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Investigating the Effect of Umbilical Cord Milking on Neonatal Outcomes among the Preterm Infants Born in Shariati Hospital of Bandar Abbas

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ABSTRACT

The annual rate of preterm birth on a global scale is 15 million which is ever-increasing. About a million of these infants die due to the outcomes of preterm birth among which anemia is on top of the list. Purpose of the study: The present research aimed to investigate the effect of delayed umbilical cord clamping and cord milking on neonatal outcomes among preterm infants. In the present interventional study (double-blinded), 80 pregnant women whose age of pregnancy ranged between 28 and 34 weeks and visited Shariati Woman's Hospital of Bandar Abbas for a vaginal or surgical labor participated. They were randomly divided into two groups. In the intervention group, an infant's umbilical cord was milked. In the control group, however, no extra action was taken. At the end, the collected data were statistically analyzed using T-test, Chi-squared test and Fisher's exact test. The two research groups shared similar demographic information. At the end of the study, such factors as birth hemoglobin and hematocrit levels, neonatal blood pressure and clinical symptoms including neonatal jaundice requiring a phototherapy and polycythemia 48 hours after the birth were higher in the intervention group than the control. On the other hand, the need for CPR and the volume of blood transfusion (in cc) and respiratory distress were higher in the control group than the intervention. Milking an delayed-clamping of the umbilical cord are effective in neonatal outcomes among preterm infants (28-34 weeks) and can be used as a well applicable method in hospitals to prevent he adverse effects of preterm birth.

Keywords: Umbilical Cord Milking, Neonatal Outcomes, Preterm Infant

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INTRODUCTION

About a tenth of all neonates are preterm. An annual rate of 15 million preterm neonates has been reported on a global scale, which is ever increasing. An annual rate of one million mortalities occurs among this population induced by the outcomes of preterm birth. A vast majority of the remainder get afflicted with a life-long disability such as in learning, vision or auditory ability [1].

About all countries with reliable data are faced with an increasing arte of preterm birth. Therefore, preterm birth is now a global issue [2].
A preterm infant is defined as one who is born in advance to the completion of 37 weeks (259 days) of pregnancy [3]. A preterm birth occurs for a variety of reasons including multiple pregnancies, genetic factors, infections, chronic diseases (e.g. diabetes, hypertension). However, in many cases the underlying cause is unknown [1]. Preterm infants are faced with the high risk of mortality induced by IVH, PVL and NEC. Delayed umbilical cord clamping is a procedure that helps to

increase fetal blood flow and prevent the side effects of preterm birth [4].

Among the adverse effects of preterm birth, anemia is a primary cause of neonatal mortality. This problem usually affects infants whose age of pregnancy is less than 33 weeks and often require a transfusion of red globules [1].

A key measure to cut down on such negative outcomes is an intervention to prevent lowered hemoglobin and hematocrit levels during and after the birth. The placenta is a source of fetal blood and can serve as useful as blood transfusion to the fetus [1]. Delayed umbilical cord clamping (DCC) during which the umbilical cord is clamped slightly after the labor as well as umbilical cord milking (UCM) during which the blood within the cord is directed and milked towards the infant are the two methods used to prevent neonatal anemia [2]. These methods restore more blood and consequently more hemoglobin to the infant and add to their iron storage [4, 5]. Delayed cord clamping can add to neonatal blood storage for 30%. It can increase the count and level of red globules for 60% which, in turn, provides enough blood to transmit oxygen to body organs and tissues. Lowered levels of blood and hemoglobin during infancy can have such outcomes as anemia, respiratory distress syndrome, cerebral palsy, mental handicap, behavioral disorders and learning disorders [3]. Despite the ever-growing scientific progress, still a tenth of infants born worldwide are preterm. An annual rate of 15 million preterm births has been reported on a global scale, which is ever increasing. About one million of these infants die annually due to the outcomes of preterm birth [6]. Therefore, the present researchers intended to investigate the effect of delayed umbilical cord clamping and milking on neonatal outcomes among preterm infants.

