	0.091	-

Abbreviations: IQR, interquartile range; AA, amplitude of accommodation; D, Diopters; AF, accommodative facility; CPM, cycle per minute; OD, right eye; OS, left eye; OU, both eyes; PRA, positive relative accommodation; NRA, negative relative accommodation; MEM, monocular estimate method. Note: *P*-values < 0.05 are shown in bold; Pre, before instillation of 5% phenylephrine; Post, 30 min after instillation of 5% phenylephrine; [1] *P*-value, within-group comparisons of accommodative values pre- and 30 min post-instillation of 5% phenylephrine; [2] *P*-value, between-group comparisons of accommodative values pre- and 30 min post-instillation of 5% phenylephrine; IQR is defined as the difference between the third quartile and the first quartile of data distribution; Range is expressed as minimum to maximum.

Table 3. Between-group comparisons of accommodative functions before and after instillation of 5% phenylephrine

Variables		Difference in opium users, Median (IQR) (Range)	Difference in non-users, Median (IQR) (Range)	*P*-value
AA (D)		0. 00 (0.00) (- 0.50 to 0.00)	0. 00 (0.00) (- 2.5 to 0.00)	0.959
AF (CPM)	**OD**	0.00 (0.00) (- 2.00 to 0.00)	0. 00 (0.00) (- 3.00 to + 2.00)	0.346
	OS	0.00 (0.00) (- 1.00 to +1.00)	0. 00 (0.00) (- 2.00 to + 12.75)	0.978
	O U	0.00 (0.00) (- 2.00 to 0.00)	0. 00 (0.00) (- 3.00 to 0.00)	0.951
PRA (D)		0.00 (0.00) (0.00 to + 0.25)	0. 00 (0.00) (- 0.25 to + 3.25)	0.771
NRA (D)		0.00 (0.00) (- 0.50 to + 0.25)	0. 00 (0.00) (- 2.75 to + 0.25)	0.113
MEM (D)	**OD**	0.00 (+ 0.25) (- 0.50 to + 0.50)	0. 00 (+ 0.25) (- 1.75 to + 1.00)	0.880
	OS	0.00 (+ 0.25) (- 0.50 to + 0.50)	0. 00 (+ 0.25) (- 0.50 to + 1.75)	0.311

Abbreviations: IQR, interquartile range; AA, amplitude of accommodation; D, Diopters; AF, accommodative facility; CPM, cycle per minute; OD, right eye; OS, left eye; OU, both eyes; PRA, positive relative accommodation; NRA, negative relative accommodation; MEM, monocular estimate method. Note: *P*-values < 0.05 are shown in bold; Difference, difference in accommodative functions between before and 30 min after instillation of 5% phenylephrine; IQR is defined as the difference between the third quartile and the first quartile of data distribution; Range is expressed as minimum to maximum.

DISCUSSION

We recruited 103 opium users and 107 age-matched non-users, with men outnumbering women among the opium users. In opium users, we observed a small but significant change in all baseline accommodative functions after the instillation of 5% phenylephrine eye drops. Specifically, their mean values decreased, except for the MEM in the right eye, which increased significantly, and the NRA, which did not change. In contrast, we found no significant changes in accommodative functions for non-users between the two time points, except for a significant decrease in AA and an increase in the right-eye MEM. Despite these differences, all measured accommodative functions—both before and after phenylephrine instillation, as well as the differences between these values—were comparable between the two groups, except for a significantly higher value of the right-eye AF in non-users at the post-instillation time point.

The primary aim of accommodation is to enhance visual performance; therefore, its most accurate measurement is subjective rather than objective [26]. In this study, we utilized subjective techniques to assess accommodative functions. We observed a significantly higher AF in the right eye of non-opium users, compared to opium users, 30 min after the instillation of 5% phenylephrine eye drops. Alabi et al. [27] reported that noxious stimulation of the cornea in healthy individuals produces a dose-dependent increase in the accommodative response, irrespective of whether the stimulation is mechanical or chemical [27]. The use of opioids for short-term pain relief following refractive surgery has been reported [28]. Because opioids serve as systemic analgesics [28], the differences we observed in the right-eye AF may be due to reduced pain sensation in opium users compared to that of healthy non-users. Further research could assess pain perception after phenylephrine instillation by measuring accommodative functions in both opium users and age- and sex-matched non-users. This may provide further insight into the effects of opium use.

