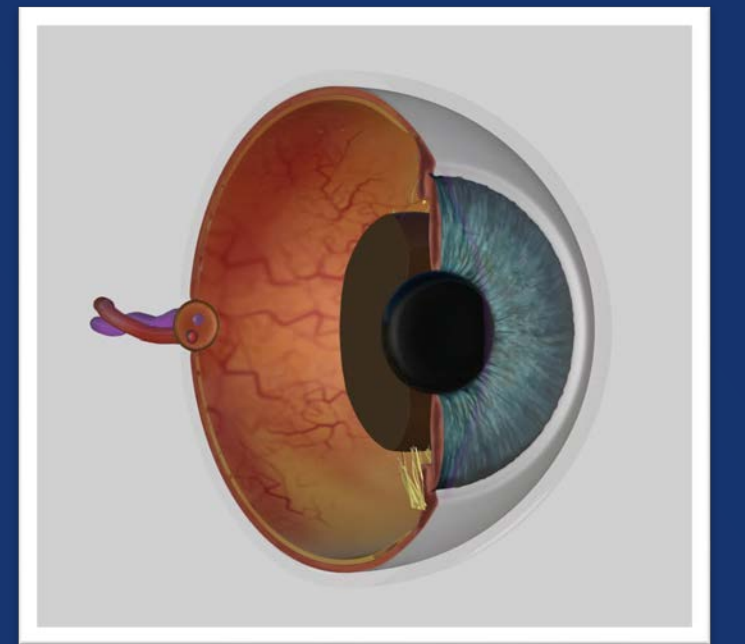


Lack of Evidence and Consequential Harm Caused by Mydriatic Regimens Used in Retinopathy of Prematurity Screening



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Introduction

- Very preterm infants require mydriatic eye drops in preparation for retinopathy of prematurity (ROP) screening.
- In New Zealand and Australia, approx. 3,500 premature infants/year are screened for ROP.
- 66% of infants screened don't have ROP.

Aims

Systematic review

- To systematically review literature for efficacy and safety of mydriatic regimens used in ROP screening.

Survey

- To determine the variation of NICU mydriatic regimens within New Zealand and Australia.
- To estimate the frequency of adverse drug events after mydriatic administration.

Methods

Systematic review

- Two review authors independently carried out the literature search.
- Publications that evaluated efficacy and safety of mydriatic regimens, in premature infants, were included in the review.
- MEDLINE via Ovid, PubMed, Web of Science, Cochrane Library and Cochrane Neonatal Review Group, Google Scholar, and Scopus databases were searched.

Survey

- A Survey Monkey questionnaire was emailed to selected nursing staff at Neonatal Intensive Care Units (NICU).
- Staff were identified in the Directory of NICU within Australia and New Zealand 2017 register.
- The target survey population were staff who administer the mydriatic medicines for ROP screening.

Results

Systematic review

- 10 papers were identified (all small sample size).
- Nine studies compared various combinations of phenylephrine and cyclopentolate and/or tropicamide.
- Irrespective of the combination of medications, pupil dilation results were above 5mm.
- 2014 Vicente et al results show a non-statistically difference in pupil dilation in all regimens (Figure 1).
- 5 studies noted an increase in blood pressure.
- 1 study noted an increase in feed intolerance.

