Original Article

Assessment of WINROP algorithm as screening tool for preterm infants in Manitoba to detect retinopathy of prematurity

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Abstract

Objective: Developing less invasive methods for early detection of retinopathy of prematurity (ROP) is vital to minimizing blindness in premature infants. Lofqvist and colleagues developed a computer-based ROP risk algorithm (WINROP) (<https://winrop.com>), which detects downtrends in postnatal weight gain that correlate with the development of sight-threatening ROP. The aim of this study is to investigate the sensitivity and specificity of the WINROP algorithm to detect vision-threatening ROP.

Methods: This is a retrospective chart review study between January 2008 and December 2013. This study was conducted in the neonatal intensive care unit in Children's Hospital at Health Sciences Centre, Winnipeg, Manitoba, Canada. The study included preterm infants, less than 32 weeks' gestation, who were admitted to the hospital during the study period. The included 215 infants were eligible for ROP screening and had sufficient data to be entered into the WINROP algorithm. Infants were screened by a paediatric ophthalmologist for retinopathy of prematurity. The body weight of infants was measured weekly and entered into the WINROP algorithm; the sensitivity and the specificity of the WINROP algorithm were assessed.

Results: The mean gestational age was 28.6 ± 1.8 weeks. The mean body weight was 1244 ± 294 g. The sensitivity of the WINROP algorithm to detect vision-threatening retinopathy of prematurity in our cohort was 90% ($P=0.021$) with a specificity of 60% ($P=0.002$).

Conclusion: The WINROP algorithm lacks sufficient sensitivity to be used clinically in our population. The algorithm needs to be reassessed in contemporary populations.

Keywords: Infants; Neonatal intensive care; Ophthalmology screening; Premature; Retinopathy of prematurity; WINROP algorithm.

Retinopathy of prematurity (ROP) is the leading cause of blindness affecting preterm infants all over the world (1). Its frequency is strongly associated with the quality of health care. In high-income countries, where many premature infants survive, sight-threatening ROP is screened for and treated effectively, making blindness rare. In middle-income countries, health care provided allows for the survival of some extremely premature infants but is less effective in preventing ROP. This has increased the prevalence of ROP in more mature infants in these countries (1,2).

With the decreasing of gestational age (GA) and birth weight (BW) in developed (core) countries, ROP is the second most common cause of blindness in childhood, after cortical blindness (3,4).

In core countries, infants born after 32 weeks are not considered at risk of developing ROP. In addition, most infants born after 28 weeks who develop ROP have mild disease that does not require treatment.

The aim of ROP screening is early detection and treatment of ROP to prevent blindness (5,6). In core countries, most premature infants less than 32 weeks receive multiple ROP screenings throughout their neonatal intensive care unit (NICU) stay (7–10). The screening consists of a comprehensive eye examination performed by a paediatric ophthalmologist with expertise in neonatal ROP. The pupil must be dilated to visualize the vitreous and retina. Both manipulations of the eye and the medications used to dilate the pupil can cause systemic sequelae (11).

Screening for ROP is a labour-intensive process with a relatively slight yield, since less than 10% of infants who are screened require treatment. Currently, BW and GA are used as selection criteria to screen infants for treatable disease (12). Although the screening guidelines differ between countries, current screening criteria do not take into account postnatal risk factors that are likely to influence the development of ROP (1,13–15). There is a need for earlier differentiation of infants at higher risk for severe ROP from those at lower risk. Integration of postnatal risk factors into the screening guidelines may decrease the need for screening. However, these methods require validation in different populations before changes to the current screening recommendations can be made.

Lofqvist and colleagues developed a computer-based ROP risk algorithm (WINROP), which detects downtrends in postnatal weight gain. This algorithm predicts need for ROP treatment and may significantly reduce the number of infants requiring examinations (12,16).

WINROP uses a cumulative-deviations statistical approach in multiple steps. Each week the infant's actual weight is compared with an expected growth curve of infants who developed no or mild ROP. The differences or deviations between the expected weight and the actual weight are accumulated from week to week, and when these cumulative deviations exceed a threshold, the program identifies the infant at high risk. The risk of severe ROP is categorized using varying levels of dichotomized cut-off for BW, gestation and postnatal age to determine the need for eye examinations. The WINROP algorithm demonstrated a sensitivity between 90% and 100% in different studies (17–23).