Dynamic retinoscopy is a simple technique for quantifying accommodation in a clinical setting. Subjective measures could overestimate the true AA [29]. Mean values of AA obtained using this technique were found to be significantly lower than for the other two subjective methods [30], the modified push down and minus lens techniques. We employed a dynamic retinoscopy procedure to assess accommodative response using MEM, which may justify the lower values we obtained in both study groups.

Ghobadi et al. [5] conducted a cross-sectional study involving 80 young men with opioid use disorder, recruited through a convenience sampling method from a specialized drug-dependence rehabilitation center in Mashhad, Iran. The participants had a mean (SD, range) age of 30.5 (3.9, 19 – 35) years [5]. In the current study, the mean (SD, range) age of opium users was 41.6 (11.0, 20 – 60) years, with a men-to-women ratio of 2.3. Ghobadi et al. [5] reported that the prevalence of accommodative disorders was 33.75% (95% confidence interval [CI]: 23.55 – 45.19) and that of convergence disorders was 25.00% (95% CI: 15.99 – 35.94). The prevalence of accommodative insufficiency was 22.5% (95% CI: 13.91 – 33.21), which was notably higher than that of accommodative excess (3.75% [95% CI: 0.78 – 10.57]) and accommodative infacility (7.50% [95% CI: 2.80 – 15.61]) [5]. Likewise, the study reported a prevalence of convergence insufficiency of 18.75% (95% CI: 10.89 – 29.03), again higher than that of convergence excess (3.75% [95% CI: 0.78 – 10.57]) and basic exophoria (2.50% [95% CI: 0.30 – 8.74]). Multiple logistic regression analysis revealed a significant inverse relationship between pupil size and accommodative insufficiency (odds ratio [OR] = 0.45), accommodative infacility (OR = 0.67), and convergence insufficiency (OR = 0.55). The study concluded that young men with opioid use disorder exhibited a higher prevalence of certain accommodative and convergence disorders [5] when compared to normal populations of a similar age range reported in previous studies [31-34]. We found no significant differences in most accommodative functions—both before and after the administration of 5% phenylephrine eye drops—between opium users and age-matched healthy controls. The only exception was that non-users exhibited a significantly higher value of the right-eye AF after the eye drop instillation. This discrepancy between our findings and those of Ghobadi et al. [5] may be due to the older participant ages and wider age ranges in our study. Additionally, our study included female participants, who comprised 30.1% of the opium user group. Furthermore, the participants in our study were restricted to those who only used Theriac [2], an opiate type different from that used in the other study [5]. Notably, the aims of the two studies differed; Ghobadi et al. [5] aimed to report the prevalence of accommodative and convergence anomalies in patients with opioid use disorder, yet we focused on measuring and reporting the changes in accommodative function before and after the instillation of 5% phenylephrine in both opium users and non-users. Other undiscovered factors may contribute to this observed discrepancy, highlighting the need for further research in this area.

Aslaksen et al. [35] conducted a cross-sectional case-control study comparing visual acuity, orthoptic status, refractive state, color vision, and visual field between 63 children aged 5 – 13 years with prenatal opioid maintenance therapy exposure and 63 non-exposed children matched for age and sex [35]. They observed a significantly higher frequency of manifest strabismus (30% in the exposed group vs. 4.8% in the control group, with 19 and 3 cases, respectively) and manifest nystagmus (16% vs. 1.6%, with 10 and 1 cases, respectively). Additionally, the exposed children had a lower mean (SD) value of AA (12.85 [2.87] D vs. 14.24 [2.69] D) and poorer visual acuity when compared to the controls; these differences persisted even after adjusting for confounding factors [35]. Within the exposure group, the children exposed to methadone exhibited poorer visual acuities, along with higher frequencies of strabismus, nystagmus, hypermetropia, and astigmatism, when compared to those exposed to buprenorphine [35]. Furthermore, impaired or absent binocular function has been reported in children with prenatal opioid exposure [36]. Despite the differences in demographic and clinical characteristics between our participants and those in the study by Aslaksen et al. [35], our findings showed a significant change in most accommodative functions after the instillation of 5% phenylephrine eye drops in opium users. However, we observed no detectable changes in most accommodative functions in non-users. This suggests that opium users may experience instability in their accommodation and ciliary muscle contraction, reducing their ability to control accommodative functions. Both our study and that of Aslaksen et al. [35] provide clinical evidence of the effects of opium use on ocular motility. There is a persistent need for multicenter longitudinal studies with larger populations to gather more evidence on the health consequences of opium use.

