Surfactant era and obstetric decision making

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Abstract

Introduction: The management of women with pregnancy complications at the peri-viability period involves a complex set of medical, ethical, emotional, and social challenges for the obstetrician. The survival rate of preterm babies has been improving along with advancement in neonatal intensive care unit (NICU) technology. Our recent experience has shown survival of even very preterm infants with the use of surfactant therapy.

Objective: This observational study was conducted in order to evaluate the survival benefit of surfactant therapy on preterm neonates, to enable straight forward decisions to be taken by the obstetricians regarding antenatal steroid prophylaxis, in-utero transfer and mode of delivery in case of inevitable preterm births.

Material and Methods: This study was conducted in the NICU of a tertiary hospital over a period of 3 years (2009-2011). We recruited only those preterm neonates who received surfactant therapy and the records were obtained and analyzed. Survival benefits of surfactant therapy, role of antenatal steroids, in utero transfer and mode of delivery were studied.

Results: Almost all (98.6%) neonates who did not receive antenatal steroids at all, landed up in respiratory distress syndrome (RDS) requiring surfactant therapy. Among the outborns 59.2% had an extended NICU stay as compared to 49.4% in the inborn group. The overall incidence of RDS was found to be more in caesarean delivery group (96.3%). However if the period of gestation at the time of delivery was less than 28 weeks, caesarean delivery had lesser incidence (12.5%) of RDS compared to vaginal delivery (27.1%). Similar finding was noted when comparing mortality. In less than 28 weeks gestation, when caesarean was done 2.5% newborn babies died, whereas in the vaginal delivery group 12.5% babies succumbed to death.

Conclusion: 1) Even in centers with facilities of surfactant therapy, steroids prophylaxis should be considered before delivery 2) Obstetricians should practice in utero transfer, to centers with NICU, having availability and technical expertise of surfactant prophylaxis 3) With the availability and wide spread usage of surfactant for premature neonates caesarean delivery should not be deferred for fetal benefit.

Key words: preterm, surfactant, neonatal intensive care unit (NICU), respiratory distress syndrome (RDS), period of gestation (POG)

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Introduction

Management of women with pregnancy complications at gestations near the "border of viability" (peri-viability period) involves a complex set of medical, ethical, emotional, and social challenges for the obstetricians.

In second trimester with pregnancy complications, when expeditious delivery becomes mandatory, after weighing the risks and benefits, decision of terminating pregnancy, depends on the period of gestation (POG). After the age of viability and before 34 completed weeks, it is prudent to wait if possible up-to 24 hours after the second dose of antenatal steroids is administered and caesarean is the preferred mode of delivery, if cervix is not favorable. Prior to the age of viability, if need of pregnancy termination arises the decision is directed more towards maternal well being. Induction of labor (if not contraindicated) is the preferred modality of management. This kind of decision owes to the fact that the rates of death and various morbidities including respiratory distress syndrome (RDS) are distressingly high in this group of neonates.

Is the scenario changing?

The survival rate of preterm babies has been improving along with advancements in development of newer generation mechanical ventilators, use of non-invasive ventilation and the wide spread use of surfactant[1,2,3].

With all this in mind the peri-viability period, becomes a perplexing area for the obstetrician to take a clinically and ethically sound decision. There is no systematic documentation on the period of viability in India. Ten years ago in the developed countries, the minimum gestational age of viability was 28 weeks and on an average we are still following the same guideline.

Surfactant usage by the neonatologists in a standard neonatal intensive care unit (NICU) has expanded the grey area for the obstetricians. Our recent experience has shown survival of even very preterm infants with the use of surfactant therapy.

We hypothesize that there is a need to rethink while taking a decision regarding the pregnancy management in a very preterm pregnancy in terms of buying time for steroid prophylaxis, mode of delivery, in utero transfer to a centre having good NICU with availability and expertise of surfactant administration.

Objective

In a tertiary care center we conducted this observational study in order to evaluate the survival benefit of surfactant therapy on very preterm neonates, in order to help the obstetricians to take the following decisions:

1) Decision to terminate a very preterm pregnancy has been taken, is there a need of in-utero transfer to a centre having good NICU with facilities and expertise for surfactant administration?

2) Is there a role of buying time for steroid prophylaxis, in presence of facilities to provide surfactant therapy after birth?

3) With the availability of surfactant therapy is there a need to give a second thought to the mode of delivery (vaginal versus caesarean delivery) for the benefit of the fetus, in cases of very preterm pregnancies?