Neonatal practices have changed since the development of the WINROP algorithm with more very immature infants surviving, improved nutritional support and improved oxygen management. Further, the criteria for screening and treatment of ROP have changed during this period with more pre-emptive management. The aim of this study is to re-evaluate the efficacy of WINROP algorithm to detect need for ROP treatment among a more contemporary population of preterm infants.

METHODS

This study is a retrospective assessment of the WINROP algorithm using data abstracted from the medical records of infants, less than 32 weeks' gestation, who were admitted to the Health Sciences Centre, Winnipeg, Manitoba, Canada between January 2008 and December 2013. The included infants had sufficient data to be entered into the WINROP algorithm. The University of Manitoba granted ethical approval for this study.

Infants who qualified for ROP examinations, according to our institutional criteria of GA and BW, were examined by paediatric ophthalmologists. During 2007 to 2008, infants less than 32 weeks and or BW less than 1501 g were screened. Since 2008, infants less than 31 weeks and or BW less than 1501 g were screened. The collected demographic data included the following: GA, BW, worst ROP stage in any eye, zone of ROP, presence or absence of plus disease, ROP treatment (either medical or laser therapy) if given, and the date of treatment. Data from the charts were entered into the WINROP program.

We used the WINROP program to categorize infants as high risk and low risk to develop ROP requiring treatment. Results from the WINROP program were compared with the results from the infants' charts. The data were analyzed using SAS software version 9.3 (SAS Institute Inc., Cary, NC) (24). Descriptive statistics, sensitivity, specificity, positive and negative predictive value of the program were calculated. Data are presented as mean $\pm$ SD.

RESULTS

During the study period, 286 infants less than 32 weeks were admitted to our institution. Infants were excluded for the following reasons: 34 died before ROP screening, 27 infants were transferred to other provincial facilities and 10 infants were excluded because of missing data (discharged before 40 weeks'

PMA). All infants who were transferred to other facilities or discharged home before 40 weeks' PMA had larger BW and higher GA and none of them developed ROP requiring treatment. Therefore, the study group was comprised of 215 infants who had sufficient data to be assessed using the WINROP algorithm. The mean GA for the included infants was 28.6 ± 1.8 weeks and the mean BW was 1244 ± 294 g. The frequency of ROP stages as detected by the routine ROP screening is shown in Table 1.

There were 10 infants (4.7%) who developed sight-threatening ROP, which required treatment based on ophthalmic examination. For those infants, GA was 25.7 ± 1.4 weeks and BW was 838 ± 140 g. The WINROP algorithm identified 89 infants (41%) as high risk to develop ROP with the mean age for alarm 30.6 ± 1.6 weeks corrected GA. The program identified 9 of 10 infants who required treatment. The mean age at identification was 30.3 ± 1.9 weeks postmenstrual age.

The sensitivity of WINROP algorithm to detect need for ROP treatment in our cohort was 90% ($P=0.021$) with a specificity of 60% ($P=0.002$). The positive predictive value was 10% and the negative predictive value was 99.2% (Table 2). The program identified all infants who developed stage 3 ROP and received treatment. However, the program missed one infant who received treatment for ROP. The infant who was missed by the program had stage 2 zone 2 ROP with plus disease. This infant had a BW of 960 g and GA of 25 weeks, Apgar scores of 4 and 6 at 1 and 5 min, respectively. The weekly weight curve in relation to infants with ROP and infants without ROP is shown in Figure 1.

DISCUSSION

We undertook a retrospective validation of the WINROP program in our centre, which could be considered as an example of a typical level 3 centre in Canada. Our patient population is heterogeneous with diverse ethnic background and a low incidence of BPD and ROP (25). Oxygen use in preterm infants in our institution is tightly regulated with the aim to keep saturation between 88% and 92%. In our institution, the WINROP program had insufficient sensitivity to detect the need for ROP treatment (90%). Despite population differences and changes in neonatal management over time, our results are similar to prior studies which had a sensitivity between 90% and 100% (17–23).

The program accurately identified all infants who developed stage 3 ROP. However, despite identifying all infants who developed stage 3 ROP, the WINROP algorithm missed one infant who was treated for ROP. This infant

Table 1. Frequency of ROP stages as diagnosed by ophthalmic exam

ROP stage	Frequency	%	Cumulative frequency	Cumulative %
0	143	66.5	143	66.5
1	39	18.1	182	84.7
2	24	11.2	206	95.8
3	9	4.2	215	100.0

ROP Retinopathy of prematurity.

