Choosing wisely babies for retinopathy of prematurity screening is more important in low resource setting

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Abstract

Design: A prospective observational study.

Setting: The study was conducted over a period of one year, from 01-07-2013 to 30-06-2014 at a hospital attached to a newly established rural medical college in India; located 45 km away from the regional eye centre.

Subjects: All babies, without exclusions, were screened for retinopathy of prematurity (ROP) as per guidelines of National Neonatology Forum (NNF) of India, i.e. babies born < 34 weeks gestation and/or < 1750 g birth weight, and the babies 34-36 [6/7] weeks gestation or 1750-2000 g birth weight, with risk factors for ROP.

Interventions: 53 babies were screened for ROP as per NNF guidelines.

Main Outcome Measures: 16 babies required laser therapy from the 53 babies that were screened over a period of one year. All weighed 1500 g or less at birth. Their GA was less than 33 weeks or less.

Conclusion: BW 1500 g or less and/ or GA less than 34 weeks, appear to be appropriate ROP screening criteria. Applying NNF criteria, no ROP would have been missed. In 19 (35.8%) babies screening could have been avoided. It is desirable to determine appropriate ROP screening criteria for a particular centre; based on local evidence.

Keywords: Blindness in children, Laser therapy, Oxygen therapy, Preterm baby, Retinopathy of Prematurity.

Introduction

Improvement in the quality of newborn care has led to enhanced survival among preterm babies. This is accompanied by increase in morbidities that include Retinopathy of Prematurity (ROP). To strike a balance between lower oxygen to prevent ROP and higher oxygen to prevent neonatal death is not easy. In preterm infants born before 28 weeks' gestation with a target oxygen saturation of 85 to 89% had a significantly higher rate of death than did those with a target of 91 to 95%.[1] Therefore, screening the high risk babies for ROP and its prompt treatment remains the only available course of action. Screening and treatment of ROP requires expertise, experience and an elaborate set up. As a result, these programmes are often not in place in low resource setting and have not always kept pace with the expansion of neonatal care. The screening centres in public hospitals are few and are over-burdened in India.[2] Therefore it is not only important that no babies with sight-threatening disease remain unidentified, it is equally important that screening of non- ROP babies is minimised.

The present study has been performed to determine appropriate ROP screening criteria for our centre; based on local evidence, in the background of National Neonatology Forum (NNF) guidelines[3] and by keeping in mind the difficulties in seeking an expert opinion and treatment.

Methods

This study was conducted at the Neonatal Intensive Care Unit (NICU) of Maharashtra Institute for Medical Education and Research (MIMER); Talegaon Dabhade, a rural medical college in India. The study was conducted over a period of one year, from 01-07-2013 to 30-06-2014. This hospital is attached to a newly established medical college, located 45 km away from a major city, Pune. It serves most often as the First Referral Unit (FRU) for the nearby primary health centres (PHC) and private maternity homes. Warmth, feeding, and antibiotic and oxygen administration receive prime attention. Inotropes and pulmonary vasodilators are administered as indicated. Management is based on established protocols, revised over time, following monthly death audits. Complete blood counts are performed on admission to Neonatal Intensive Care Unit. Chest x-ray is obtained if there is respiratory distress. A portable x-ray machine is available. However, blood gas analysis, surfactant administration, mechanical ventilation and mechanised CPAP delivery units are not available. CPAP was delivered by a "home- made", inexpensive (costing US $3), and easy-to use version of CPAP delivery system.[4, 5] For an average bed-occupancy of 13 babies, generally two staff nurses are on duty round-the-clock. One junior and one senior resident are present per shift of 8 hours. They are supervised by three consultants. All the doctors are responsible for the paediatric outpatient and inpatient care as well. The consultants are also involved in under graduate and post graduate teaching.

All babies, without exclusions, were screened for ROP as per NNF guidelines that recommend screening all the preterm neonates who are born < 34 weeks gestation and/or < 1750 grams birth weight; as well as babies 34-36$^{6/7}$ weeks gestation or 1750-2000 grams birth weight, if they have risk factors for ROP.[3] The screening was performed after weaning from continuous positive airways pressure (CPAP) and follow up head box oxygen. No baby received surfactant therapy or mechanical ventilation. ROP examinations were done first by the ophthalmic consultants at the study centre and later, at the regional eye centre, where treatment was also possible. The screening at our institute was done by ophthalmic consultants by indirect ophthalmoscopy. A wide-field digital camera (RetCam) was not available.