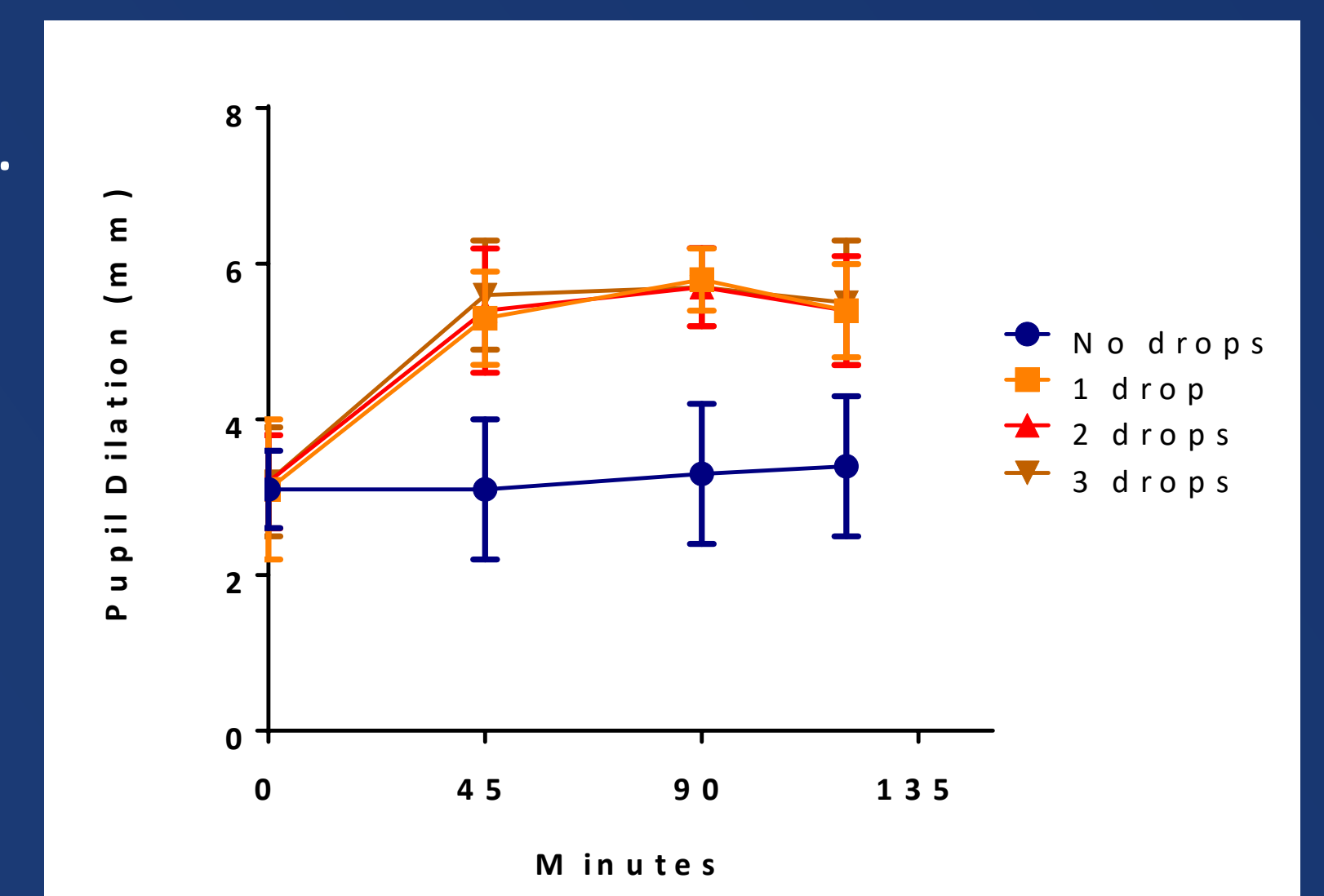


Figure 1. Vicente et al¹ Mean pupil size for phenylephrine 1% and cyclopentolate 0.2%

Survey

- 46 neonatal nurses from Australia (n= 30) and New Zealand (n= 16) participated in the survey.
- 11 different mydriatic regimens were identified (Tables 1).
- Regimens F and G were the most common regimens (n=18).
- Phenylephrine dosing ranged from 70 µg to 1950 µg (28 fold difference).
- Cyclopentolate dosing ranged from 14 µg to 260 µg (18 fold difference).
- Tropicamide dosing ranged from 260 µg to 780 µg (3 fold difference).
- Very often skin blanching apnoea, tachycardia, feed intolerance occurred (Figure 2).
- Sometimes hypertension, tachycardia, apnoea, feed intolerance, skin blanching occurred (Figure 2).
- Rarely NEC, HTN, tachyapnoea, feed intolerance, seizure, skin blanching occurred.
- Nursing staff reported seeing additional adverse effects following mydriatic administration; bradycardia, abdominal distension and death.

Regimen	Phenylephrine total dose µg (%*)	Cyclopentolate total dose µg (%*)	Number of admin.	Drop volume (µL)
A	70 (1%)	14 (0.2%)	1	7
B	520 (1%)	104 (0.2%)	2	35
C	260 (1.25%)	65 (0.25%)	1	35
D	87.5 (1.25%)	17.5 (0.25%)	1	7
E	650 (2.5%)	65 (0.25%)	1	35
F	650 (2.5%)	130 (0.5%)	1	35
G	1300 (2.5%)	260 (0.5%)	2	35

Regimen	Phenylephrine total dose µg (%*)	Tropicamide total dose µg (%*)	Number of admin.	Drop volume (µL)
H	1300 (2.5%)	260 (0.5%)	2	35
I	1950 (2.5%)	390 (0.5%)	3	35
J	1300 (2.5%)	520 (1%)	2	35
K	1950 (2.5%)	780 (1%)	3	35

*concentration expressed as percentage

Table 1. Reported mydriatic regimens in New Zealand and Australia.