Firth et al. [37] recruited 83 heroin users before detoxification and 69 after, along with a control group of 10 individuals. They reported mean (SD) binocular AA values of 12.93 (4.58) D in heroin users and 13.1 (3.2) D in non-users, with repeated measures showing values of 12.2 (4.16) D for heroin users and 14.5 (6.85) D for non-users, indicating no significant differences between the groups [37]. The mean (SD) binocular AA and repeated binocular AA values increased to 14.15 (6.68) D and 13 (5.1) D, after detoxification and before discharge for heroin users, again showing no significant difference [37]. A key finding of their study was a shift in the distance angle of deviation in the esotropic direction. This change was attributed to involvement of the sixth cranial nerve and divergence insufficiency [37]. Differences between the findings of their research [37] and those of the current study may arise from variations in addiction types, participant demographics, or measurement techniques, which warrant further investigation.

Pupil size can influence accommodative gain [38]. Pupillary diameter is significantly and independently associated with AA in individuals aged less than 44 years; however, this association does not hold for those aged 45 or more years [39]. Furthermore, pupil size has a significant impact on AA [40]. Therefore, addressing differences in pupillary diameter could serve as an early treatment target for presbyopia [39]. In the current study, within-group comparisons among non-users found a significant decrease in AA post-instillation of 5% phenylephrine.

The effects of phenylephrine eye drop on the accommodative system have been documented at concentrations ranging from 0.1% to 10% [41]. Phenylephrine is a pharmacological option for the treatment of presbyopia, particularly when used in a mixed combination at a concentration of 0.78%, which causes ciliary muscle contraction and mydriasis [42]. A 0.5% phenylephrine eye drop combined with 0.5% tropicamide can relax accommodation [43]. This combination is widely used as a cycloplegic agent because of its safety, rapid onset, and quick recovery [44, 45]. The mydriatic effect of phenylephrine eye drops can lead to a decrease in both objective and subjective measurements of accommodation [46]. Reductions in accommodative performance with concentrations of 2.5%, 5%, and 10% of the drug, combined with pupil diameter, suggest an independent role of pupil size in determining accommodative performance [24]. We administered 5% phenylephrine and assessed accommodative function 30 min after instillation. No significant differences were detected in most accommodative functions between opium users and healthy non-users, except for a significantly higher value of the right-eye AF in non-users at the post-instillation time point.

Richdale et al. [47] conducted a cross-sectional study involving 25 healthy young adults, in which they measured pupil size, accommodation, and ciliary muscle thickness both before and 30 min after the instillation of 1% proparacaine and 2.5% phenylephrine. The study found a significant reduction in AA, approximately 1 D, using the push-up test with phenylephrine. However, phenylephrine did not alter the accommodative response to a 4 D Badal target, as measured by either autorefraction or photorefraction [47].

Additionally, phenylephrine had no significant impact on baseline ciliary muscle thickness or the muscle's accommodative contraction. The researchers concluded that low-dose phenylephrine does not affect ciliary muscle dimensions and contractility, or the accommodative response to a 4 D near target [47]. We observed small but significant changes in binocular AA and MEM of the right eye 30 min after administering 5% phenylephrine in healthy non-opium users. The mean (SD) values for AA were

5.80 (3.28) D before instillation and 5.76 (3.25) D afterward. For the right-eye MEM, the values were 0.84 (0.36) D before and 0.92 (0.42) D after instillation.

Data from 1357 young students in Iran with a mean (SD, range) age of 22.71 (3.0, 18 – 39) years showed a decreasing trend in AA with age [17]. Data from 1113 individuals aged 6 – 30 years living in rural northern Iran indicated a mean (95% CI) binocular AF of 9.84 (9.63 – 10.06) CPM [48]. Among 382 Iranian university students with a mean (SD, range) age of 22.5 (4.4, 18 – 35) years, the mean (SD) NRA and PRA were + 2.08 (0.33) D and - 2.92 (0.76) D, respectively [20]. In a study involving 382 young adults in Iran [49], results showed the following means (SD) and medians for various accommodative functions: monocular AF, 11.33 (5.58) 12 CPM; binocular AF, 8.84 (4.47) 9 CPM; NRA, 2.08 (0.33) 2.25 D; PRA, - 2.92 (0.76) - 2.75 D; and AA, 11.14 (2.6) 11.11 D, respectively [49]. Notably, these values for our healthy controls, who were two decades older and had a broader age range, were substantially lower, highlighting the impact of age on accommodative functions in normal individuals. Accordingly, Ramamurthy et al. [50] reported that younger adolescents have significantly lower near monocular AF than older adolescents, with values of 5.87 (3.72) CPM compared to 8.11 (4.11) CPM, respectively [50]. Additionally, a significant direct correlation has been found between the cumulative amount of near work and decreased AF [51]. This suggests that factors other than age may influence the measured values for accommodative functions, and this should be further investigated. On a positive note, training has been shown to improve the facility rate [52].

