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Full Length Research Paper

Effect of timing of cord clamping on neonatal venous hematocrit and clinical outcome at term–hospital based randomized control trial

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Abstract

The study was conducted at the department of Obstetrics and Gynecology at Jawaharlal Nehru Medical College, Aligarh India from June 2008 to October 2010. 200 mothers were selected for the study and informed consent using a predesigned proforma. The subjects were divided into 4 groups of 50 each wherein the umbilical cord was clamped at 15 seconds, 30 seconds, 1 minute and 2 minutes respectively. The neonatal venous hematocrit and clinical outcome was assessed. The primary objective was to study the effect of timing of cord clamping on neonatal venous hematocrit at 6 and 24 hours of life. The other neonatal parameters assessed were blood glucose at 6 and 24 hours, serum calcium at 6 hours, serum total bilirubin at 24 hours, oxygen saturation, temperature and duration of NICU stay. The maternal parameters studied were pre and post delivery hemoglobin, pre and post delivery hematocrit and blood loss during delivery. Data was analyzed using statistical package for social service software – SPSS version 11.5. A p value of less than 0.05 was considered statistically significant. Our study showed a rising trend in neonatal hematocrit values with progressive delay in clamping of the umbilical cord. A high indience of anemia was seen among the newborns if the cord was clamped at 15 seconds. No infant was reported to have anemia if the cord was clamped at 2 minutes. Ony asymptomatic polycythemia was seen in this category. A beneficial effect of delayed cord clamping on neonatal hematocrit at both 1 and 2 minutes but it is significantly higher at 2 minute clamping group as compared to 1 minute clamping group.

Keywords: Anemia, Hematocrit, Term Baby, Clinical Outcome

INTRODUCTION

The timing of cord clamping and cutting is frequently regarded as one of the components of active management of the third stage of labour. However, there is no consensus on the precise meaning of the words "early", "late" or "delayed" cord clamping and cutting. Since there is evidence of potential benefits for the baby when cord clamping is delayed after birth it is important to ascertain the exact timing of cord clamping. A study undertaken by Van (Rheenen et al., 2006) showed an obvious benefit of late cord clamping in term infants as it resulted in an increase in the average hemoglobin concentration at 4 months of age thereby improving the anemic status of newborns.

The neonatal outcome of delayed cord clamping (3 to 5 minutes after birth) with serious consequences was observed in a study undertaken by (Yao et al., 1971) where 13 out of 33 infants suffered from respiratory distress owing to an over distended neonatal circulation. (Linderkamp et al., 1992) found that if the cord is clamped after it stops pulsating, the babies had blood volumes 32 % higher than those in which the cord was clamped immediately after birth. In a study undertaken by (Geethanath et al., 1997), it was observed that iron stores at 3 months were not influenced by the timing of cord clamping at birth. These studies point towards the fact that early cord clamping produces a physiologically

correct blood volume and prevents the likelihood of neonatal complications.

However delayed cord clamping was also shown to improve the hematologic status of infants at 2 months of age (Gradeja et al., 1997). Delayed cord clamping was also associated with fewer blood transfusions for neonatal anemia and less incidence of intraventricular hemorrhage (Heike, 1998).

There is now considerable evidence that early cord clamping does not benefit mothers or babies and may even be harmful. Both the World Health Organization (WHO) and the International Federation of Gynecology and Obstetrics (FIGO) have dropped the practice from their guidelines. In actual practice, the timing of ligation of the cord is a matter of great variation, and it has been a common opinion that there is no proof that the infant may be harmed by any procedures of clamping the cord. So the exact timing of umbilical cord clamping continues to be a matter of great debate amongst professionals across the globe and is indeed a raging topic of discussion in the modern era. The irony is that cord clamping per se is a simple intervention, however there is no agreement on the meaning of terms like “early clamping” and “late clamping” though these are used so liberally in day to day practice. It is therefore important to assess how the effect of timing of cord clamping can have a bearing on the neonatal hematocrit and other clinical outcomes.

Our study attempts to determine the optimal timing of cord clamping which can have a reasonably favorable neonatal and maternal outcome.

MATERIALS AND METHODS

The study was conducted at the department of Obstetrics and Gynecology at JNMC from June 2008 to October 2010.

Subjects with the following inclusion criteria were chosen for the study: 1). gestational age 37 to 41 weeks 2). Singleton pregnancy 3). Uneventful cephalic vaginal delivery. Mothers with evidence of clinical disease (diabetes, preeclampsia, hypertension) or any other complications, multiple pregnancy, babies with congenital malformations or intrauterine growth restriction and tight nuchal cord were excluded from the study. This study was approved by the Institutional Ethics Committee of Jawaharlal Nehru Medical College, Aligarh

200 mothers were selected for the study and informed consent using a predesigned proforma. The subjects were divided into 4 groups of 50 each wherein the umbilical cord was clamped at 15 seconds, 30 seconds, 1 minute and 2 minutes respectively. The neonatal venous hematocrit and clinical outcome was assessed.