The team from the regional centre also visited the study centre once a week. Their services were also available on other days at the regional centre if a need for an urgent consultation was felt. In such a situation, a junior resident accompanied the baby. The baby was transported in a Styrofoam box to keep her warm[6] along with a resuscitation kit; portable oxygen cylinder and a syringe loaded for enteral feed. A nurse could not be spared for the transport. The regional centre team performed screening with a binocular indirect ophthalmoscope using an infant speculum and a scleral depressor. Eyes were examined under topical anaesthesia using 2% proparacaine drops. Pupils were dilated by using 0.5% tropicamide +2.5% phenyl ephedrine eye drops 2 or 3 times. Retinopathy was documented using the International Classification for Retinopathy of Prematurity.[7] Laser therapy was performed as per early treatment for retinopathy of prematurity (ETROP) guidelines[8] and follow up was conducted as per pre-determined schedule of the regional eye centre.

The presence of following parameters was compared in the group that required laser therapy and that did not: GA, BW, mode of delivery, need for resuscitation at birth, presence of respiratory distress, presence of clinical sepsis, lowest haemoglobin, duration of CPAP, duration of weaning to head box oxygen, length of hospital stay and outcome. Odds ratio (OR), confidence interval (CI) were derived. Pearson's chi square test or Fisher' exact test was applied as a test of significance.

Our study conformed to the Helsinki Declaration and to local legislation. The ethics committee of MIMER Medical College and Hospital, Talegaon Dabhade approved the permission to conduct this research study. A written informed consent was obtained from the mother/father of the participant.

Results

Of the 409 babies admitted to the NICU during the study period, 77 (18.8%) qualified for screening. Of these, 24 (31.1%) babies died before the ROP screening. A typical profile of the babies that passed away is: weight <1200g/gestational age <29 weeks and had hyaline membrane disease, based on clinical and radiological findings. The remaining 53 babies were screened for ROP. Sixteen babies (30.2%) required laser therapy. The therapy was indicated in 3 babies following first screening, in10 following second screening and in 3 following third screening. All of them weighed 1500 g or less at birth and all except three, were born with GA less than 32 weeks. Three babies were born at 33 weeks and appeared growth restricted. The risk of getting laser therapy was higher in presence of BW 1500 g and less (p=.000), GA 32 weeks (p=.008) and less; and length of hospital days more than 21 days (p-.000). Male gender, CPAP delivery for more than 10 days, twin delivery, out- born status, mode of delivery, need for resuscitation, respiratory distress, lowest haemoglobin % less than 15 g, duration of weaning to head box oxygen (more than 3 days), presence of sepsis and adverse outcome (death) did not carry a significant risk for laser therapy (Table).

Table 1:

	Comparison of Clinical Features of Cases of ROP* with & without Laser Therapy					
Sr. No	**Parameters**	**Laser Therapy**		**Odds Ratio**	**Confidence**	**Significance**
		Yes (%)	**No (%)**		**Interval**	
1	**Birth weight**					
	≤1500g	16 (47.1)	18(52.9)	0.52	0.38-0.72	0.00
	>1500g	0(0.0)	19(100)			
2	**Gestational age**					
	≤ 32 weeks	13(54.2)	11(44.8)	10.24	2.42-43.22	0.00
	>32 weeks	3(10.3)	26(89.7)			
3	**Gender**					
	Male	10(41.7)	14(58.3)	2.73	0.81-9.18	0.08
	Female	6(20.7)	23(79.3)			
4	**Multiple births**					
	Singleton	13(27.7)	34(72.3)	2.61	0.46-14.65	0.25
	Twins	3(50)	3(50)			

5	**Place of delivery**					
	Out- born	8(38.1)	13(61.9)	1.84	0.56-6.06	0.23
	In- born	8(25)	24(75)			
6	**Mode of delivery**					
	Vaginal	10(25)	30(75)	0.38	0.10-1.43	0.13
	C - Section	6(46.2)	7(53.8)			
7	**Resuscitation**					
	Yes	3(37.5)	5(62.5)	1.47	0.3-7.09	0.45
	No	13(28.9)	32(71.1)			
8	**Respiratory distress**					
	Yes	12(32.4)	25(67.6)	1.44	0.3-5.42	0.45
	No	4(25%)	12(75)			
9	**Lowest Hb%**					
	≤ 15 g	10(33.3)	20(66.7)	1.25	0.37-4.20	0.52
	> 15 g	6(28.6)	15(71.4)			
10	**CPAP duration**					
	≤ 10 days	4(15.4)	22(84.6)	0.21	0.05-0.79	0.17
	> 10 days	12(46.2)	14(53.8)			
11	**Weaning to head box oxygen**					
	≤ 3 days	10(26.3)	28(73.7)	0.53	0.15-1.88	0.48
	> 3 days	6(40)	9(60)			
12	**Sepsis**					
	Yes	6(27.3)	16(22.7)	0.78	0.23-2.62	0.46
	No	10(32.3)	21(66.7)			
13	**Hospital stay**					
	≤ 21 days	3(9.1)	30(90.9)	0.54	0.12-0.24	0.00
	> 21 days	13(65)	7(35)			
14	**Outcome**					
	Death	1(100)	0	3.46	2.26-5.31	0.31
	Discharge	15(28.8)	37(71.2)			