A study involving 713 Iranian university students with a mean (SD, range) age of 21.35 (1.87, 18 – 25) years found statistically significant differences in AA, monocular AF, and accommodative response between individuals with and without accommodative insufficiency. In a multiple regression analysis, only sex demonstrated a significant association with accommodative insufficiency, with an OR of 3.14 (95% CI: 1.33 – 7.45) [53]. The current study compared the accommodative functions of opium users with that of age-matched controls, addressing the confounding effects of age [49]. The rates of fusional vergence dysfunction are similar in male and female individuals in Iran [54]. According to the National Burden of Eye Diseases report on Iran from 1990 to 2010, a point-by-point comparison of disability-adjusted life years attributed to accommodation disorders showed a slight decrease across all specific age groups for both sexes. This trend is consistent for both men and women [55], which may reduce the need to consider a similar sex ratio when assessing accommodation functions. However, owing to the significantly different sex ratios of the two groups, this confounding factor could undermine the robustness of our conclusion regarding the comparable accommodative functions. Therefore, further research with balanced sex ratios among opium users and non-users is necessary to validate our findings.

The current study presents a novel comparison of accommodative functions between users of a specific type of opium, known as Theriac, and age-matched healthy non-users. This comparison was conducted before and after the instillation of 5% phenylephrine. However, the study has certain limitations. As a single-center, cross-sectional study, it does not provide longitudinal assessments of accommodative functions. Additionally, it did not evaluate the effects of orthoptic training on improvements in these functions, the effects of other concentrations of phenylephrine, or other aspects of binocular vision, such as vergence anomalies. Further research addressing these limitations could yield more reliable and applicable outcomes for managing potential binocular abnormalities in opium users.

CONCLUSIONS

We observed significant, albeit minimal, changes in most baseline accommodative functions after the application of 5% phenylephrine eye drops in opium users. In contrast, most parameters in healthy non-users remained unchanged, except for a significant decrease in AA and an increase in the right-eye MEM. When compared to healthy non-users, considering the difference in values of accommodative functions before and after the instillation of phenylephrine, opium users exhibited similar accommodative functions. Likewise, before and after the instillation of phenylephrine, opium users exhibited similar accommodative functions, except for a significantly lower value for the right-eye AF at the post-instillation time point. Further longitudinal studies, matched for age and sex, should investigate additional aspects of binocular vision and ocular motility to further explore potential binocular anomalies in opium users.

ETHICAL DECLARATIONS

Ethical approval: The study protocol received approval from the ethics committee of Shahid Beheshti University of Medical Sciences and adhered to the ethical standards outlined in the Declaration of Helsinki. After a thorough briefing about the study, all participants provided written informed consent prior to their involvement.

Conflict of interests: None.