MATERIALS AND METHODS

To this aim a double-blinded clinical trial was designed with 80 patient participants who visited Shariati Hospital of Bandar Abbas (affiliated with Hormozgan University of medical sciences) from the beginning of 2014 to the end of the same year. All those meeting the inclusion criteria and who consented to take part entered the study and were randomly assigned to two groups. Each research group consisted of 40 subjects (N=40).

The inclusion criteria were women with 28 to 34 weeks of pregnancy (shown by ultrasound results at the first or third trimester of pregnancy). The exclusion criteria were: short umbilical cord (<25 cm), vigorous newborns, those born in meconium-stained amniotic fluid, primary congenital anomalies, umbilical cord prolapse, fetal hydrops, multiple pregnancies, a mother who is ABO or Rh-, a mother with a placenta Previa, placental expulsion, abnormal umbilical cord such as a true umbilical cord knot or a mother with background diseases such as diabetes, hypertension, residence out of the province or lack of follow-up. In the intervention group, immediately after birth, the infant born through vaginal delivery was kept at the surface of the uterine and one born through surgical labor was held beside the thigh and then the umbilical cord was cut at a distance of 25 cm. The infant was kept only then under a warmer; the cord was held up; it was milked three times at a pace of 10 cm/s towards the infant; finally it was cut at a distance of 2 cm from body and was clamped and cut. In the control group, immediately after birth, the infant born through vaginal delivery was kept at the surface of the uterine and one born through surgical labor was held beside the thigh and the umbilical cord was cut at a distance of 25 cm from body. Then the infant was held under a warmer and the umbilical cord was cut without milking at the distance of 2 cm from body and was clamped. The primary outcomes were the hemoglobin and hematocrit levels while the secondary outcomes were: 1) vital signs such as blood pressure 2) clinical parameters such as respiratory distress, jaundice requiring a phototherapy 3) blood parameters such as hemoglobin (Hb), hematocrit (HCT) and the need for phototherapy based on the level of bilirubin in the first 48 hours of birth. These data were collected and recorded. Besides, in the case of low Hb in infants, blood transfusion was done.

Once the data were collected they were analyzed statistically via SPSS. The statistical tests included the T-test, Chi-squared test and Fisher's exact test.

RESULTS

In the present research, 80 subjects whose age of pregnancy was 28-34 weeks were candidates for pregnancy termination. If they did not meet the exclusion criteria, they entered the study. For a double-blinded design, the umbilical cord of the first 40 visitors was first milked and then clamped

with a delay. That of the second 40 subjects were clamped without milking or any delay.

From among the 80 labors, 65 (80.2%) were vaginal (NVD) and 15 (18.5%) were surgical. The result was the birth of 42 (51.9%) male neonates and 38 (46.9%) female neonates.

According to the data presented in table 1, the two groups did not diverge significantly in terms of the birth weight, age of pregnancy, mother's parity.

Table 1: Comparison of the two research groups in terms of the birth weight, age of pregnancy and mother's parity

Variable	Group	Mean	Standard deviation	p-value
Birth weight	intervention	2089.50	259.81	.395
	control	2145.25	319.77	
Age of pregnancy	intervention	31.25	1.56	.795
	control	31.35	1.86	
Mother's parity	intervention	2.10	.95	.601
	control	2.22	1.16	

Data analysis revealed that in both the intervention (n=32, 80%) and the control groups (n=33, 82.5%), the highest frequency was that of vaginal childbirth. It is noteworthy that the frequency of birth in the former group was 8 (20%) and in the latter group it was 7 (17.5%). The difference between the two groups was not statistically significant in terms of the type of delivery (p=1).

Table 2: Comparison of the two research groups in terms of blood factors

Variable		Group	Mean	Standard Deviation	p-value
Serum level of potassium		Intervention	5.01	.153	.508
		control	4.96	.474	
Bilirubin	total	Intervention	3.63	.426	.000
		control	2.73	.589	
	direct	Intervention	.55	.88	.004
		control	.50	.08	
Hemoglobin		Intervention	17.09	.87	.000
		control	15.24	1.32	
hematocrit		Intervention	51.16	1.57	.000
		control	45.59	4.86	
Systolic blood pressure		Intervention	70.95	5.67	.000
		control	62.97	6.01	

According to the data presented in table 2, the mean serum level of potassium was 5.01 me/l and 4.96 me/l in the intervention group and control groups respectively. The two groups did not diverge significantly in terms of potassium level (p=.508).