*ROP= Retinopathy of Prematurity

Discussion

BW 1500 g or less and/ or GA less than 34 weeks, appear to be appropriate ROP screening criteria at our centre based on local evidence. This will ensure that no case of severe ROP is missed and importantly, the screening of non- ROP babies is minimised. Usually ROP screening protocols are based on post-conception age (PCA), since ROP onset and progression are mainly determined by it. However, in India, accurate GA and hence PCA, GA+ Chronological age estimation is not possible many a time. This results in babies with intrauterine growth retardation (IUGR) cluttering up the screening program, leading to a lot of unnecessary screenings.[9] BW criterion is preferable at our centre since, it is not uncommon for a mother to not know her dates correctly nor have ultrasound study during pregnancy.

Narrowing of NNF criteria is thus possible. This finding is particularly important since accessing these specialized services is not easy from our centre, located 45 km from the regional eye centre. There are difficulties in arranging transportation, both the availability and the affordability especially because the screening process is time-bound and the window period for action is small. Secondly, transportation is not without risks of hypothermia, hypoglycaemia and hypoxemia during transportation and hospital procedures, for a baby born say with a BW 1200 g during the first 2-3 weeks of age. The transportation and hospital procedures often take 4-5 hours. Managing any set back, should it set in during transportation or at the eye centre, which has no neonatal/paediatric wing, may be challenging for the accompanying junior resident. Some patients may have to make two or even three such visits. The referral services are extended at a subsidized cost. Yet, some patients cannot afford it. Among the patients coming to our hospital, virtually no one has a medical insurance.

Use of survival rates as a proxy to decide screening criteria is advocated.[9] It is suggested that screening criteria for a NICU with high survival rate i.e., more than 80% among babies weighing less than 1500 g , would be 1500 g or less or GA less than 32 weeks. For NICU with lower survival rate, the criteria would be BW less than 1500 g or less or GA 35 weeks or less.[10] During the present study period, the survival rate for 1000-1500 g weight category has been 75.5% (34 out of 45) and no baby weighing more than 1500 g required laser therapy. Hence, we tend to agree with suggestion of linking survival rates in babies weighing less than 1500 g and ROP screening criteria. In absence of surfactant therapy and mechanical ventilation facility, few babies with BW less than 1000 g, especially those with respiratory distress, stand a chance of survival at our centre.

It has been well- recognized that sight-threatening ROP can affect more mature infants in some settings. This is reflected in variation in the criteria for ROP screening in various studies. The birth weight range reported in various studies is as follows: Vinekar:[11] 1251-2750 g, Jalali:[12] 710-2000g, Shah:[13] 850-2290 g. It is also suggested that the unstable clinical course of the infant is also an important determinant for the development of ROP.[14, 15] Difference in the survival of unstable babies may explain the difference in occurrence of ROP. Thus, it is important that screening criteria are developed locally and revised following survival audit. A study from Iran recommended locally developed criteria when it found that 8.4% of cases of ROP requiring treatment would have been missed by the application of American Academy of Paediatrics guidelines.[16]

Low GA, low BW, and factors related to general illness such as length of hospital stay, duration of artificial ventilation, and the administration of supplemental oxygen are established risk factors.[17]Predictably, our study too found a higher risk with low BW, low GA and length of hospital stay, and need for laser therapy (Table). In absence of surfactant therapy or mechanical ventilation NICU stay may be getting prolonged.

In summary, the development of screening criteria for ROP, based on local evidence, should be encouraged. These criteria will need revision from time to time with changes in the neonatal care. One size does not fit all.[18] The existing NNF criteria may not be a reflection of the situation in entirety of a vast and diverse country such as India where accessing the specialized care and transportation involved are variable. There is an urgent need for telemedicine for ROP screening.[19] In the meanwhile, for a remotely located neonatal centre like ours, it is not only important that we do not miss a case of ROP; it is equally important that we reduce the burden of screening of non-ROP cases by using appropriate criteria developed on the basis of a local evidence.

What is known?

National Neonatology Forum of India recommends ROP screening for neonates who are born < 34 weeks gestation and/or < 1750 g birth weight.

What we add?

BW 1500 g or less and/ or GA less than 34 weeks, appear to be the appropriate ROP screening criteria at our centre.

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