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REFERENCES

1. Dhingra D, Kaur S, Ram J. Illicit drugs: Effects on eye. Indian J Med Res. 2019 Sep;150(3):228-238. doi: 10.4103/ijmr.IJMR_1210_17. PMID: 31719293; PMCID: PMC6886135.
2. Kamali M, Kamali H, Doustmohammadi M, Sheikhbardsiri H, Moghadari M. Treatment of opium addiction in persian medicine: A review study. J Educ Health Promot. 2021 May 20;10:157. doi: 10.4103/jehp.jehp_5_21. PMID: 34222532; PMCID: PMC8224515.
3. Shiferaw B, Bekele E, Syed S, Fan L, Patel N, Qazi S, Biro N. A Case Report of Acute Esotropia in a Young Woman following Heroin Withdrawal. Case Rep Med. 2015;2015:740710. doi: 10.1155/2015/740710. Epub 2015 May 17. PMID: 26074969; PMCID: PMC4449923.
4. Rottach KG, Wohlgemuth WA, Dzaja AE, Eggert T, Straube A. Effects of intravenous opioids on eye movements in humans: possible mechanisms. J Neurol. 2002 Sep;249(9):1200-5. doi: 10.1007/s00415-002-0806-1. PMID: 12242539.
5. Ghobadi M, Nabovati P, Hashemi H, Talaei A, Fathi HR, Yekta Y, Ostadimoghaddam H, Yekta A, Khabazkhoob M. Accommodative and convergence anomalies in patients with opioid use disorder. Clin Exp Optom. 2022 May;105(4):392-397. doi: 10.1080/08164622.2021.1932431. Epub 2021 Jun 24. PMID: 34167446.
6. Firth AY. Heroin and diplopia. Addiction. 2005 Jan;100(1):46-50. doi: 10.1111/j.1360-0443.2005.00915.x. PMID: 15598191.
7. Sutter FK, Landau K. Heroin and strabismus. Swiss Med Wkly. 2003 May 17;133(19-20):293-4. doi: 10.4414/smw.2003.10206. PMID: 12844273.
8. Mehmandoost S, Sharifi A, Tohidinik HR, Shafa S, Hayati N, Sharifi M, McFarland W, Sharifi H. Opium Use and the Risk of Cataract: a Hospital-based, Group-matched, Case-control Study in Iran. Ophthalmic Epidemiol. 2023 Feb;30(1):66-73. doi: 10.1080/09286586.2022.2028296. Epub 2022 Jan 26. PMID: 35081859.
9. Shah RJ, Cherney EF. Diffuse retinal ischemia following intravenous crushed oxymorphone abuse. JAMA Ophthalmol. 2014 Jun;132(6):780-1. doi: 10.1001/jamaophthalmol.2014.324. PMID: 24921173.
10. Cacho-Martínez P, García-Muñoz Á, Ruiz-Cantero MT. Is there any evidence for the validity of diagnostic criteria used for accommodative and nonstrabismic binocular dysfunctions? J Optom. 2014 Jan-Mar;7(1):2-21. doi: 10.1016/j.optom.2013.01.004. Epub 2013 Mar 9. PMID: 24646897; PMCID: PMC3938740.
11. Porcar E, Montalt JC, Pons ÁM, España-Gregori E. Symptomatic accommodative and binocular dysfunctions from the use of flat-panel displays. Int J Ophthalmol. 2018 Mar 18;11(3):501-505. doi: 10.18240/ijo.2018.03.22. PMID: 29600186; PMCID: PMC5861242.
12. Chase C, Tosha C, Borsting E, Ridder WH 3rd. Visual discomfort and objective measures of static accommodation. Optom Vis Sci. 2009 Jul;86(7):883-9. doi: 10.1097/OPX.0b013e3181ae1b7c. PMID: 19521268.
13. Scheetz J, Koklanis K, Long M, Morris ME. Accuracy and Efficiency of Orthoptists in Comprehensive Pediatric Eye Examinations. Am Orthopt J. 2016 Jan;66(1):98-106. doi: 10.3368/aoj.66.1.98. PMID: 27799583.
14. Hamou S, Ghiaee S, Chung C, Lloyd M, Khem K, Chi Zhang X. Emergency Department Slit Lamp Interdisciplinary Training Via Longitudinal Assessment in Medical Practice. West J Emerg Med. 2024 Sep;25(5):725-734. doi: 10.5811/westjem.18514. PMID: 39319803; PMCID: PMC11418879.
15. Collis S, Yung M, Parikh N. Evaluation of an Instructional Video and Simulation Model for Teaching Slit Lamp Examination to Medical Students. J Acad Ophthalmol (2017). 2023 Sep 26;15(2):e215-e222. doi: 10.1055/s-0043-1775577. PMID: 37766880; PMCID: PMC10522417.
16. Antona B, Barra F, Barrio A, Gonzalez E, Sanchez I. Repeatability intraexaminer and agreement in amplitude of accommodation measurements. Graefes Arch Clin Exp Ophthalmol. 2009 Jan;247(1):121-7. doi: 10.1007/s00417-008-0938-9. Epub 2008 Sep 13. PMID: 18791730.
17. Hashemi H, Pakbin M, Ali B, Yekta A, Ostadimoghaddam H, Asharlous A, Aghamirsalim M, Khabazkhoob M. Near Points of Convergence and Accommodation in a Population of University Students in Iran. J Ophthalmic Vis Res. 2019 Jul 18;14(3):306-314. doi: 10.18502/jovr.v14i3.4787. PMID: 31660110; PMCID: PMC6815340.
18. Manion GN, Stokkermans TJ. The Effect of Pupil Size on Visual Resolution. 2024 Feb 28. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan–. PMID: 38753941.
19. Momeni-Moghaddam H, McAlinden C, Azimi A, Sobhani M, Skiadaresi E. Comparing accommodative function between the dominant and non-dominant eye. Graefes Arch Clin Exp Ophthalmol. 2014 Mar;252(3):509-14. doi: 10.1007/s00417-013-2480-7. Epub 2013 Oct 26. PMID: 24158371.
20. Yekta A, Hashemi H, Khabazkhoob M, Ostadimoghaddam H, Ghasemi-Moghaddam S, Jafarzadehpur E, Shokrollahzadeh F. The distribution of negative and positive relative accommodation and their relationship with binocular and refractive indices in a young population. J Curr Ophthalmol. 2017 Jan 21;29(3):204-209. doi: 10.1016/j.joco.2017.01.001. PMID: 28913512; PMCID: PMC5587222.
21. Abraham LM, Kuriakose T, Sivanandam V, Venkatesan N, Thomas R, Muliyil J. Amplitude of accommodation and its relation to refractive errors. Indian J Ophthalmol. 2005 Jun;53(2):105-8. doi: 10.4103/0301-4738.16173. PMID: 15976465.
22. Redondo B, Serramito M, Vera J, Alguacil-Espejo M, Rubio-Martínez M, Molina R, Jiménez R. Diurnal Variation in Accommodation, Binocular Vergence, and Pupil Size. Optom Vis Sci. 2023 Dec 1;100(12):847-854. doi: 10.1097/OPX.0000000000002091. Epub 2023 Nov 27. PMID: 38019970.
23. Park SM, Moon BY, Kim SY, Yu DS. Diurnal variations of amplitude of accommodation in different age groups. PLoS One. 2019 Nov 26;14(11):e0225754. doi: 10.1371/journal.pone.0225754. PMID: 31770414; PMCID: PMC6879161.
24. Sarkar S, Hasnat AM, Bharadwaj SR. Revisiting the impact of phenylephrine hydrochloride on static and dynamic accommodation. Indian J Ophthalmol. 2012 Nov-Dec;60(6):503-9. doi: 10.4103/0301-4738.103773. PMID: 23202387; PMCID: PMC3545125.
25. Lesack K, Naugler C. An open-source software program for performing Bonferroni and related corrections for multiple comparisons. J Pathol Inform. 2011;2:52. doi: 10.4103/2153-3539.91130. Epub 2011 Dec 26. PMID: 22276243; PMCID: PMC3263024.
26. Labhishetty V, Cholewiak SA, Roorda A, Banks MS. Lags and leads of accommodation in humans: Fact or fiction? J Vis. 2021 Mar 1;21(3):21. doi: 10.1167/jov.21.3.21. PMID: 33764384; PMCID: PMC7995353.