Material and methods

We analyzed the data of preterm infants admitted in the NICU of a tertiary hospital, over a period of 3 years (2009-2011). All neonates included in the study were below 34 weeks period of gestation and received surfactant therapy either as prophylaxis and/or rescue therapy. We included all these 128 neonates in our study. Surfactant therapy was administered either as prophylaxis or rescue. Prophylactic surfactant was given to those newborns who were either less than 28 weeks period of gestation or had birth weight of less than 1000 gm. It was given to those preterm neonates also who had respiratory distress and required ventilation at birth. Rescue surfactant therapy was administered for those neonates who required FiO2 of more than 40% on non-invasive ventilation (CPAP – continuous positive airway pressure) with respiratory distress score of 5 or more. Survival benefits of surfactant therapy, role of additional antenatal steroids, and adverse effects were studied.

Results

In last three years, we had 340 preterm neonates admitted in our NICU, out of which 128 had received surfactant therapy. Mean age of mothers of these neonates was 26.5 years (95% confidence interval: 25.8-27.2), with 47.6% of mothers being in the age group of 25-30 years. For more than half (54.7%) of these mothers this was their first pregnancy. Around a third of these (31.3%) neonates were delivered at 30 to 32 weeks POG. This was followed by neonates delivered at 28 to 30 weeks and 32 to 34 weeks (24.2% and 21.1% respectively). Notably all these babies were the result of singleton pregnancy. Most common antenatal complication found in our study was pre eclampsia (defined as blood pressure of 140/90 mmHg or more with proteinuria after 20th week of period of gestation in a previously normotensive and non proteinuric woman- 35.2%), followed by preterm pre-labor rupture of membranes (PPROM: spontaneous rupture of membranes, anytime beyond 28th week but before 37th completed weeks of pregnancy and before the onset of labor- 21.1%), intrauterine growth restriction (IUGR- taken as estimated fetal weight below 10th percentile of the average for the gestational age) and antepartum hemorrhage (APH- bleeding from or into the genital tract after the 28th week of pregnancy either due to placenta previa or abruption), gestational diabetes mellitus (GDM- glucose intolerance of variable severity with onset or first identified during the present pregnancy-9.4%) and polyhydramnios (amniotic fluid index (AFI) 25 cm or more 3.1%) (Table 1).

In the study group as a whole we met with a total mortality of 21 neonates (16.4%). RDS occurred in 93.8% of neonates. Other morbidities were due to intraventricular hemorrhage (IVH-defined as is bleeding inside or around the ventricles, the spaces in the brain containing the cerebral spinal fluid) 11 (8.6%), necrotizing enterocolitis (NEC- is a medical condition where portions of the bowel undergo necrosis (tissue death) 3 (2.3%) and retinopathy of prematurity (ROP- is a disease that affects immature vasculature in the eyes of premature babies) 21 (16.4%).

A quarter of pregnant women (26.6%) had received full dose of antenatal steroid prophylaxis (either betamethasone or dexamethasone), while 18.8% could receive incomplete dose (single injection) of prophylactic steroids before they delivered. More than half (54.7%) women had not received even a single steroid injection before delivery (no steroid prophylaxis group) (Table 2). Almost all (98.6%) neonates who did not receive antenatal steroids at all landed up with RDS requiring surfactant therapy. Even with incomplete dose of antenatal steroids 87.5% of babies developed RDS as compared to 82.4% who had received the complete dose. Interesting fact to be noted is 6 of those babies who delivered after 34 weeks developed RDS. All of these belonged to the group where antenatal steroid prophylaxis was not administered. It is evident in Table 2 that giving incomplete course of antenatal steroids was as good as giving no steroids, in term of mortality, major morbidities and extended NICU stay.

In order to evaluate the role of in utero transfer of preterm babies to a center with facilities of NICU care, we analyzed the outcome of babies who delivered with us compared to those who were delivered outside and brought directly to NICU (Table 3). We found that 49 (38.3%) neonates were born outside and then brought to our Institution for NICU care. Incidence of RDS was found to be higher in babies who were outborn (97.9% versus 91.9%). Among the outborns 59.2% had an extended NICU stay as compared to 49.4% in the inborn group. Major morbidities like IVH, NEC and ROP was comparable between the two groups. The point to be appreciated is that mortality though seems to be higher in babies who were either booked with us or were transferred in utero, had an overall survival advantage of higher POG and birth weight. The mean POG of the outborn babies as well as the birth weight (mean POG 31.5 ± 2.4 weeks; mean birth weight 1567.4 ± 518.6 gms) was better as compared to that of inborn babies (mean POG 30.3 ± 2.6weeks; mean birth weight 1361.8 ± 535.2 gms).

