·Clinical Research·

Comparative study measuring the dilatory effect of a mydriatic device (Mydriasert®) versus topical drops

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Abstract

• AIM: To compare the mydriatic efficacy of an ophthalmic insert (Mydriasert, MY) versus phenylephrine and tropicamide (PT) eye drops.

• METHODS: Two controlled, prospective, randomized, single-blind studies were performed. In the first study, a total of 80 eyes from 40 outpatient-clinic patients were analyzed. PT drops were applied to the right eye, and a MY device was inserted in the left eye for 30min. Time until maximal pupil dilation for each eye was then assessed. In the second study, 80 eyes from 80 patients undergoing cataract surgery were analyzed. Pupil dilation was achieved using either PT drops three-times for one hour prior to surgery (40 patients), or a MY device was inserted one hour prior to surgery (40 patients).

• RESULTS: In the first study, MY achieved superior mydriasis compared to PT eye drops at 90min (9.04±1.33mm *vs* 8.78±1.37mm, *P*=0.012). However MY took longer than PT drops to achieve maximal dilation, and mydriasis was inferior in eyes with MY compared to PT drops at 30min (7.21±1.73mm *vs* 8.22±1.43mm, *P*<0.001), the two groups only becoming similar by 60min (8.85±1.44mm *vs* 8.71±1.27mm, *P*=0.236). In the second study, both MY and PT achieved similar levels of mydriasis at the beginning of surgery (8.75±0.76mm with MY *vs* 8.77±0.63mm with PT), and also at the end of surgery (7.96±1.06mm with MY *vs* 8.32±0.72mm with PT), with no significant difference between groups (*P*=0.08). MY was well tolerated and cardiovascular effects were not influenced by dilation method.

• CONLUSION: MY could be a safe and efficacious alternative for mydriasis. The mydriatic effect of MY is as good as conventional PT eye drops after 60min, and is superior after 90min. MY also maintains good pupil dilation during cataract surgery.

• **KEYWORDS:** Mydriasert® ; mydriasis; pupil dilation; cataract surgery; device

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INTRODUCTION

Mydriasis, or pupil dilation, is an important tool used extensively in ophthalmological clinical practice. Achieving good mydriasis is necessary not only for complete funduscopic examinations, but also to successfully perform procedures such as fluorescein angiography, laser photocoagulation and cataract or retinal surgeries. Poor mydriasis can increase the risk of intraoperative complications during cataract surgery[1]. Currently, mydriasis is obtained using eye drops which elicit anticholinergic and sympathicomimetic effects. Phenylephrine and tropicamide (PT) are most commonly used, either alone or in combination[2]. Full dilation is achieved faster when both drugs are used together [3]. However, repeated doses of these drops are necessary, which is both time consuming and may also damage the corneal epithelium [4,5]. Furthermore, tear clearance can adversely affect local efficacy of the drops, and repeated doses are sometimes required. Systemic absorption of mydriatic solution may increase cardiovascular risks in predisposed patients[6,7]. In order to overcome these problems several other dilating methods have been proposed, including the use of medicated pledget sponges or wicks, and intracameral injections [4,5,8]. Mydriasert® (MY) is an ophthalmic drug insert containing 0.28mg tropicamide and 5.4mg phenylephrine. As with all inserts, the bioavailability of MY is higher than with traditional mydriatic drops, meaning adequate local efficacy is achieved with only limited systemic absorption [9]. There is consensus among ophthalmologist that MY might be a timesaving and safe alternative to the use of dilating eye drops. However, the use of MY has not extended probably because there are doubts

about the best time to place the device and its efficacy to maintain mydriasis long enough to perform procedures such as cataract surgery.

Here, results of two studies investigating the effect of MY versus topical PT eye drops are reported. The first study involved patients attending the department of Ophthalmology at the University of Navarra's Clinic, the second involved patients undergoing cataract surgery. The aim of both of these studies was to compare and define the optimal dosing regimen needed to achieve maximal mydriasis using either a MY opthalmological device or conventional topical drops.

SUBJECTS AND METHODS

Informed consent was obtained from all patients. Study protocols were approved by the ethics and scientific committees of the University of Navarra and also the Government of Navarra's Department of Education and Research.

