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Comparison of Mydriatic Efficacy of Homatropine and Xylocaine as Single and Combined Therapy

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Abstract

Background: Study was conducted to compare efficacy in pupil dilatation between 2% Homatropine(2H) alone and alternate application of 2% Homatropine with 4% Xylocaine(2H/4X) eye drops for easy estimation of refractive error and posterior segment examination. *Methods:* Over 6 months, after obtaining waiver of consent in 100 eyes of 50 patients age between 5-20years (14.26±3.06), one drop of Xylocaine 4% was applied to left eye (study eye). After 60 seconds 1 drop of 2% Homatropine was applied in both right (control eye) and left (study eye). Pupil diameter was measured via transparent scale before instillation of first drop. At every 15 minutes interval, pupillary size was measured and subsequent instillations were done, upto one hour. *Results:* There was a statistical significant difference in pupil diameter between eyes dilated with 2H/4X and 2H alone at 30-60minutes ($p<0.001$). 31 patients (62%) developed maximum pupillary dilatation of (7.42±0.84) in left eye by 45minutes, while only 4 patients (8%) in right eye. Mean dilatation at 60 minutes in study eye was 7.94±0.24 but in control eye was 7.00±0.83 with $p<0.001$. *Conclusion:* Combination of 2H/4X potentiates mydriatic effect produced by Homatropine alone causing quicker onset of action, increases patient comfort level by reducing stinging effect of Homatropine and reducing the chances of side effects of Homatropine like delirium, hallucination, dry mouth by reducing the number of drop instillations. So, combination of 2H/4X can reduce patient's waiting time in OPD and quicker examination of interior of eye and refractive error with ease.

Keywords: Homatropine; Mydriasis; Xylocaine.

Introduction

Pupillary dilatation or mydriasis is of great significance in screening of various ophthalmological conditions [1]. Cycloplegia is needed for assessing the accommodation and obtaining accurate refraction in young children who have strong accommodation; in all children with tropias, hyperopia, pseudomyopia etc. The objectivity & consistency of cycloplegic refraction is unbeatable. The incidental effect of cycloplegia is mydriasis, necessary for detailed examination of lens, vitreous & fundus examination in all patients [2]. The factors which influence mydriasis are pupillary hippus, iris pigmentation, emotional status, diseases- local & systemic, drugs- systemic & topical ophthalmic medications [3]. The ability & magnitude of agent for producing mydriasis depends on balance between sphincter and radial muscle of pupil which are controlled by parasympathetic and sympathetic nervous system respectively. Loads of studies have investigated the time course and maximal mydriasis for different topical drugs in these categories in an

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effort to look which drug provide a quick, adequate dilatation with the least potential for untoward side effects in patients [4-6].

Parasymaptholytic and sympathomimetic drops are commonly used for pupil dilatation in clinical settings routinely [7]. An ideal mydriatic will cause quicker onset of dilatation with quick recovery but lesser side effects. Additionally for cataract surgery, an adequate, sufficient and sustained dilatation is mandatory. In general, the cycloplegic drugs which causes both mydriasis & cycloplegia takes longer time to act. It has been documented that in light irides patients, drugs takes shorter time course for dilatation, which speeds up in dark irides patients when drugs with two different mechanism of action are combined [7].

Homatropine is an anticholinergic agent acting as an antagonist of muscarinic acetylcholine receptors, causing parasympatholytic effect. The cycloplegic effect need not necessarily correlate with mydriatic effect.

Refractive error is most common condition in ophthalmological practice, which is detected by instilling cycloplegic-mydriatic drugs in conjunctival sac to achieve cycloplegia & pupillary dilation. Most of cycloplegic-mydriatic drugs take variable time for onset of action and have irritant effect topically, causing patient discomfort. Also they are instilled frequently, often more than necessary, usually by the paramedical ophthalmic assistants. This may cause side effects & affect patient compliance adversely and also prolongs the time spent by the patient in OPD.

Xylocaine is a local anaesthetic agent which has membrane stabilizing effect, thereby improving the effect of the topical drug, hasten the time of action and thereby probably reduce the frequency of instillations.

This study is an effort to study maximal or optimal mydriasis irrespective of cycloplegic effect. Mydriatic examination has to be carried out by the Ophthalmologist, while refraction after onset of cycloplegia can be carried out by the Optometrist. The onset and amount of cycloplegia was not the purview of this study.