Table 1. Demographic characteristics of the studied population (n=128)

Variables	Absolute numbers (n)	Percentage
Maternal demographic data		
Mean Age (95% CI) 26.5 (25.8 to 27.2)		
<20 years	04	03.1%
20 - 24 years	36	28.1%
25 - 29 years	60	46.9%
30 - 34 years	24	18.8%
35 years and above	04	03.1%
Parity		
Primiparous	70	54.7%
Period of gestation (POG) at delivery (in weeks)		
Less than 28	23	18.0%
28+1 to 30	31	24.2%
30+1 to 32	40	31.3%
32+1 to 34	27	21.1%
34+1 and more	07	05.5%
Pregnancy complications		
PPROM	27	21.1%
GDM	12	09.4%
Pre eclampsia	45	35.2%
IUGR	17	13.3%
Polyhydramnios	04	03.1%
APH	14	10.9%

PPROM – Prelabor preterm rupture of membranes, GDM – gestational diabetes mellitus, IUGR - intra uterine growth restriction, APH – antepartum hemorrhage.

Table 2. Effect of antenatal corticosteroids on neonatal outcome

Neonatal outcome	No steroid prophylaxis (n=70)	Incomplete dose (n=24)	Complete dose (n=34)
Respiratory distress Syndrome (RDS)	69 (98.6%)	21 (87.5%)	28 (82.4%)
Less than 28 (n=23)	11	05	07
28+1 to 30 (n=31)	08	10	12
30+1 to 32 (n=40)	26	03	08
32+1 to 34 (n=27)	18	03	02
More than 34 (n=07)	06	00	01
Morbidity (NEC + IVH+ROP)	15 (21.4%)	7 (29.2 %)	8 (23.5%)
Less than 28 (n=23)	03	03	03
28+1 to 30 (n=31)	03	02	02
30+1 to 32 (n=40)	05	02	03
32+1 to 34 (n=27)	04	00	00
Extended NICU stay (>15 days)	42 (60%)	09 (37.5%)	17 (50%)
Less than 28	07	02	04
28+1 to 30	06	03	08
30+1 to 32	16	03	04
32+1 to 34	11	01	01
More than 34	02	00	00
Mortality	11 (15.7%)	05 (20.8%)	05 (14.7%)
Less than 28	06	01	01
28+1 to 30	01	04	04
30+1 to 32	03	00	00
32+1 to 34	00	00	00
More than 34	01	00	00

RDS - Respiratory distress syndrome, NICU - neonatal intensive care unit, NEC - necrotizing enterocolitis, IVH - intra-ventricular hemorrhage, ROP - retinopathy of prematurity.

Table 3. Role of inutero transfer in preventing complications/ improving outcome

Neonatal outcome Mean POG in wks (95% CI) Mean Birth weight in gms (95% CI)	Inborn (n=79) 30.3 (29.8 to 30.9) 1361.8 (1241.9 to 1481.7)	Outborn (n= 49) 31.5 (30.8 to 32.2) 1567.4 (1418.4 to 1716.3)
Respiratory distress syndrome (RDS)	72 (91.1%)	48 (97.9%)
Less than 28 (n=23)	17	06
28+1 to 30 (n=31)	24	06
30+1 to 32 (n=40)	17	20
32+1 to 34 (n=27)	11	12
More than 34 (n=07)	03	04
Morbidity (NEC + IVH+ROP)	18 (22.8%)	11 (22.4%)
Less than 28 (n=23)	6	3
28+1 to 30 (n=31)	5	2
30+1 to 32 (n=40)	4	6
32+1 to 34 (n=27)	3	0

(Continued)

Neonatal outcome	Inborn (n=79)	Outborn (n= 49)
Mean POG in wks (95% CI)	30.3 (29.8 to 30.9)	31.5 (30.8 to 32.2)
Mean Birth weightin gms(95% CI)	1361.8 (1241.9 to 1481.7)	1567.4 (1418.4 to 1716.3)
Extended NICU stay (>15 days)	39 (49.4%)	29 (59.2%)
Less than 28	09	04
28+1 to 30	13	04
30+1 to 32	10	13
32+1 to 34	06	07
More than 34 (n=07)	1	1
Mortality	14 (17.7%)	07 (14.3%)
Less than 28	6	2
28+1 to 30	8	1
30+1 to 32	0	3
32+1 to 34	0	0
More than 34 (n=07)	0	1

RDS - respiratory distress syndrome, NICU - neonatal intensive care unit, NEC - necrotizing enterocolitis, IVH - intra-ventricular hemorrhage, ROP - retinopathy of prematurity.