Outpatient Clinic Study An initial prospective study was performed in 40 patients (80 eyes), who attended the department of ophthalmology in the University of Navarra's Clinic. The main inclusion criterion was that patients had no ophthalmologic or systemic disease. Both eyes of each patient were dilated with either one drop of 10% phenylephrine and one drop of 1% tropicamide (PT drops, the right eye), or using a MY insert (the left eye). The MY device was placed in the inferior conjunctival sac for thirty minutes.

The primary outcome measure was mean pupil diameter obtained by either PT drops or the MY insert. Secondary variables also measured included mean near best corrected visual acuity (NBCVA), which is an indirect measurement of cycloplegia, and objective signs (scored by masked observers) such as keratitis, conjunctiva redness, conjunctiva swelling, reading capacity and light adaptation. Subjective symptoms such as foreign body sensation, itchiness, stinging, irritation and tearing were also scored by patients at 0-, 30-, 60- and 90-min time points. (Scores 0-4, 0: None, 1: Mild, 2: Moderate, 3: Severe, 4: Incapacitating). Six hours after dilation, reading capacity recovery was assessed and subjective preferred dilation method was recorded.

Cataract Surgery Study The second study was a controlled, prospective, randomized study involving 80 eyes from 80 consecutive patients who were scheduled for routine unilateral cataract surgery.

The main inclusion criterion was a Lens Opacities Classification System III (LOCS-III) nuclear opacity (NO) /nuclear color (NC) score of 3 or higher. Patients with pseudoexfoliation syndrome, diabetes, intraoperative floppy iris syndrome (IFIS) associated with systemic alpha-1 blockers, and previous ophthalmic surgery were excluded. Patients with intrasurgical requirements of iris retractors, or intracameral phenylephrine or acetylcholine, were also excluded.

Table 1 Mean (±standard deviation) pupil diameter (mm) at 30, 60 and 90min using Mydriasert® or conventional eye drops in the outpatient clinic study

	Mydriasert®	Phenylephrine+Tropicamide	*P*
30min	7.21±1.73	8.22±1.43	<0.001
60min	8.85±1.44	8.71±1.27	0.236
90min	9.04±1.33	8.78±1.37	0.012

Mydriasis was achieved in the PT treatment group using the center's current standard procedure of administering PT drops (n=40 patients) three times every ten minutes, starting one hour prior to surgery. In the MY treatment group (n=40 patients), a MY device was inserted into the inferior conjunctival sac one hour before surgery.

Topical anesthesia was performed using a combination of 0.1% tetracaine and 0.4% oxybuprocaine topical eye drops twice every five minutes in both groups. A 2.4mm clear corneal incision was made and intracameral anesthesia was performed using 0.5mL lidocaine (1%). Different nuclear cracking procedures were performed according to the experience of the surgeon and cataract grade. In all cases, a foldable posterior chamber intraocular lens was implanted. Self-sealing corneal incisions were not sutured.

Main outcome measure was mean pupil diameter at the beginning and at the end of surgery. The volume of fluid employed through the phacoemulsification machine was measured in order to determine if there were differences in the difficulty of surgeries between both groups. Blood pressure and heart rate were also measured at the beginning and at the end of surgery to determine and compare the cardiovascular effects of both dilating methods.

Statistical Analysis Descriptive statistics are given as mean±standard deviation. Differences in mean values among the groups were compared by Student's t-test for all pairwise comparisons. Statistical analysis was performed using SPSS, version 15.0 (SPSS Inc, Chicago, Illinois, USA). Statistical significance was considered as P<0.05.

RESULTS

Outpatient clinic results A total of 80 eyes from 40 patients (32 males and 48 females) were evaluated. Mean patient age was 56 years. No patients were lost to follow up and none were excluded from analysis.