So this study aims to compare the mydriatic efficacy of homatropine alone vs combination of homatropine and xylocaine in patients attending Ophthalmology OPD at Sri Siddhartha Medical College and Hospital, Tumkur. This will be achieved by:

1. Considering Right eye as the control eye(A) & Left as the test eye(B).
2. Comparing onset of action–mydriasis.
3. Comparing time of peak mydriasis.
4. Comparing frequency of drug instillation.
5. Studying the discomfort experienced in patients.

Methods

This study was conducted in outpatient department of Ophthalmology in SSMC Hospital and Research centre in patients requiring routine testing of the refractive error.

This case-control study was an observational clinical study, consisting of total 100 eyes of 50 patients aged between 5-20 years attending Ophthalmology outpatient department in SSMC, Tumkur, for routine refraction. The study was approved by the Institutional ethics committee & a waiver of informed consent was taken, as the procedure is a part of routine Ophthalmic evaluation for refractive error.

After obtaining verbal consent from parents and assent from patient, their simple random sampling was done and their primary demographic data was noted. Brief history was taken & initial examination of both eyes with diffuse light was done. Snellen's Visual acuity was recorded. First baseline pupil size was recorded in both eyes using transparent scale as 0 minutes. Then one drop of Xylocaine 4% was instilled in left eye (study eye), after 60 seconds or after the subsidence of stinging sensation, 1 drop of 2% Homatropine was instilled in both eyes. So, the drug regimen assigned consist of instillation of Homatropine 2% in right eye(A)-control eye & Homatropine 2% with Xylocaine 4% in left eye(B)-study eye, noting the time of instillation. A 15 minute interval was given between subsequent pupillary measurement and administration of Homatropine drops upto one hour.

Exclusion Criteria Included

1. History of intra-ocular inflammation,
2. History of any intra-ocular procedure/ surgery,
3. Use of any topical medication,
4. History of juvenile diabetes,
5. Patient unable to comprehend/ assent.
6. Uncooperative child.

Data is obtained by recording the pupillary size using transparent scale having grading from 0-15mm. It was recorded by the same observer at the

eye level of the patient, avoiding any parallax error, prior to instillation of eye drops, then every 15 minutes, for 1 hour. All the drops were instilled into the inferior fornix by gently pulling the lower lid down & the patients were instructed to keep their eyes closed. They were also instructed to keep their head tilted backwards, resting on the back of the seat. At the completion of the process, the patient was asked to give a comparison of the discomfort/any unpleasant sensation between the two eyes.

The difference in the average duration of Homatropine alone(A) and Homatropine with Xylocaine(B) in pupil dilatation was tested for its statistical significance by mean ± standard deviation. Student t test (two tailed, dependent) has been used to find the significance of study parameters on continuous scale within each group. Significance is assessed at 5% level of significance

Results

A total of 100 eyes of 50 patients were enrolled in this study with left eye as study eye(B) and right eye as control eye(A). (Table 1, Figure 1).

Patient age ranged from 5 years to 20 years, with the mean ± standard deviation (SD) of 14.26±3.06 (Table 2, Figure 2).

Twenty-five patients were male and twenty-five were females (Table 3, Figure 3). So there was no significant difference in baseline gender distribution.

Pupil size assessment of maximum-minimum size at 0, 20, 30, 45, 60 minutes in both study and control eye in (Table 4, Figure 4) showing statistical significant difference in pupil size ($p<0.001$) at all intervals.

In all patients, baseline pupil size at 0 minute was 2-3mm. In most patients 47 out of 50 (94%) pupil started dilating from baseline at 20minutes in study eye-B, while only 7 out of 50 (14%) in control eye-A.

In this study maximum pupillary size was defined as 8mm size measured with transparent scale. 31 out of 50 patients in study eye (62%) developed maximum pupillary size in 45 minutes while only 4 out of 50 patients (8%) in control eye ($p<0.001$). Total of 47 out of 50 patients(94%) developed 8mm dilatation in study eye while only 17 out of 50 patients (34%) in control eye($p<0.001$) in 60minutes (Table 5).

Comparison of pupil size of study and control eye at 0, 20, 30, 45, 60 minutes (Table 6, Figure 5a) demonstrates that mydriasis produced when combining Homatropine with Xylocaine (B) was significant ($p<0.001$) at 20, 30, 45 and 60minutes.

