Tropicamide
Newborn use only

2022

Alert	Watch for apnoeas and abdominal distension following administration. Lower concentration solutions and regimens minimising number of additional drops are recommended.
Indication	Induction of mydriasis and cycloplegia for diagnostic and therapeutic ophthalmic procedures.
Action	Anticholinergic drug that produces pupillary dilatation by inhibiting the sphincter pupillae muscle and paralysis of accommodation.
Drug type	Antimuscarinic
Trade name	Minims Tropicamide Eye Drops Mydriacyl Eye drops
Presentation	Minims Tropicamide Eye Drops 0.5%, 1% 0.5 mL (single use).[16] Mydriacyl Eye drops 0.5%, 1% 15 mL (multi-dose).[17]
Dose	Use in combination with phenylephrine 2.5% with or without cyclopentolate 0.5%. **<u>REGIMEN 1 (3 agents):</u>** Phenylephrine 2.5% + cyclopentolate 0.5% + tropicamide 0.5% eye drops.[1-4] Instil one drop of each agent (5 minutes apart) into each eye 60 minutes prior to examination. **<u>REGIMEN 2 (2 agents):</u>** Phenylephrine 2.5% + tropicamide 0.5% eye drops.[5-7] Instil one drop of each agent (5 minutes apart) into each eye 60 minutes prior to examination. Dark irides may require additional drops.
Dose adjustment	Therapeutic hypothermia – No information. ECMO – No information. Renal impairment – No information. Hepatic impairment – No information.
Maximum dose	REGIMEN 1: 3 drops of each agent. REGIMEN 2: 4 drops of each agent.
Total cumulative dose	
Route	Topical instillation into the eyes from the container or use a microdrop (5–7 microL) cannula
Preparation	
Administration	Instil one drop of each agent (5 minutes apart) into each eye. Apply pressure to the lacrimal sac during and for 60 seconds after instillation of eye drop to minimise systemic absorption. Wipe away excess medication. Repeat if pupillary dilatation inadequate. Perform examination 60 to 120 minutes after instillation. Consider withholding feeds for four hours from administration of the last drops to reduce incidence of feed intolerance.
Monitoring	Blood pressure, heart rate, oxygen saturation in infants with bronchopulmonary dysplasia or at risk of apnoea. Signs of ileus.
Contraindications	Necrotising enterocolitis (NEC) at the time of examination. Hypersensitivity to tropicamide or any other component listed in the formulation. Narrow angle glaucoma.
Precautions	Bronchopulmonary dysplasia. Severe neurological impairment—may increase risk of seizures. Feeding intolerance. Lower concentration solutions and regimens minimising number of additional drops are recommended to minimise toxicity.
Drug interactions	
Adverse reactions	Feeding intolerance, abdominal distension and increased gastric residuals. Apnoea, transient bradycardia (especially infants on respiratory support). Stinging or burning of eye, photophobia.