Table 2. Sensitivity, specificity, positive predictive value and negative predictive value of the WINROP algorithm

	Physician' screening		
	ROP requiring treatment	No ROP/ROP not requiring treatment	Total
WINROP positive alarm	9	80	8989
WINROP no alarm	1	125	126
Total infants	10	205	215

ROP Retinopathy of prematurity.

Figure 1. Weight curve of the infant who was treated for retinopathy of prematurity (ROP) and was not identified as high risk by the WINROP algorithm in relation to other infants. Triangles depict the weekly weight curve of the missed infant; boxes depict the weight curve of infants with no ROP/nontreated ROP and diamonds depict infants with ROP that required treatment.

had adequate weight gain throughout the initial weeks of life and yet developed stage 2 ROP with plus disease and needed treatment.

As all infants with significant ROP in our centre are less than 28 weeks of gestation, this study could not assess the validity of the program in older infants. Additionally, WINROP is not suitable for infants less than 24 weeks as these were not included in the development of the algorithm. The program generally identified those infants at risk for severe ROP at 30 weeks' PMA, which is 2 weeks prior to the routine ophthalmic examination. Early prediction of the development of severe ROP may in the future be used to initiate novel treatments to prevent disease progression such as beta-blockers (26).

In populations different from the reference population, the WINROP algorithm has lower sensitivity (27–31). The algorithm used in WINROP was developed using a Swedish population with mean GA of 29 weeks and upper limit set at 32 weeks (29,32). Differences in resources availability or the ethnic make up may account for the lower sensitivity observed in these studies. Our study population is likely different from the population for which the WINROP algorithm was derived. Our study population is ethnically and socioeconomically diverse.

A large part of WINROP's convenience is that it depends only on the weight measurements of the infants, a measurement that is already done as a part of clinical practice all over the world (29). However, since the measurement only takes into account the weight, it fails to include other health and medical factors that may affect the weight measurements. For example, factors such as intraventricular hemorrhage, bronchopulmonary dysplasia, necrotizing enterocolitis, sepsis and hydrocephalus could induce excessive weight gain that would alter the ability of the algorithm to detect those at risk for severe ROP (30). Furthermore, many premature infants have higher morbidity and weekly weight measurements are not always possible to perform due to instability (33). This was not the case in our population as all infants who remained in hospital until 40 weeks had weekly weights available. Once there is a missed weight, the WINROP program can no longer be applied. Thus, when using WINROP to complement established screening schedules, the clinical judgment regarding an infant's risk of developing severe ROP must always supersede the WINROP outcome (23).

The strength of this study lies in the fact that it has been conducted in a centre with a low rate of ROP, restricted oxygen use and routine ROP screening by a paediatric ophthalmologist. Although the previous multicentre trial was conducted between 2006 and 2009 in North America and included 1706 infants, the results may not be comparable to our more contemporary cohort as neonatal care practices have been continually evolving (21). Since the time of the prior study, lower limits for oxygen saturation are being used, infants are progressively ventilated less, infants are fed earlier with higher amounts of protein and the ductus ligated much less. These are some of the many changes that have occurred. This allows for accurate assessment of the sensitivity and the specificity of the WINROP program, especially in preterm infants less than 28 weeks' GA. However, these results are limited by small sample size and the scarcity

of infants greater than 28 weeks who developed ROP, which limits our ability to assess the validity of the WINROP algorithm in older preterm infants and consequently the generalizability of our results.

Our screening criteria as well as the CPS guidelines have changed during the period involved in this study. Our data include nine infants that would not be screened by the current CPS recommendations. All of these infants were 31 weeks' gestation and were screened between 2007 and 2008 in accordance to the CPS guideline at that time. None of them developed ROP and the inclusion of these infants only minimally affects the specificity and has no effect on the sensitivity.

In conclusion, the consequence of missing a treatable case of ROP is so significant that we conclude that the use of the WINROP algorithm lacks sufficient sensitivity to be used clinically in our population. Because the nature of the population that are at risk and the fact that neonatal intensive care is changing, the algorithm needs to be reassessed in contemporary populations. Additional prospective multicentre studies examining the usefulness of WINROP in current practice are needed. These could readily be done with the advent of electronic patient records and large national databases.

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Conflict of Interest

There is no conflict of interest.

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