Figure 5b showing gradual increase in pupil size in study group (B) with time from baseline to 60minutes with most increase at 30-45minute interval while in control group increase in pupil size starts after 20minutes.

Also 45 out of 50 (90%) patients reported that despite initial stinging, the Left eye (B) felt comfortable at completion of the procedure.

Table 1: Eye Involved of patients studied

Eye Involved	No. of Eyes	%
Left Eye	50	50.0
Right Eye	50	50.0
Total	100	100.0

Table 2: Age distribution of patients studied

Age in years	No. of patients	%
<10	3	6.0
10-15	28	56.0
16-20	19	38.0
Total	50	100.0

Mean ± SD: 14.26±3.06

Table 3: Gender distribution of patients studied

Gender	No. of patients	%
Female	25	50.0
Male	25	50.0
Total	50	100.0

Table 4: Pupil size : An assessment at 0 min, 20 min , 30 min, 45 min and 60 min

Pupil Size	Min-Max	Mean ± SD	difference	t value	P value
0 min	2.00-2.00	2.00±0.00	-	-	-
20 min	2.00-5.00	2.85±0.86	-0.850	-9.916	<0.001**
30 min	3.00-7.00	4.54±1.01	-2.540	-25.167	<0.001**
45 min	5.00-8.00	6.50±1.25	-4.500	-35.964	<0.001**
60 min	6.00-8.00	7.47±0.77	-5.470	-70.910	<0.001**

** Strongly significant (P value: P≤0.01)

Table 5: Time taken to achieve 8mm dilatation

Time(min)	Group-B	Group-A
30	0	0
45	31 (62)	4 (8)
60	47 (94)	17 (34)

Table 6: Pupil size: A Comparison between study group-B and control group-A (Left eye Vs Right eye)

Pupil Size	Group-B	Group-A	t value	P value
0 min	2.00±0.00	2.00±0.00	-	-
20 min	3.52±0.61	2.18±0.44	15.983	<0.001**
30 min	5.28±0.76	3.80±0.61	16.188	<0.001**
45 min	7.42±0.84	5.58±0.86	13.324	<0.001**
60 min	7.94±0.24	7.00±0.83	8.122	<0.001**