The primary objective was to study the effect of timing of cord clamping on neonatal venous hematocrit at 6 and 24 hours of life. The other neonatal parameters assessed were blood glucose at 6 and 24 hours, serum calcium at 6 hours, serum total bilirubin at 24 hours, oxygen saturation, temperature and duration of NICU stay. The maternal parameters studied were pre and post delivery hemoglobin, pre and post delivery hematocrit and blood loss during delivery.

Data was analyzed using statistical package for social service software – SPSS version 11.5. A p value of less than 0.05 was considered statistically significant.

RESULTS

Baseline maternal characteristics

The maternal baseline characteristics have been tabulated in the table. The table shows that there were no significant differences in the baseline characteristics of the 4 groups studied.

Maternal age and parity were comparable in all the 4 groups.

A. Maternal outcome

- It was noted that average blood loss post delivery in each group was 243.5 ml. No mother was reported to suffer from postpartum hemorrhage.
- No significant difference was noted between the pre and post delivery hemoglobin and hematocrit values.

B. Neonatal outcome

Venous hematocrit at 6 hours

The mean neonatal venous hematocrit values were higher at 6 hours of life when cord was clamped late. In groups 1, 2, 3 and 4 it was found to be 52.34%, 52.28%, 57.26% and 59.26% respectively. Statistical difference was found between groups 1 and 3, 1 and 4 and 3 and 4. There was no difference in groups 1 and 2.

Venous hematocrit at 24 hours

The mean venous hematocrit values in each group at 24 hours of life were found to be 50.52, 52.44, 53.26 and 56.14 % respectively. Statistical difference was found between groups 1 and 3, 1 and 4 and 3 and 4.

Prevalence of anemia and polycythemia at 6 hours

Neonatal anemia was more when cord was clamped early. In group 1, 8% neonates were found to be anemic with no incidence of polycythemia. In group 2, the incidence of anemia was 6%. There was no incidence of polycythemia in this group also. Only 4 % of the neonates in group 3 were found to be anemic. Polycythemia

Table 1: Baseline maternal characteristics

Characteristics	Group 1	Group 2	Group 3	Group 4
Mean maternal age ± SD (yrs)	25.36±3.958	24.36±4.070	25.50±4.306	25.26±3.784
Pre delivery maternal Hb ±SD (g/dl)	9.670±0.911	9.590±0.8493	9.596±1.043	9.670±0.824
Pre delivery maternal HCT ±SD (%)	29.88±1.430	30.07±3.029	29.77±2.444	29.90±0.5878

Table 2: Venous hematocrit at 6 hours

GROUP	MEAN Hct (%)	SD	Max – Min (%)
1	52.34	3.778	57 - 41
2	52.28	4.204	68 - 40
3	57.26	4.571	69 - 42
4	59.26	4.222	70 - 47

Table 3: Venous hematocrit at 24 hours

GROUP	MEAN HCT (%)	SD	Min – max (%)
1	50.52	4.176	38 - 56
2	52.44	4.708	37 - 65
3	53.26	3.680	39 - 65
4	56.14	3.897	44 - 68

Table 4: Prevalence of anemia and polycythemia at 6 hours

CATEGORY	GROUP 1		GROUP 2		GROUP 3		GROUP 4	
	N	%	N	%	N	%	N	%
Anemia	4	8	3	6	2	4	0	0
Normal	46	92	47	94	45	90	46	92
Polycythemia	0	0	0	0	3	6	4	8
Total	50	100	50	100	50	100	50	100

Table 4: Prevalence of anemia and polycythemia at 24 hours

CATEGORY	GROUP 1		GROUP 2		GROUP 3		GROUP 4	
	N	%	N	%	N	%	N	%
Anemia	8	16	5	10	1	2	1	2
Normal	42	84	44	88	48	96	45	90
Polycythemia	0	0	1	2	1	2	4	8
Total	50	100	50	100	50	100	50	100

occurred in 6% of cases. In group 4, no newborn was found to be anemic whereas polycythemia occurred in 8 % of the newborns.

Prevalence of anemia and polycythemia at 24 hours

Anemia was more in the early group. At 24 hours of life, 16% of the neonates were anemic in group 1. There was no incidence of polycythemia. In group 2, 10% of neonates were anemic. One neonate developed polycythemia. In group 3, only 2 % of the neonates were anemic. One neonate developed polycythemia. In group 4, only 1 neonate was found to be anemic whereas 8% were polycythemic.