After 30min of mydriatic treatment, mean pupil diameter was slightly larger in with PT eye drops (8.22 ±1.43mm) compared to MY 7.21 ±1.73mm, P<0.001. However, after 60min of treatment, mydriasis was similar between both treatment groups; with a mean pupil diameter of 8.85 ± 1.44mm in with MY and 8.71±1.27mm in with PT drops (P= 0.236). After 90min of treatment, MY achieved significantly greater mydriasis (9.04 ±1.33mm) compared to PT drops (8.78±1.37mm, P=0.012) (Table 1).

Table 2 Objective signs and subjective symptoms mean scores at 30, 60 and 90min using Mydriasert® or conventional eye drops in the outpatient clinic study

Signs & Symptoms	30min			60min			90min		
	Mydriasert®	Phenylephrine+ Tropicamide	*P*	Mydriasert®	Phenylephrine+ Tropicamide	P	Mydriasert®	Phenylephrine+ Tropicamide	*P*
Keratitis	0.28±0.59	0.13±0.33	NS	0.30±0.60	0.13±0.33	0.088	0.30±0.60	0.15±0.36	NS
Conjunctival redness	0.00±0.00	0.00±0.00	NS	0.03±0.15	0.00±0.00	NS	0.03±0.60	0.00±0.00	NS
Conjunctival swelling	0.00±0.00	0.00±0.00	NS	0.00±0.00	0.00±0.00	NS	0.00±0.00	0.00±0.00	NS
Reading capacity	1.38±1.39	1.95±1.43	0.006	1.68±1.43	1.90±1.54	NS	1.70±1.45	1.78±1.52	NS
Light adaptation	0.43±0.93	0.75±1.10	0.018	0.75±1.10	1.00±1.21	NS	1.30±1.20	1.18±1.23	NS
Foreign body sensation	0.55±0.84	0.23±0.57	0.03	0.23±0.48	0.08±0.35	NS	0.08±0.26	0.00±0.00	0.083
Itching	0.23±0.57	0.10±0.30	NS	0.13±0.40	0.13±0.46	NS	0.08±0.26	0.05±0.31	NS
Stinging	0.25±0.67	0.18±0.44	NS	0.13±0.46	0.15±0.53	NS	0.08±0.26	0.10±0.44	NS
Irritation	0.38±0.80	0.38±0.80	NS	0.20±0.51	0.08±0.35	NS	0.08±0.26	0.03±0.15	NS
Tearing	0.08±0.26	0.23±0.62	NS	0.23±0.53	0.18±0.54	NS	0.05±0.31	0.05±0.31	NS
NBCVA	0.87±0.17	0.82±0.20	0.04	0.79±0.21	0.76±0.22	0.25	0.83±0.17	0.80±0.24	0.37
Complete reading capacity recovery at 6h	4.28±2.4	3.75±2.03	0.022						

Mean±standard deviation; NS: Not significant differences; NBCVA: Mean near best corrected visual acuity.

No significant difference in NBCVA was noted between treatment groups at any time point except for 30min, when MY elicited a small but significantly better NBCVA; 0.87±0.17 with MY *vs* 0.82±0.20 with PT drops (P=0.04, Table 2).

At 30min, some objective signs and subjective symptoms varied slightly between treatment groups. However, all differences in objective and subjective parameters analyzed had resolved by 60 and 90min, with no significant differences noted between the two treatment groups (Table 2). Reading capacity recovery was slightly delayed with MY compared to PT drops (4.28±2.4h *vs* 3.75±2.03h respectively; P=0.022).

Overall, 50% of patients preferred MY as a dilation method, and 50% preferred PT drops. In summary, both MY and PT drops were safe and well-tolerated in these small cohorts and no complications were observed.

Cataract surgery study results In this second study, 80 eyes from 80 patients scheduled for routine unilateral cataract surgery were randomized to be treated either with MY or PT eye drops. The study comprised 35 males (23 with MY and 12 with PT drops) and 45 females (17 in with MY and 28 with PT); mean patient age was 69 years. At the start of surgery, mean pupil diameter was 8.75±0.76mm with MY compared to 8.77±0.63mm with PT drops, with no significant difference between both methods (P=0.91). At the end of surgery, mean pupil diameter was 7.96±1.06mm with MY and 8.32±0.72mm in with PT drops (P=0.08).