	Rarely dry mouth, urinary retention, fever, tachycardia, vasodilatation, restlessness, agitation, seizures.
Compatibility	Phenylephrine, cyclopentolate, tetracaine (amethocaine)
Incompatibility	
Stability	Minims Tropicamide: Discard immediately after use. Mydriacyl: Discard container 28 days after opening.
Storage	Minims Tropicamide: Store between 2°C to 8°C. Do not freeze. Protect from light. Mydriacyl: Store below 25°C. Do not refrigerate. Protect from light. Keep tightly closed.
Excipients	Minims Tropicamide: Sodium hydroxide, hydrochloric acid and purified water.(16) Mydriacyl: Benzalkonium chloride 0.01%, sodium chloride, disodium edetate, hydrochloric acid and/or sodium hydroxide, purified water).(17)
Special comments	Without lacrimal sac occlusion, approximately 80% of each drop may pass through the nasolacrimal system and be available for rapid systemic absorption by the nasal mucosa. Consider withholding feeds for four hours from administration of the last drops. Used in conjunction with topical anaesthetic, e.g. tetracaine (amethocaine). Use with caution in an inflamed eye as the hyperaemia greatly increases the rate of systemic absorption through the conjunctiva.
Evidence	**<u>Efficacy and safety</u>** **Tropicamide alone (muscarinic antagonist):** Two controlled trials have compared tropicamide 0.5% to 1% versus other individual eye drops (phenylephrine [adrenergic agonist] or cyclopentolate [muscarinic antagonist]) or combination eye drops. Caputo et al reported tropicamide 1% (3 drops) produced inadequate mydriasis for peripheral retinal examination.[4] Ogut et al reported least mydriasis and side effects was achieved with use of tropicamide 1% (2 drops).[2] **Conclusion:** Tropicamide 1% produces insufficient mydriasis for use alone although it is associated with the least systemic physiological effects. [LOE II GOR B] **Tropicamide versus phenylephrine + tropicamide combination:** Lux et al, in an RCT in 30 preterm infants, reported the pupil surface area was 1.9 times greater with a regimen of phenylephrine 5% (1 drop) + tropicamide 0.5% (2 drops) compared to tropicamide 0.5% (3 drops). Visualisation of the retinal periphery was possible for 30 of 30 eyes dilated with the PTT regimen and for 16 of 30 eyes dilated with the TTT regimen.[8] Fleck et al, in an RCT in 23 preterm infants, reported the mydriatic effect of phenylephrine 2.5% + tropicamide 0.5% was superior to tropicamide 0.5% alone (mean 6 mm versus 2.7 mm; p <.001). Adequate mydriasis in phenylephrine 2.5% + tropicamide 0.5% group only.[5] **Conclusion:** Phenylephrine 2.5% (1 drop) + tropicamide 0.5% (2 drops) is an effective mydriatic combination and produces greater mydriasis compared to tropicamide 0.5% alone. [LOE II GOR B] **Tropicamide combinations:** Several RCTs have reported the efficacy of various tropicamide combinations in preterm infants undergoing ROP screening. Merritt et al, in a crossover RCT in 30 preterm infants, reported phenylephrine 2.5% + tropicamide 0.5% + cyclopentolate 0.5% (1 drop each) produced maximal mydriasis at 75–90 minutes with adequate fundoscopy at 120 minutes and no significant effect on systolic BP.[1] Ogut et al, in an RCT in 80 preterm infants, reported maximum mydriasis was achieved with cyclopentolate 0.5% + tropicamide 0.5% + phenylephrine 2.5% (1 drop each); whereas adequate mydriasis without side effects was achieved with cyclopentolate 1% + tropicamide 1% (1 drop each). Maximum side effects (increased heart rate and BP) were seen with phenylephrine 2.5%; the safest was tropicamide 1%.[2] Chew et al, in an RCT in 39 preterm infants with dark irides, reported similar pupillary dilatation at 45 and 60 minutes after combinations of cyclopentolate 1% + phenylephrine 2.5% (3 drops) compared to tropicamide 1% + phenylephrine 2.5% (3 drops) and cyclopentolate 0.2% + phenylephrine 1% (3 drops). Combination cyclopentolate 1% + phenylephrine 2.5% and tropicamide 1% + phenylephrine 2.5% were associated with increased BP, and cyclopentolate 1% + phenylephrine 2.5% was associated with feed intolerance.[9] Khoo et al, in an RCT in 28 preterm infants, reported similar mydriasis from cyclopentolate 0.2% + phenylephrine 1% (3 drops) compared to tropicamide 0.5% + phenylephrine 2.5% (3 drops). No significant difference in blood pressure over baseline values was reported.[6]