27. Alabi EB, Simpson TL. Accommodative response to ocular surface pain. Clin Exp Optom. 2022 Aug;105(6):624-630. doi: 10.1080/08164622.2021.1951600. Epub 2021 Jul 28. PMID: 34320330.
28. Pereira VB, Garcia R, Torricelli AA, Bechara SJ. Opioids for Ocular Pain - A Narrative Review. Pain Physician. 2017 Jul;20(5):429-436. PMID: 28727706.
29. Wold JE, Hu A, Chen S, Glasser A. Subjective and objective measurement of human accommodative amplitude. J Cataract Refract Surg. 2003 Oct;29(10):1878-88. doi: 10.1016/s0886-3350(03)00667-9. PMID: 14604706.
30. León A, Estrada JM, Rosenfield M. Age and the amplitude of accommodation measured using dynamic retinoscopy. Ophthalmic Physiol Opt. 2016 Jan;36(1):5-12. doi: 10.1111/opo.12244. Epub 2015 Sep 9. Erratum in: Ophthalmic Physiol Opt. 2016 Jul;36(4):512. doi: 10.1111/opo.12308. PMID: 26353999.
31. Lara F, Cacho P, García A, Megías R. General binocular disorders: prevalence in a clinic population. Ophthalmic Physiol Opt. 2001 Jan;21(1):70-4. doi: 10.1046/j.1475-1313.2001.00540.x. PMID: 11220042.
32. Hoseini-Yazdi SH, Yekta A, Nouri H, Heravian J, Ostadimoghaddam H, Khabazkhoob M. Frequency of convergence and accommodative disorders in a clinical population of Mashhad, Iran. Strabismus. 2015;23(1):22-9. doi: 10.3109/09273972.2014.1002622. Epub 2015 Mar 19. PMID: 25789965.
33. García-Muñoz Á, Carbonell-Bonete S, Cantó-Cerdán M, Cacho-Martínez P. Accommodative and binocular dysfunctions: prevalence in a randomised sample of university students. Clin Exp Optom. 2016 Jul;99(4):313-21. doi: 10.1111/cxo.12376. Epub 2016 Mar 29. PMID: 27027297.
34. Ma MM, Yeo ACH, Scheiman M, Chen X. Vergence and Accommodative Dysfunctions in Emmetropic and Myopic Chinese Young Adults. J Ophthalmol. 2019 Jul 17;2019:5904903. doi: 10.1155/2019/5904903. PMID: 31396411; PMCID: PMC6664731.
35. Aslaksen AK, Vikesdal GH, Voie MT, Rowlands M, Skranes J, Haugen OH. Visual function in Norwegian children aged 5-13 years with prenatal exposure to opioid maintenance therapy: A case-control study. Acta Ophthalmol. 2024 Jun;102(4):409-420. doi: 10.1111/aos.15764. Epub 2023 Sep 13. PMID: 37702266.
36. Mactier H, Hamilton R. Prenatal opioid exposure - Increasing evidence of harm. Early Hum Dev. 2020 Nov;150:105188. doi: 10.1016/j.earlhumdev.2020.105188. Epub 2020 Sep 10. PMID: 32958331.
37. Firth AY, Pulling S, Carr MP, Beaini AY. Orthoptic status before and immediately after heroin detoxification. Br J Ophthalmol. 2004 Sep;88(9):1186-90. doi: 10.1136/bjo.2003.032334. PMID: 15317713; PMCID: PMC1772312.
38. Huang CT, Satou T, Niida T. Effect of Pupil Size and Binocular Viewing on Accommodative Gain in Emmetropia and Myopia. J Binocul Vis Ocul Motil. 2020 Jul-Sep;70(3):103-108. doi: 10.1080/2576117X.2020.1780878. Epub 2020 Jul 2. PMID: 32615879.
39. Kubota M, Kubota S, Kobashi H, Ayaki M, Negishi K, Tsubota K. Difference in Pupillary Diameter as an Important Factor for Evaluating Amplitude of Accommodation: A Prospective Observational Study. J Clin Med. 2020 Aug 18;9(8):2678. doi: 10.3390/jcm9082678. PMID: 32824849; PMCID: PMC7465210.
