Tropicamide
Newborn Use Only

2018

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% solution. Mydriacyl Eye drops 0.5%, 1.0% 15 mL (multidose—excipients benzalkonium chloride 0.01%, sodium chloride, disodium edetate, hydrochloric acid and/or sodium hydroxide, purified water).
Dosage/Interval	Use in combination with phenylephrine 2.5% with or without cyclopentolate 0.5%. **<u>REGIMEN 1:</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. Repeat if pupillary dilatation inadequate. Perform examination 60 to 120 minutes after instillation. **<u>REGIMEN 2:</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. Repeat if pupillary dilatation inadequate. Perform examination 60 to 120 minutes after instillation. Dark irides may require additional drops.
Maximum daily dose	REGIMEN 1: 3 drops of each agent. REGIMEN 2: 4 drops of each agent.
Route	Topical instillation into the eyes from the container or use a microdrop (5–7 microL) cannula.
Preparation/Dilution	
Administration	Apply pressure to the lacrimal sac during and for 60 seconds after instillation of eye drop to minimise systemic absorption. Wipe away excess medication. 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.
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	Cyclopentolate, phenylephrine, tetracaine (amethocaine)
Adverse Reactions	Feeding intolerance, abdominal distension and increased gastric residuals. Apnoea, transient bradycardia (especially infants on respiratory support). Stinging or burning of eye. Rarely dry mouth, urinary retention, fever, tachycardia, vasodilatation, restlessness, agitation, seizures.
Compatibility	Phenylephrine, cyclopentolate, tetracaine (amethocaine)
Incompatibility	No information.

Stability	Discard immediately after use.
Storage	Store in refrigerator at 2°C to 8°C. Do not freeze. Protect from light.
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).
Evidence summary	**Efficacy and safety** **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% + 2.5% phenylephrine (1 drop each); whereas adequate mydriasis without side effects was achieved with 1% cyclopentolate + 1% tropicamide (1 drop each). Maximum side effects (increased heart rate and BP) were seen with 2.5% phenylephrine; the safest was 1% tropicamide.[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 1.0% + tropicamide 1.0% (2 drops) was significantly smaller than phenylephrine 2.5% + tropicamide 1.0% (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). P and HR increased transiently in all groups receiving mydriatic but returned to baseline values in 25 minutes. This increase was significant with 2.5% phenylephrine. **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 1.0% (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 1% cyclopentolate + 1% tropicamide (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% + 2.5% phenylephrine eye drops.[11] 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 0.75% tropicamide + 2.5% phenylephrine 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 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)
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Authors Contribution

Original author/s	Himanshu Popat
Expert review	Mark Jacobs, Hughie Tsang, Kimberley Tan
Evidence Review	David Osborn
Nursing Review	Eszter Jozsa
Pharmacy Review	Jing Xiao, Mariella De Rosa
Final content and editing review of the original	Ian Whyte
Electronic version	Mariella De Rosa, Cindy Chen, Ian Callander
Facilitator	Srinivas Bolisetty