Other neonatal parameters

Significant difference was observed between groups 1 and 3 with respect to blood glucose levels at both 6 and

Table 5: Other relevant neonatal markers

Parameters studied	Group 1	Group 2	Group 3	Group 4
NEONATAL PARAMETERS (mean values)				
1. Blood glucose at 6 hrs (g/dl)	65.80	70.00	78.22	68.62
2. Blood glucose at 24 hrs (g/dl)	67.46	70.46	75.30	72.54
3. Calcium at 6 hrs (mg/dl)	8.57	8.36	8.36	8.67
4. Serum bilirubin at 24 hrs (mg/dl)	3.050	2.692	2.810	3.060
5. Temperature (°C)	36.838	37.006	37.006	36.744
6. Oxygen saturation (%)	98.02	98.02	98.02	96.80
NICU stay				
a). No. of admissions, n/N(%)	5/50 (10)	4/50 (8)	2/50 (4)	2/50 (4)
b). Mean duration(days)	4.8	6.5	4	3

24 hours of life. Significant differences were also observed between groups 3 and 4 at 6 hours of life. This is primarily attributed to stress responses in term neonates. Furthermore there is no definite correlation between the effect of timing of cord clamping and neonatal glycemic values observed in our study.

- No significant difference in the neonatal calcium levels among the groups. The finding of asymptomatic hypocalcemia correlates well with full term neonates included in our study.
- In our study, a total of 9 newborns developed hyperbilirubinemia requiring phototherapy. There was no statistical difference of the mean bilirubin levels between the groups. There is no definite evidence to suggest that the cases in our study which required phototherapy were due to the result of the interventions done in cord clamping. None of the babies registered bilirubin levels high enough to warrant exchange transfusion.
- None of the newborns were found to be hypothermic. Also there was no statistical difference between the groups with respect to newborn temperature on the first day of life.
- In all groups, the mean oxygen saturation falls in the normal range for a full term neonate. In other words, the newborns in each group were well oxygenated and oxygen saturation did not change with delay in the clamping of the cord.
- No significant differences were observed in the number of NICU admissions and the duration of stay in our study group.

DISCUSSION

As per the WHO guidelines on anemia published in 1998, the term pregnancy cut off is 11 g/dl**.** If we take this report into consideration, none of the pregnant women had normal hemoglobin levels prior to delivery. In terms of maternal hemoglobin status, our study can be compared to the Indian study undertaken by (Gupta and Ramji, 2002) wherein all the mothers recruited for the study had mean hemoglobin levels less than 10 g/dl. Since in both the studies, mean hemoglobin values were similar, we cannot consider maternal anemia to be a possible confounder in our final work up for results.

It needs to be pointed out that no study has been done in the past wherein both pre and post delivery maternal hematocrit values have been taken for each group and subsequently compared for any significant difference.

(Ceriani et al., 2006) studied only post delivery hematocrit values and assessed for any significant difference only among the groups. The maternal hematocrit 24 hours postpartum was 29.9% (SD: 3.5) in group 1, 30.9% (SD: 4.5) in group 2, and 30.6% (SD: 3.6) in group 3.No differences were observed among the groups with respect to post delivery hematocrit values at 24 hours.

The study by Ceriani also recorded cases which suffered from post partum hemorrhage. Postpartum hemorrhage (blood loss >500 ml) was 26.8% in the early-cord-clamping group, 22.2% in the 1-minute cord-clamping group, and 25.4% in the 3-minute cord-clamping group. Severe postpartum hemorrhage (blood loss >1000 ml) was 3.6%, 5.6%, and 3.2% in each group, respectively. In our study, however, no case was reported to have post partum hemorrhage (>500ml).

Our study results match with those of (Van Rheenen et al., 2007), wherein no significant difference was found between the early and late cord clamping groups with respect to maternal blood loss. However a limitation of this study was a small sample size, i.e. a total of only 91 cases were studied. Our study closely matches with the findings obtained by (Ceriani et al., 2006) in which mean neonatal hematocrit measured in blood samples from the newborns at 6 hours after birth was higher for those allocated to late cord clamping groups.

Our study recorded a fall in the neonatal hematocrit values at 24 hours of life when compared to 6 hours of life in groups 1, 3 and 4. However we did not observe a uniform pattern of decrease in neonatal hematocrit values as seen in the classic study on hematological parameters in full term neonates by Otwin Linderkamp (1992).