The mean total scores of bilirubin for the intervention and control group were respectively 3.63 and 2.73 mg/dl. The mean scores of direct bilirubin for the two groups were .55 and .50, respectively. According to the numerical value of the standard deviation, this divergence is statistically significant. Moreover, the statistical test confirmed this significant difference (p<.05). The mean total scores of hemoglobin level for the intervention and control groups were respectively 17.09 and 15.24 which is evidently higher in the former group. In other words, the milking process led to an increased hemoglobin level (p=.000). The results revealed that the mean score of hematocrit was 51.16 in the intervention and 45.59 in the control group. Evidently, this level is higher in the intervention group. In fact, milking contributed to an increase in the hematocrit percentage (p=.000). According to the data within table 4.2, the mean score of systolic blood pressure was 70.95 in the intervention group and 62.97 in the control group which is higher in the former. It appears that the milking technique managed to increase systolic blood pressure significantly (p=.000).

According to the data presented in table 4.3, from among the total of 80 neonates born, upon birth, 34 cases (42%, 2 from the intervention and 32 from the control group) received blood while on the 28th day of birth, 26 cases (32.5%, 4 from the intervention and 32 from the control) received blood. In other words, 90% of the intervention group received no blood whereas only 45% of the control required no blood. Therefore, it was shown that the milking technique managed to reduce the need for blood transfusion.

Table 3: Comparison of the two research groups in terms of the need for certain measures

Variable		Group	Need for measure	f.	%	p-value
Need for blood	Upon birth	Intervention	Yes	2	5	.000
		control	No	38	95	
	In 28 days	Intervention	Yes	32	80	
		control	No	8	20	
Need for phototherapy		intervention	Yes	39	97.5	.000
			No	1	2.5	
		control	Yes	9	22.5	
			No	31	77.5	
Need for CPR		intervention	Yes	5	12.5	.755
			No	35	87.5	
		control	Yes	7	17.5	
			No	33	82.5	

According to the data summarized in table 3, from among the 80 neonate participants, 48 cases (59.3%) underwent a phototherapy, 39 of whom

belonged to the intervention and 9 of whom to the control groups. Moreover, from among the 32 neonates (39.5%) who did not undergo a phototherapy 31 belonged to the control group and only 1 belonged to the intervention. In other words, the milking procedure helped to increase the need for a phototherapy (p=.000). According to the data presented in the table, from among the overall 80 neonates, 12% (14.8%) had a CPR 5 of whom were in the intervention and 7 in the control groups. 68 cases (84%) required no CPR from whom 35 cases belonged to the intervention and 33 to the control groups. As the analysis showed, the milking technique had no effect on the need for CPR among the neonates (p=.755).

According to the information summarized in table 4, from among the 40 neonates of the intervention group, 10 (25%) and from among the 40 neonates in the control group, 15 (37.5%) were afflicted with respiratory distress syndrome. In other words, umbilical cord milking led to a decrease in the frequency of occurrence of RDS in neonates (p=.000).

Table 4: Comparison of the two research groups in terms of the frequency of RDS

Group	RDS	f.	%	p-value
Intervention	Yes	10	25	.000
	No	30	75	
Control	Yes	15	37.5	
	No	25	62.5	

Table 5: Comparison of the two research groups in terms of IVH

Age of pregnancy	f.		IVH		p-value
	Inter-vention	control	f.	%	
28-30 weeks	5	9	9	11.25	.000
30-32 weeks	15	9	0	0	
32-34 weeks	20	22	1	1.25	
Total	40	40	10	12.5	

According to the information presented in table 4.5, from among the 80 neonates participating in this research, 10 (12.5%) got afflicted with intraventricular hemorrhage (IVH) 9 of whom had an age of pregnancy of 18-30 weeks. Only 1 case had an age of pregnancy of 32-34 weeks. From this total number, 3 cases belonged to the intervention group while 7 others were in the control group. Therefore, the milking procedure seems to manage to reduce intraventricular hemorrhage (p=.000).