Volume of fluid employed during surgery was not different between groups; 101.93±54.27mL with MY and 102.58±30.75mL with PT drops (P=0.95).

There was no significant difference between treatment groups in any cardiovascular parameters (Table 3). Both MY and PT drops were shown to be safe in these small groups in a surgical setting. No complications related to mydriatic procedures were observed.

Table 3 Comparative statistical analysis during cataract surgery

Parameters	Mydriasert® (n=40)	PT (n=40)	*P*
Age (a)	67.95 (9.52)	70.10 (10.22)	0.33
Sex (%)			0.013
F	42.50	70	
M	57.50	30	
Initial dilation (mm)	8.75 (0.76)	8.77 (0.63)	0.91
Final dilation (mm)	7.96 (1.06)	8.32 (0.72)	0.08
Dilation difference (mm)	0.79 (0.75)	0.45 (0.56)	0.025
Volume of fluid (mL)	101.93 (54.27)	102.58 (30.75)	0.95
Initial systolic pressure (mmHg)	135 (17.10)	140.25 (21.93)	0.36
Initial diastolic pressure (mmHg)	76.97 (10.58)	75.33 (8.69)	0.49
Final systolic pressure (mmHg)	139.28 (16.67)	141.62 (21.40)	0.62
Final diastolic pressure (mmHg)	79.66 (9.37)	77.47 (9.08)	0.34
Initial heart rate	66.19 (10.99)	66.81 (10.11)	0.81
Final heart rate	64.97 (9.73)	66.08 (9.85)	0.64

Mean±standard deviation; PT: Phenylephrine and tropicamide.

DISCUSSION

Good mydriasis is required for thorough ophthalmic examinations and for procedures such as laser photocoagulation. Furthermore, adequate dilation is of great importance in cataract surgery. In current standard practice mydriasis is obtained through mydriatic eye drops eliciting anticholinergic and sympathomimetic effects. Phenylephrine (10%) and tropicamide (1%), alone or in combination, are the most frequently used drugs, and repeated application are usually required to get a good pupil dilatation [10]. Several studies have tried to achieve better mydriasis using lower concentrations, in order to decrease associated cardiovascular effects in predisposed patients[11-13].

Mydriasert(is an insoluble ophthalmic drug insert containing 0.28mg tropicamide and 5.4mg phenylephrine, measuring 4.3mm×2.3mm×1.6mm. As with all inserts, bioavailability is higher with MY compared to drops, producing improved local effect with lower local and systemic concentrations.

Some studies have demonstrated that phenylephrine plasmatic concentrations using MY are inferior compared to eye drops [14]. Other devices have been used to achieve mydriasis, including wicks and pledget sponges saturated in dilating drops. Although the mydriatic effect of these methods has been shown to be as good as conventional eye drops, topical anesthetic must be used with these methods leading to risk of corneal and conjunctival abrasions [4,15,16]. In the studies reported here, no topical anesthetic was necessary for placement of the insert, and the procedure was well tolerated by most patients.

Based on the results of this study, MY represents a suitable alternative as a mydriatic device. The mydriatic effect of MY is at least as good as conventional PT eye drops after 60min of application, and its efficacy is actually superior to PT drops after 90min of application. These results are important as they show MY is capable of exerting a sustained mydriatic effect over a length of time where repeated doses of conventional eye drops are needed to sustain the same effect, potentially increasing the risk of cardiovascular side effects. This study also confirms that pupil dilation prior to cataract surgery can be adequately and safely achieved using MY. The device was well tolerated by all patients and all side effects were mild in severity and reversible after one hour. Other groups have reported that application of MY for 40min achieved mydriasis as good or better than conventional dilating drops[17-19].

Although MY can take slightly longer than eye drops to achieve maximal pupil dilation, the device is efficacious and elicits good mydriasis for significantly longer duration than conventional PT eye drops. Mydriasis using PT eye drops before cataract surgery can be a time consuming procedure, as often several drugs must repeatedly be applied. One MY device can produce a similar level of pupil dilation as three applications of PT drops, significantly saving time. Use of ophthalmic mydriatic devices could potentially help reduce economic costs and improve throughput, especially in high-volume surgical centers.

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