Table 4. Role of mode of delivery in preventing complications/ improving outcome

Neonatal outcome	Vaginal delivery (n=48)	Cesarean delivery (n= 80)
Mean POG (95% CI)	30.0 (29.2 to 30.9)	31.3 (30.7 to 31.8)
Mean birth weight (95% CI)	1434.7 (1263.8 to 1605.7)	1444.0 (1331.3 to 1556.6)
Respiratory distress syndrome (RDS)	43 (89.6%)	77 (96.3%)
Less than 28 (n=23)	13	10
28+1 to 30 (n=31)	12	18
30+1 to 32 (n=40)	12	27
32+1 to 34 (n=27)	03	20
More than 34 (n=07)	03	04
Morbidity (NEC+IVH+ROP)	12 (25%)	18 (22.5%)
Less than 28	03	06
28+1 to 30	02	05
30+1 to 32	07	03
32+1 to 34	00	04
Extended NICU stay (>15 days)	22 (45.8%)	46 (57.5%)
Less than 28	06	07
28+1 to 30	05	12
30+1 to 32	09	14
32+1 to 34	01	12
More than 34	01	0
Mortality	8 (16.7%)	13 (16.3%)
Less than 28	06	02
28+1 to 30	02	07
30+1 to 32	00	03
32+1 to 34	00	00
More than 34	00	01

RDS - respiratory distress syndrome, NICU - neonatal intensive care unit, NEC - necrotizing enterocolitis, IVH - intra-ventricular hemorrhage, ROP - retinopathy of prematurity.

Next we tried to compare the outcome of different modes of delivery (i.e., vaginal delivery versus caesarean delivery). The overall incidence of RDS was found to be more in caesarean delivery group (96.3%) as compared to vaginal delivery group (89.6%). However if the period of gestation at the time of delivery was less than 28 weeks, caesarean delivery had 12.5% incidence of RDS compared to vaginal delivery which was more than double of this (27.1%). Similar finding was noted when comparing mortality. In less than 28 weeks gestation, when caesarean was done 2 out of 80 (2.5%) newborn babies died, whereas in the vaginal delivery group 6 out of 48 (12.5%) babies succumbed to death. The reason for a poor outcome in the caesarean group can be because of the fact that most of the caesareans in preterm are emergency caesareans and so already many of the babies in this group were compromised. However comparing neonatal outcome based on the indication of caesarean was out of the scope of present study.

Discussion

Use of surfactant has definitely revolutionized the prognosis of even very preterm babies. Our study shows that still obstetrician has a great role in improving survival and decreasing morbidity of these neonates. We emphasize here the role of antenatal steroids (full dose even after 34 weeks of gestation), in utero transfer and caesarean delivery for babies less than 28 weeks, to optimize the outcome where preterm delivery is imminent.

In 1959, for the first time, Avery and Mead[4] reported that the deficiency of surface-active material in the lungs of preterm babies is the cause of RDS. This led to a chain reaction of clinical trials on artificial surface-active materials in neonates with RDS[5,6].

According to Society of Obstetricians and Gynaecologists of Canada (SOGC) guidelines, expectant mothers with threatened preterm labor should be given a course of steroid prophylaxis even with the availability of surfactant therapy[7]. Large cohort studies indicate that the combination of surfactant and steroids is more effective than exogenous surfactant alone[8]. Two independent randomized controlled trials[9,10] have confirmed that antenatal steroids continue to reduce the risk of poor outcome, even in centers where surfactant is available. Notably in our study group 6 babies who delivered after 34 weeks and were not given steroid prophylaxis developed RDS. This observation makes us rethink about the usual policy to administer steroids upto 34 weeks period of gestation only. Similar concept has also been advocated that antenatal steroid administration might be beneficial even after 34 weeks, in selected cases [11,12,13].

When the question of prophylactic versus rescue surfactant therapy arises the recommendation is for infants at significant risk of RDS should receive prophylactic surfactant as soon as they are stable within a few minutes after intubation[14]. Surfactant replacement therapy should not be administered by anyone, anywhere rather it should be directed by physicians qualified and trained in its use and administration[15]. Keeping these factors in mind the obstetricians should practice in utero transfer, to centers with NICU with availability and technical expertise of surfactant prophylaxis, when the need to deliver a very preterm fetus arises.

Short-term risks of surfactant replacement therapy have been reported including bradycardia and hypoxemia during instillation, as well as blockage of the endotracheal tube[16] and pulmonary hemorrhage following surfactant treatment; however, and overall mortality is definitely lower after surfactant therapy[17].

Conclusion

1) Even in centers with facilities of surfactant therapy, steroids prophylaxis should be considered before a preterm delivery. Administration of antenatal steroids beyond 34 weeks should be considered in selected cases.

2) Obstetricians should practice in utero transfer, to centers with NICU having availability and technical expertise of surfactant prophylaxis, when the need to deliver a very preterm fetus arises.

3) With the availability and wide spread usage of surfactant for premature neonates caesarean delivery should not be deferred for fetal benefit.

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