Concerning the data presented in table 6, the mean Apgar scores of the first minute were 6.42 and 5.15 in the intervention and control groups, respectively. The mean Apgar scores of the fifth minute were 7.42 and 6.15 for the two groups respectively. In other words, the mean Apgar scores of the first and fifth minutes were higher in the first group than the second. In fact, the milking technique showed to increase Apgar score (p=.000).

Table 6: Comparison of the two research groups in terms of Apgar score

Group	Apgar	mean	SD	p-value
Intervention	1st minute	6.42	1.08	.000
	5th minute	7.42	.90	
Control	1st minute	5.15	1	
	5th minute	6.15	.92	

Data analysis revealed that the mean PH scores were 7.05±.11 and 6.91 in the intervention and control groups respectively (SD=.11). In fact, the milking procedure did not only fail to reduce the PH and the acidity of the umbilical cord, but rather led to an increase in it (p=.000).

DISCUSSION

As the present findings showed, the two research groups diverged significantly from each other in terms of the need for blood transfusion, the 1st and 5th minute Apgar score, PH of the umbilical cord blood, systolic blood pressure, need for phototherapy, frequency of IVH, the initial level of hemoglobin, hematocrit, bilirubin (total and direct) and the frequency of RDS. However, the two groups did not differ significantly in terms of such factors as the age of pregnancy, birth weight, need for CPR and the level of potassium.

All the participants in this research were healthy pregnant women who had either a vaginal or surgical delivery. However, in Gupta's research [2], anemic mothers participated. Another investigation by Van Rheene [7] was set in a malaria-endemic region. The study conducted by Middleton [8] was only focused on vaginal deliveries.

In the present research, the umbilical cord was milked three times from the trimmed end towards the infant's body at a rate of 10 cm/s. Finally it was cut at a distance of 2 cm from the body. In the control group, no milking action was taken and

the cord was cut at the distance of 2 cm from the root with no delay. In Saigal's research [9], the delay time was 1 minute; in Chaparro's study [10], it was 2 minutes; in Cernadas's [11], Oxford Midwives' [12] and Spears' [13] it was 3 minutes. In their investigations, Emhamed [14], Van Rheenen [7] clamped the umbilical cord only when its pulse stopped. In another study, McDonald (8) clamped the umbilical cord five minutes later or when the pulse stopped.

There was a body of similar research that also reported a positive effect of milking on the reduced need for blood transfusion. These studies were conducted by Hulton [1], Gupta [2], Upadhyay [5], Kurdi [15], Hosono [4], Van Rheenen [7], Ruben [16] and Jahazi [17]. In some other research, Linderkamp [18] not only mentioned the umbilical cord clamping but also the infant's postpartum positioning as effective in its blood condition. In fact, a vast majority of research found delayed umbilical cord clamping effective in preventing the occurrence of anemia. With this concern, it should be reminded that preterm children are exposed to the risk of anemia. They do not enjoy sufficient iron as a term infant does. The importance of iron insufficiency lies not only in the fact that it leads to anemia, but also in its adverse effects on child behavior and cognition [2]. An infant population is among those more prevalently in need of blood products during hospital stay [1]. Blood transfusion to infants requires much more care than adults due to the blood volume inside their veins and the unique characteristics of their immune system as compared to adults [4]. Considering the various outcomes of blood transfusion and disruptions in neonatal immune system, the probability of occurrence of transfusion side effects showed to be positively correlated with the frequency of blood product transfusion. The side effects of blood transfusion to preterm infants include: transmission of CMV, hyperkalemia, GVH induced by blood transfusion, hemolytic reactions to blood transfusion, exposure to preservatives of blood products and other toxins, transmission of HIV, hepatitis B, C, etc. [5].

The mean hemoglobin level was 17.09 g/dl in the intervention group (milking+delayed clamping) whereas it was 15.24 in the control group (only clamping). In Rabe's [19] investigation, these values were respectively 17.5 and 17.3 g/l). This divergence was not statistically significant (p=.71). In Hosono' (4) study, this value was reported as 16.5 for the milking+delayed clamping group which was higher than the other group. This finding was also confirmed by Emhamed [14], Cernadas [11], Chaparro [10] and Saigal [9]. In some other research, Rabe [19], inferred that suggested that rather than a 30-second delay in clamping, the umbilical cord be milked four times. This researcher also suggested further investigation with a group in which the umbilical cord is immediately clamped after birth with no delay to find more precise results. However, this researcher reminded that umbilical cord clamping earlier than 30 seconds might be unethical.