40. Lara F, Bernal-Molina P, Fernández-Sánchez V, López-Gil N. Changes in the objective amplitude of accommodation with pupil size. Optom Vis Sci. 2014 Oct;91(10):1215-20. doi: 10.1097/OPX.0000000000000383. PMID: 25207484.
41. Esteve-Taboada JJ, Del Águila-Carrasco AJ, Bernal-Molina P, Ferrer-Blasco T, López-Gil N, Montés-Micó R. Effect of Phenylephrine on the Accommodative System. J Ophthalmol. 2016;2016:7968918. doi: 10.1155/2016/7968918. Epub 2016 Dec 7. PMID: 28053778; PMCID: PMC5174178.
42. Haghpanah N, Alany R. Pharmacological treatment of presbyopia: A systematic review. Eur J Transl Myol. 2022 Sep 19;32(3):10781. doi: 10.4081/ejtm.2022.10781. PMID: 36121117; PMCID: PMC9580536.
43. Zhu X, Chen M, Dai J, Lu Y. The effect of 0.5% tropicamide/0.5% phenylephrine mixed eye drop in Chinese adults with myopia and its inter-eye difference in refractive outcomes. Curr Med Res Opin. 2014 Mar;30(3):481-7. doi: 10.1185/03007995.2013.861348. Epub 2013 Nov 15. PMID: 24215472.
44. Fan DS, Rao SK, Ng JS, Yu CB, Lam DS. Comparative study on the safety and efficacy of different cycloplegic agents in children with darkly pigmented irides. Clin Exp Ophthalmol. 2004 Oct;32(5):462-7. doi: 10.1111/j.1442-9071.2004.00863.x. PMID: 15498055.
45. Lyu IJ, Park KA, Oh SY. Increase in esodeviation under cycloplegia with 0.5% tropicamide and 0.5% phenylephrine mixed eye drops in patients with hyperopia and esotropia. BMC Ophthalmol. 2017 Dec 12;17(1):247. doi: 10.1186/s12886-017-0644-7. PMID: 29233124; PMCID: PMC5727972.
46. Del Águila-Carrasco AJ, Lara F, Bernal-Molina P, Riquelme-Nicolás R, Marín-Franch I, Esteve-Taboada JJ, Montés-Micó R, Kruger PB, López-Gil N. Effect of phenylephrine on static and dynamic accommodation. J Optom. 2019 Jan-Mar;12(1):30-37. doi: 10.1016/j.optom.2018.01.005. Epub 2018 Mar 27. PMID: 29602687; PMCID: PMC6318542.
47. Richdale K, Bailey MD, Sinnott LT, Kao CY, Zadnik K, Bullimore MA. The effect of phenylephrine on the ciliary muscle and accommodation. Optom Vis Sci. 2012 Oct;89(10):1507-11. doi: 10.1097/OPX.0b013e318269c8d0. PMID: 22922779; PMCID: PMC3607430.
48. Zakian A, Heydarian S, Mirzajani A, Jafarzadehpur E, Yekta A, Khabazkhoob M. Distribution of near Point of Convergence, near Point of Accommodation, Accommodative Facility and Refractive Errors in a Rural Population Living in Northern Iran. J Binocul Vis Ocul Motil. 2021 Jul-Sep;71(3):104-109. doi: 10.1080/2576117X.2021.1927291. Epub 2021 May 25. PMID: 34032560.
49. Yekta A, Khabazkhoob M, Hashemi H, Ostadimoghaddam H, Ghasemi-Moghaddam S, Heravian J, Doostdar A, Nabovati P. Binocular and Accommodative Characteristics in a Normal Population. Strabismus. 2017 Mar;25(1):5-11. doi: 10.1080/09273972.2016.1276937. Epub 2017 Jan 17. PMID: 28095087.
50. Ramamurthy D, Radhakrishnan H, Pardhan S. Associations between Accommodative Facility, Age, and Refractive Errors in Early, Older Adolescent Myopes and Emmetropes. Br Ir Orthopt J. 2023 Mar 31;19(1):15-25. doi: 10.22599/bioj.284. PMID: 37008825; PMCID: PMC10064887.
51. Iribarren R, Fornaciari A, Hung GK. Effect of cumulative nearwork on accommodative facility and asthenopia. Int Ophthalmol. 2001;24(4):205-12. doi: 10.1023/a:1022521228541. PMID: 12678397.