	Bolt et al, in an RCT in 39 preterm infants, reported the mydriatic effect of the phenylephrine 2.5% + tropicamide 0.5% combination (2 drops) was significantly superior to that of the cyclopentolate 0.5% + tropicamide 0.5% combination (2 drops). A significant increase of BP and HR occurred within 7 to 10 minutes after the cyclopentolate 0.5% + tropicamide 0.5% combination only.[7] Sindel et al, in an RCT in 34 preterm infants, reported that, on exposure to bright light, the pupillary size with phenylephrine 1% + tropicamide 1% (2 drops) was significantly smaller than phenylephrine 2.5% + tropicamide 1% (2 drops) or phenylephrine 2.5% + tropicamide 0.5% + cyclopentolate 0.5% (2 drops).[3] Dilatation was sufficient to allow appropriate examination in all infants (pupillary diameter > 6.0 mm). BP and HR increased transiently in all groups receiving mydriatic but returned to baseline values in 25 minutes. This increase was significant with phenylephrine 2.5%. **Conclusion:** Tropicamide is well tolerated but produces inadequate mydriasis by itself.[2, 4] Most effective combinations are: phenylephrine 2.5% + tropicamide 0.5% + cyclopentolate 0.5% (1 drop each)[1-3] and phenylephrine 2.5% + tropicamide 1% (2 drops each)[3], although these regimens may be associated with acute physiological effects. Adequate mydriasis with lower risk of side effects is achieved with cyclopentolate 1% + tropicamide 1% (1 drop each)[2]. [LOE II GOR B] Three-drop regimens of combination eye drops were associated with more acute physiological effects and feed intolerance.[6] [LOE II GOR B] **Safety** Ogut et al reported least side effects were achieved with use of tropicamide 1% (2 drops) compared to cyclopentolate 1% and phenylephrine 2.5%.[2] Three-drop regimens of combination eye drops were associated with more acute physiological effects and feed intolerance.[6] Instillation of tropicamide 1% + phenylephrine 2.5% causes infant pain (increase in PIPP score).[10] Acute ileus has been reported after instillation of tropicamide 0.5% + phenylephrine 2.5% eye drops.[11-13] More severe reactions have not been reported in newborn infants from use of tropicamide alone. **Pharmacokinetics/pharmacodynamics** Absorption and pharmacokinetics in newborns have not been reported. Combined tropicamide 0.75% + phenylephrine 2.5% resulted in a mean time to pupillary diameter 7 mm of 46 minutes.[12] Phenylephrine 2.5% + tropicamide 0.5% + cyclopentolate 0.5% (1 drop of each agent) produced maximal mydriasis at 75–90 minutes with adequate fundoscopy at 120 minutes.[1] Approximately 80% of each drop may pass through the nasolacrimal system and be available for rapid systemic absorption by nasal mucosa without lacrimal sac occlusion.[13] (LOE III GOR C)
Practice points	
References	1. Merritt JC, Kraybill EN. Effect of mydriatics on blood pressure in premature infants. Journal of Pediatric Ophthalmology and Strabismus. 1981;18:42-6. 2. Ogut MS, Bozkurt N, Ozek E, Birgen H, Kazokoglu H, Ogut M. Effects and side effects of mydriatic eyedrops in neonates. European Journal of Ophthalmology. 1996;6:192-6. 3. Sindel BD, Baker MD, Maisels MJ, Weinstein J. A comparison of the pupillary and cardiovascular effects of various mydriatic agents in preterm infants. Journal of Pediatric Ophthalmology and Strabismus. 1986;23:273-6. 4. Caputo AR, Schnitzer RE. Systemic response to mydriatic eyedrops in neonates: Mydriatics in neonates. Journal of Pediatric Ophthalmology and Strabismus. 1978;15:109-22. 5. Fleck BW, Dhillon B, Mitchell A. Additive mydriatic effect of 2.5% phenylephrine and 0.5% tropicamide eyedrops in premature babies. Journal of Pediatric Ophthalmology and Strabismus. 1994;31:130. 6. Khoo BK, Koh A, Cheong P, Ho NK. Combination cyclopentolate and phenylephrine for mydriasis in premature infants with heavily pigmented irides. Journal of Pediatric Ophthalmology and Strabismus. 2000;37:15-20. 7. Bolt B, Benz B, Koerner F, Bossi E. A mydriatic eye-drop combination without systemic effects for premature infants: A prospective double-blind study. Journal of Pediatric Ophthalmology and Strabismus. 1992;29:157-62.

8. Lux AL, Degoumois A, Barjol A, Mouriaux F, Denion E. Combination of 5% phenylephrine and 0.5% tropicamide eyedrops for pupil dilation in neonates is twice as effective as 0.5% tropicamide eyedrops alone. Acta Ophthalmologica. 2017;95:165-9.
9. Chew C, Rahman RA, Shafie SM, Mohamad Z. Comparison of mydriatic regimens used in screening for retinopathy of prematurity in preterm infants with dark irides. Journal of Pediatric Ophthalmology and Strabismus. 2005;42:166-73.
10. Cohen AM, Cook N, Harris MC, Ying GS, Binenbaum G. The pain response to mydriatic eyedrops in preterm infants. Journal of Perinatology. 2013;33:462-5.
11. Degirmencioglu H, Oncel MY, Calisici E, Say B, Uras N, Dilmen U. Transient ileus associated with the use of mydriatics after screening for retinopathy of prematurity in a very low birth weight infant. Journal of pediatric ophthalmology and strabismus. 2014;51 Online:e44-e7.
12. Obata S, Imamura T, Kakinoki M, et al. Systemic adverse events after screening of retinopathy of prematurity with mydriatic. PLoS One. 2021 Sep 9; 16(9):e0256878
13. Alpay A, Canturk Ugurbas S, Aydemir C. Efficiency and safety of phenylephrine and tropicamide used in premature retinopathy: a prospective observational study. BMC Pediatr. 2019 Nov 6;19(1):415.
14. Phamonvaechavan P, Chutasmit K, Damrongrak P, Koukiatkul S, Wongkiatkajorn T, Ngerncham S. Comparison of the effectiveness of mydriasis by two instillation methods of combined 0.75% tropicamide and 2.5% phenylephrine eye drop in preterm infants. Journal of the Medical Association of Thailand = Chotmaihet thangphaet. 2012;95 Suppl 4:S1-7.
15. Gray C. Systemic toxicity with topical ophthalmic medications in children. Paediatric and Perinatal Drug Therapy. 2006;7:23-9.
16. Minims Tropicamide Eye Drops. Bausch & Lomb (Australia) Pty Ltd. MIMS online accessed online on 19 May 2022.
17. Mydriacyl Tropicamide Eye Drops. Alcon Laboratories (Australia) Pty Ltd. MIMS online accessed online on 19 May 2022.

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