In the present research, 20% of the deliveries in the group of delayed clamping plus milking. 17.5% belonged to the group with immediate clamping after a surgical delivery. These values were respectively reported in Rabe's research [19] as 78% and 58%. In some other research, Aladanady [20] reported a lower rate of red cells in the vaginal delivery group.

The mean Apgar's scores were reported as 6.42 and 5.15 in the intervention and control groups respectively. The mean Apgar's scores I the 5th minute was 7.42 in the intervention group and 6.15 in the control group. It was significantly higher in the delayed clamping plus milking group than the mere clamping group. Middleton [8] reported an Apgar's score lower than 7 in the first five minutes. This researcher reported no statistically significant difference between the two groups. The same finding was reported by Rabe [19] and Spears [13].

In the present study, umbilical cord milking managed to significantly reduce the frequency of RDS. In Middleton's study [8], the number of infants hospitalized in NICUdue to RDS was about the same in both groups (1-3 cases). In Spear's [13] investigation a similar number of neonates showed to have symptoms of RDS. Postpartum respiratory care is currently changing from intubation to Continuous Positive Airway Pressure ventilator (CPAP) or intubation and prescription of surfactant, immediate removal of the tube and CPAP [12].

In the present study, the milking procedure led to an increase in bilirubin level. However, no statistically significant difference was observed between the two groups in terms of clinical

jaundice by Cernads [11], Emhamed [14], McDonald [8] and Oxford Midwives [12].

In s body of research by Emhad [14], McDonald [8], Van Rheenen [7] and Rabe [19], the number of infants born in need of phototherapy was lower in the immediate clamping group than the delayed group. Middleton [8] reported the percentage of those in need of phototherapy 5% in the delayed clamping group and 3% in the other group. In the present research, the need for phototherapy was significantly higher in the delayed clamping and milking group than the immediate clamping group. This finding can be explained by the significant increase in the hemoglobin level of those whose umbilical cord was clamped with a delay. However, this effect does not remain longer than six months. Furthermore, the ferritin level turned out higher in delayed clamping group [5]. A ferritin level lower than 50 mg/l in neonates younger than 3 months expose them to iron deficiency [1]. It was shown in the present research that the milking procedure managed to reduce IVH in neonates. In a similar fashion, Mercr [21] and Emhamed [14] reported that delayed clamping was effective in reducing the frequency of occurrence of IVH. The advantages and disadvantages of umbilical cord clamping can be justified by an increase in the count of red cells. Besides the fact that the red cells in neonates can reinforce iron supply, they can improve metabolism, bilirubin level and eventually the cranicectrosis. Therefore, if an early treatment of mild to intense jaundice is not possible for an infant, or if the side effects of jaundice are not predictable, the delayed clamping should not be used. The World health Organization has recently suggested that the umbilical cord should not be clamped sooner than needed [8].

An increased concentration of hemoglobin and consequently higher blood volume raises the risk of hyperbilirubinemia and lengthened hospitalization for phototherapy. Moreover, delayed clamping might cease early and timely CPR. Overall, delayed umbilical cord clamping does not reduce the Apgar's score, PH of the cord blood and the RDS induced by polycythemia [7]. A cofactor of delayed clamping is polycythemia which is often unmarked [3]. In VLBW neonates (of very low birth weight), delayed umbilical cord clamping and holding the neonate lower than the placenta helps to transmit the placental blood to the neonate. It cuts down on the need for blood transfusion upon birth. This maneuver is not expected to delay the CPR [3].

Suggestions

Further research requires more strength and precision so as to be able to indicate the real advantages and disadvantages of delayed umbilical cord clamping. Moreover, further research needs to investigate and compare maternal outcomes such as PPH and long term postpartum effects on mother's iron supply, physical health and mental state. Furthermore, neonatal outcomes such as the neural development in long term follow-ups need to be considered.

Limitations

Among the main limitations of this study are the limited population size and the short time span included.

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