52. Allen PM, Charman WN, Radhakrishnan H. Changes in dynamics of accommodation after accommodative facility training in myopes and emmetropes. Vision Res. 2010 May 12;50(10):947-55. doi: 10.1016/j.visres.2010.03.007. Epub 2010 Mar 19. PMID: 20304003.

53. Hashemi H, Khabazkhoob M, Nabovati P, Shahraki FA, Ostadimoghaddam H, Faghihi M, Aghamirsalim M, Doostdar A, Yekta A. Accommodative insufficiency in a student population in Iran. J Optom. 2019 Jul-Sep;12(3):161-167. doi: 10.1016/j.optom.2018.03.006. Epub 2018 May 22. PMID: 29802027; PMCID: PMC6612034.

54. Hashemi H, Nabovati P, Khabazkhoob M, Yekta A, Ostadimoghaddam H, Doostdar A, Ramin S, Aghamirsalim M. The Prevalence of Fusional Vergence Dysfunction in a Population in Iran. J Curr Ophthalmol. 2021 Jul 5;33(2):112-117. doi: 10.4103/JOCO.JOCO_61_20. PMID: 34409219; PMCID: PMC8365572.

55. Hatef E, Mohammadi SF, Alinia C, Ashrafi E, Mohammadi SM, Lashay A, Sadeghi-Tari A. National Burden of Eye Diseases in Iran, 1990-2010; Findings from the Global Burden of Diseases Study 2010. Middle East Afr J Ophthalmol. 2016 Jan-Mar;23(1):89-95. doi: 10.4103/0974-9233.171781. PMID: 26957846; PMCID: PMC4759911.