** Strongly significant (P value: P≤0.01)

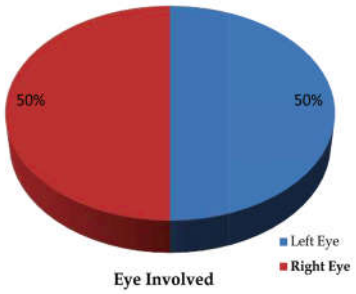

Fig. 1: Eye Involved of patients studied

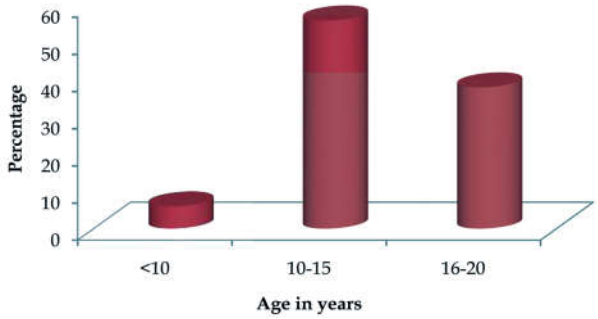

Fig. 2: Age distribution of patients studied

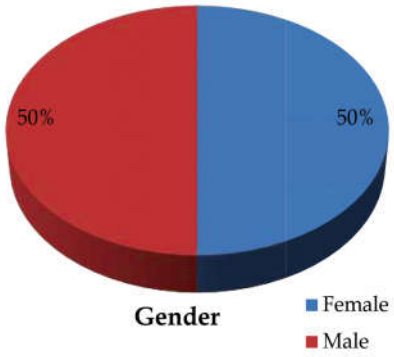

Fig. 3: Gender distribution of patients studied

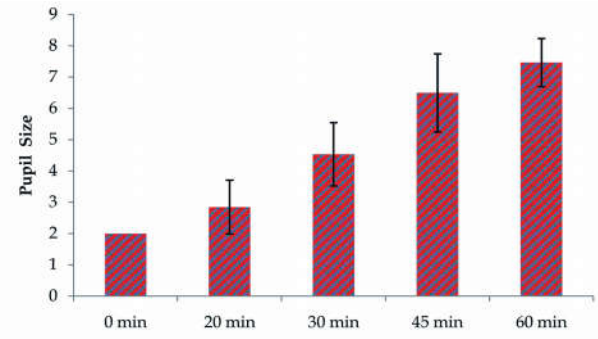

Fig. 4: Pupil size: An assessment at 0 min, 20 min , 30 min, 45 min and 60 min

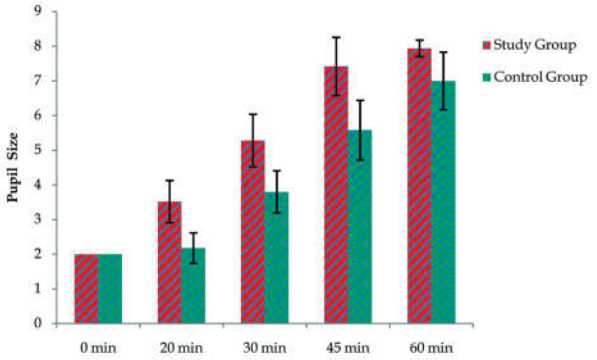

Fig. 5a: Pupil size: A Comparison between Group B and Group A (Left eye-study Vs Right eye- control)

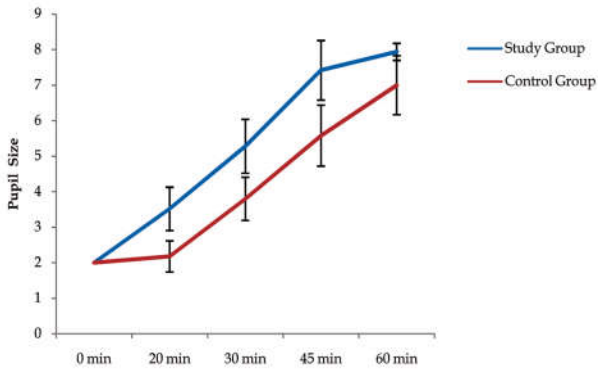

Fig. 5b: Pupil size: A Comparison between Group B and Group A (Left eye-study Vs Right eye- control)

Discussion

Globally visual impairment due to uncorrected refractive error is 158million [8]. Among 5-15years old children, uncorrected refractive error is main cause of visual impairment [9]. So,comprehensive screening and refracting children in school going age group is a common, essential clinical test in Ophthalmology. Use of an effective, solo or combination of mydriatic and cycloplegic eye drops can facilitate this procedure. Compliance can be poor due to the time taken for the pupillary dilatation and the discomfort associated with the instillation of eye drops.

There is no literature till date which showed effectiveness of mydriasis or pupil dilatation on combining local anaesthetic with Homatropine. So,

present study was done to show if prior application of Xylocaine augments the mydriatic efficacy of Homatropine.

Pupil is a dynamic structure whose size is controlled by sympathetic & parasympathetic nervous system. Parasympathetic regulation dominates over sympathetic effects in control of pupil size of eye [10]. Parasympatholytic & sympathomimetic drugs are main class of drugs used as mydriatic & cycloplegics in day to day practice to screen for refractive error, cataract surgery, photocoagulation procedures, detailed examination of fundus, relieve ciliary spasm in acute inflammation & to prevent formation of posterior synechiae in uveitis.

Homatropine in the form of Homatropine hydrobromide is colourless crystal, can be used as mydriatic & cycloplegic drug [11]. It is available in concentration of 0.25%, 0.5% as mydriatic & 1%, 2%, 5% for cycloplegics [11]. It acts by inhibiting acetylcholine action leading to paralysis of sphincter pupillae & unopposed adrenergic innervations of dilator pupillae leading to dilatation of pupil.

The onset of mydriasis & cycloplegia has variable latency, 30- 60 minutes. Siu et al (1999) reported that prior application of local anaesthetic could shorten the time to full cycloplegia for Chinese patients with dark irides [12].

Local anaesthetic acts by inhibiting rate of corneal epithelial cell migration & decreasing permeability of chloride channels thus blocking nerve impulse transmission & destroying superficial epithelial microvilli. Thus potentiates pupillary dilatation induced by routinely used mydriatics [13].

An important observation made in this study was, the shape of pupil on dilatation with homatropine. This was found to be circular unlike, vertically oval pupil on using sympathomimetic agents for dilatation [14].