The latter study classified neonates into early (cord clamping within 10 seconds) and late cord clamping groups (cord clamping at 3 minutes). In the infants with early cord-clamping, the hematocrit decreased from 0.48±0.04 1/1 at birth to 0.43±0.61/1 after 24 h ($p< 0.05$). After late cord-clamping, the hematocrit dropped to 0.59±0.51/1 at 24 h ($p< 0.05$). This could be attributed to increased blood volume with age resulting in hemodilution and reduced erythropoietin response.

Our result closely matches with the study done by (Ceriani et al., 2006).The prevalence of newborn infants with anemia (hematocrit level of<45%) at 6 hours was significantly higher in the early-cord-clamping group (8.9%) versus groups with cord clamping at 1 or 3 minutes (1% and 0%, respectively).

Our study reported 8 anemic newborns in group 1(16%), 5 in group 2(10%), 1 in group 3 (2%) and 1 in group 4 (2%). One newborn each in groups 2 and 3 developed polycythemia. Group 4 documented 4 polycythemic neonates (8%).

In a similar study undertaken by (Nelle et al.,1993) on the effect of Leboyer delivery on hematologic parameters in term neonates, the hematocrit value rose from 48% ± 5% at birth to 56% ± 7% at 24 hours of life.

A study by (Amir et al., 2007) on preterm babies did not find any difference between the early (cord clamping at 10 seconds) and late (cord clamping at 1 minute after delivery) cord clamping groups with respect to neonatal blood glucose values.

Clinically significant hypocalcemia occurs in premature infants (Sang et al., 1973) asphyxiated newborns, and infants of diabetic mothers (Wandrup et al., 1988).

Our study involved only full term neonates hence the finding of asymptomatic hypocalcemia is in agreement to the studies done by the above authors.

The study by (Emhamed et al., 2004) found no significant difference was found between the delayed and immediate cord clamping groups in total serum bilirubin levels at 24 hours, the number of infants requiring phototherapy, or the prevalence of plethoric skin and polycythemia.

In our study, the mean temperature of the newborn was assessed in each group and was found to be statistically insignificant. No newborn was detected to have hypothermia (<36.5℃) or hyperthermia (>37.5℃). In a randomized control trial done by (Kinmond et al., 1993) on the effect of timing of cord clamping on preterm infants, no significant differences between the random (early cord clamping) and regulated (cord clamping at 30 seconds) with respect to newborn temperature on day 1 of life.

Our study found the oxygen saturation of newborns to be similar in all the groups with no statistical difference in the values in between the groups. In other words oxygen saturation did not change with delay in the clamping of cord. This result supports the finding obtained by (Patrizia Zaramella et al., 2007**)** who conducted a study on the effect of timing of cord clamping on peripheral blood flow and cardiac function in term infants. They discovered no changes in calf blood flow, oxygen delivery, oxygen consumption or fractional oxygen extraction calculated from the Near-infrared spectroscopy measurements, or in foot perfusion index.

No significant differences were found in the admission rate to the NICU or length of hospital stay in our study. This supports the findings obtained by (Ceriani et al., 2006)

CONCLUSION

Present study shows a rising trend in neonatal hematocrit values with progressive delay in clamping of the umbilical cord. It further reveals that if the cord is clamped too early, i.e. at 15 seconds, there is a high incidence of anemia among the newborns. On the other hand, if the cord is clamped late, i.e. at 2 minutes, no infant is reported to have anemia, only asymptomatic polycythemia is seen. It can be deduced from our study that the 30 second cord clamping group offers no added advantage over the 15 second cord clamping group in terms of an increment in neonatal venous hematocrit levels and decreasing the prevalence of neonatal anemia as no statistical difference was found between group 1 and group 2. Furthermore, there is beneficial effect of delayed cord clamping on neonatal hematocrit at both 1 and 2 minutes but it is significantly higher at 2 minute clamping group as compared to 1 minute clamping group.

Some studies have delayed the cord clamping up to 3 minutes and reported beneficial effect. Whether delay in the cord clamping to 3 minutes has any significant advantage over clamping at 2 minutes may be analysed.

Other secondary neonatal outcomes need to be highlighted. There was no correlation between timing of cord clamping, neonatal serum bilirubin, serum calcium and blood glucose levels. Newborn temperature and oxygen saturation were also not affected by timing of cord clamping. More detailed and large scale studies are needed to conclusively draw an inference.

As far as the maternal outcome of the study is concerned, we found no correlation between the effect of timing of clamping of umbilical cord and the amount of blood loss during delivery. There is no evidence to suggest that early cord clamping is associated with less maternal hemorrhage.

Hence, as this study supports, the clamping of the umbilical cord maybe delayed at least up to 2 minutes to get the optimal benefit.

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