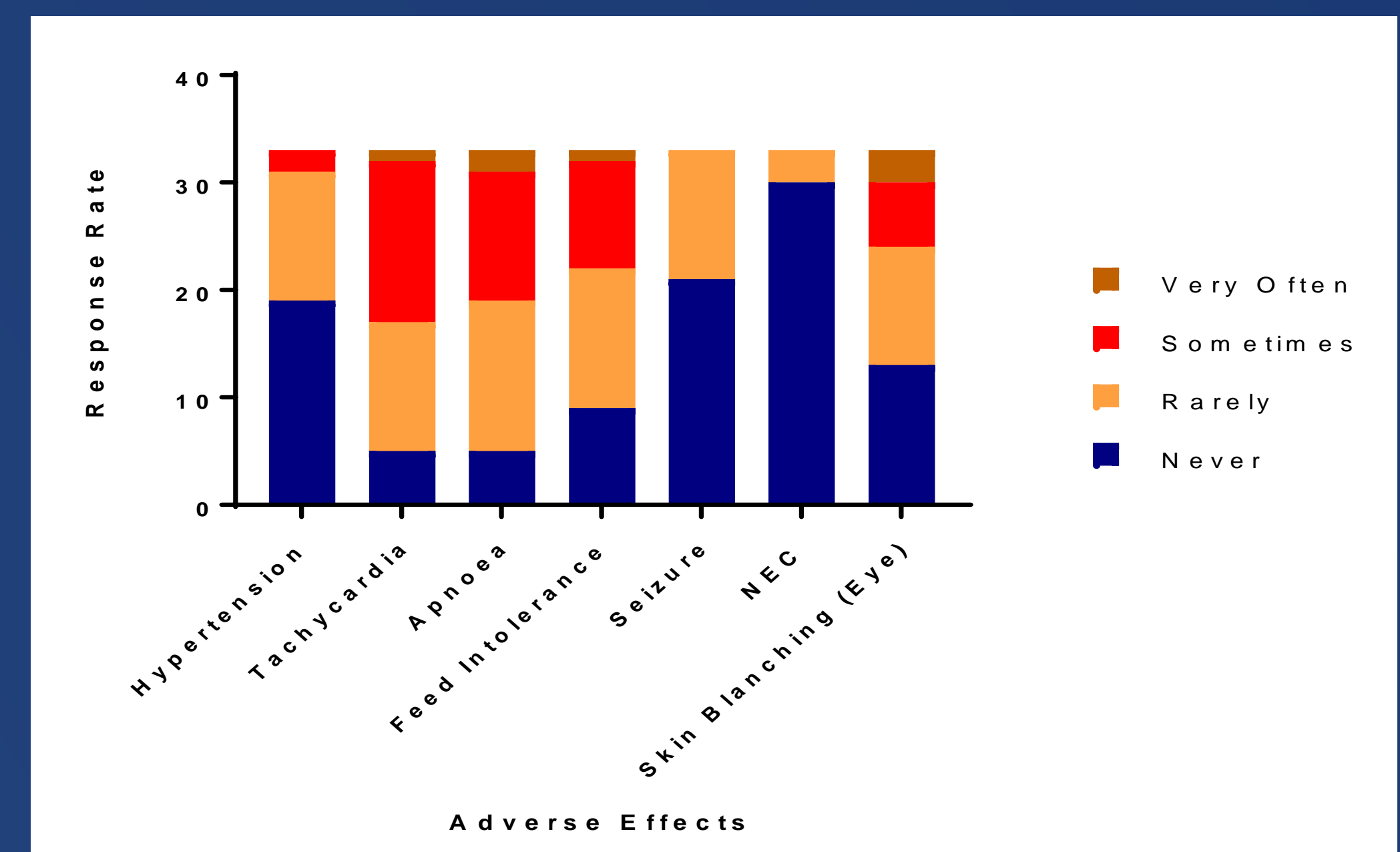


Figure 2. Reported adverse effects, by nursing staff, following mydriatic eye drop administration

Discussion

- Results from pilot studies suggest that there is very little benefit in administering larger doses when smaller doses are effective.
 - A robust data set is lacking.
 - Neonatal nurses associate mydriatics with significant harm, including NEC and death.
 - Side effects are seen if systemic or transdermal absorption occurs.
 - Consequential harm caused by mydriatic medicines used in ROP screening should not be occurring.

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Conclusions

- A sufficiently powered data set is required to a) establish low dose efficacy of mydriatic medicines, b) incidence of adverse drug effects, with a focus on the most vulnerable infants.

References

1. Vicente G.V., et al. *Journal of American Association for Pediatric Ophthalmology and Strabismus*. 2012;16(4):365-9

Further information

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