There is no literature till date which showed effectiveness of mydriasis or pupil dilatation on combining local anaesthetic with homatropine. So, present study was done to show if prior application of one drop of Xylocaine augments the mydriatic efficacy of homatropine.

In using more than one drug, time gap between drops may affect amount of drug absorption in the eye. Initial drug used requires some contact time for ocular penetration. Early instillation of second drug may dilute or washout the first drug from cul-de-sac, thereby, reducing the chances of first drug penetration into the eye. So here in this study a time gap of 60 seconds was allowed between instillation of Xylocaine followed by Homatropine eye drops.

It was observed in this study that Xylocaine potentiates mydriatic efficacy of Homatropine by decreasing time of onset, number of drop instillation & causes effective pupil dilatation. Also, it gave better comfort to the patients despite the initial irritation.

So, it is believed in present study that combined use of 2% homatropine with 4% xylocaine is more effective as mydriatic than 2% homatropine alone.

Regarding concern for limitation of current study was that measurement of pupil size in our study was conducted in bright light using transparent scale. The pupillary size is only an apparent measurement as it is visualized through the cornea. Hence, magnification factor has to be kept in mind. Randomised trials with larger sample size may be required for confirmation. Also, 2% topical Xylocaine may be tried.

Conclusion

Combination of 2% homatropine & 4% xylocaine (2H/4X) potentiates mydriatic effect produced by homatropine alone causing quicker onset of action, increases patient comfort level by reducing stinging effect of homatropine and reducing the chances of side effects of homatropine like delirium, hallucination, dry mouth by reducing the number of drop instillations. So, combination of 2H/4X can reduce patient's waiting time in OPD and quicker examination of interior of eye and refractive error with ease.

References

1. Rajanandh MG, Kumar MSP, Chaparala V, Teja R, Chakravarthi NNK, Molekunnel JJ, Ramasamy C. Mydriatic effect of tropicamide, proparacaine and lignocaine : a mono and combination therapy. Int J Pharma and Biosciences. 2011; 2(3): 128-132.
2. Leonard apt and william m gaffney, Cyclolegic refraction. [Online]. Available from: www.oculist.net/downaton502/prof/ebook/duanes/.../v1c041.html [Accessed].
3. Novitskaya ES, Dean SJ, Moore JE, Moore T CB, Nagendran S, Sharma A. Effects of some ophthalmic medications on pupil size; a literature review. Can J Ophthalmol. 2009; 44(2): 193-7.
4. Levine L. Mydriatic effectiveness of dilute combinations of phenyephrine and tropicamide. Am J Optom Physiol Opt. 1982; 59(7): 580-94. [PubMed].

5. Apt L, Henrick A. Pupillary dilatation with single eyedrop mydriatic combinations. Am J Ophthalmol. 1980; 89(4): 553-9. [PubMed].
6. Lyle WM, Bobier WR. Effects of topical anaesthetics on phenylephrine-induced mydriasis. Am J Optom Physiol Opt. 1977; 54(5): 276-81. [PubMed].
7. Anderson HA, Bertrand KC, Manny RE, Hu YS, Fern KD. A comparison of two drug combinations for dilating dark irides. Optom Vis Sci. 2010; 87(2): 120-4.
8. Vora U, Khandekar R, Natrajan S, Al-Hadrami K. Refractive error and visual functions in children with special needs compared with the first grade school students in onam. Middle East Afr J ophthalmol. 2010; 17(4): 297-302.
9. Smith TS, Frick KD, Holden BA, Fricke TR, Naidoo KS. Potential lost productivity resulting from global burden of uncorrected refractive error. Bull world health organ. 2009; 87(6): 431-7.
10. Kardon R. The pupil. In: Kaufman PL, Alm A, editors. Adler's physiology of the eye. St. Louis: Mosby; 2003; p713-43.
11. Rosenfield M, Logan N. Optometery science technology and clinical management. (2nd ed.). London: Elsevier; 2009.
12. Siu AW, Sum AC, Lee DT. Prior topical anaesthesia reduces time to full cycloplegia in chinese. Japanese J ophthlmol. 1999; 43(6): 466-471.
13. Burns RP. Toxic effects of local anaesthetics. JAMA. 1978; 240(4): 347.
14. Jain IS, Nagpal KC, Sharma PL. A study of pupil shape and size by symapthomimetics. Indian J Ophthalmol . 1973; 21(4): 156-60.