

**Efficacy of intraumbilical vein (IUV) injection of oxytocin in active management of the third stage of labor**Farideh Movahed<sup>1</sup>, Reyhaneh Ramazan Nejjhad<sup>1</sup>, Ezzatalsadat Haji Seid Javadi<sup>1</sup>, Amir Javadi<sup>2</sup>, Fatemeh Lalooha<sup>1</sup>, Sepehr Taghizadeh<sup>3</sup><sup>1</sup>. Assistan professor of Obstetrics and gynecology, Department of Obstetrics and gynecology, Faculty of Medicine, Qazvin University of Medical Sciences, Qazvin, Iran.<sup>2</sup>. Faculty of Medicine, Qazvin University of Medical Sciences, Qazvin, Iran.<sup>3</sup>. Infectious and Tropical disease research center, Infectious diseases department, Tabriz university of medical sciences, Tabriz, Iran.

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**Abstract:** Assessment of the efficacy of using intraumbilical vein (IUV) injection of Oxytocin in active management of the third stage of labor and reducing blood loss and length of the third stage. In a randomized double-blind clinical trial, 200 women undergoing vaginal delivery without any risk factor for postpartum hemorrhage recruited. 100 assigned to receive 10 international units (IU) oxytocin diluted in 9cc ringer by IUV injection and 10cc ringer by peripheral vein injection and 100 assigned to receive 10cc ringer by IUV injection and 10 international units (IU) oxytocin diluted in 9cc ringer by peripheral vein injection. Active management of labor (prophylactic injection of 20IU oxytocin after clamping of umbilical cord and controlled cord traction) was used in both groups. Pre delivery and post delivery hemoglobin level was assessed. The primary outcome was change in hemoglobin levels and duration of the third stage of labor. The third stage of labor was significantly shorter in IUV injection group ( $4.2 \pm 4.1$  minutes compared with  $5.5 \pm 4.5$  minutes, respectively;  $p=0.03$ ). An additional uterotonic agent in case group was needed less than the controlled group ( $P=0.03$ ). Mean drop in hemoglobin levels in intervention group was  $1.5 \pm 0.96$  (95% CI 1.16-1.53) and in control group was  $1.35 \pm 0.94$  (95% CI 1.3-1.7) and there was significantly difference in this respect in two groups ( $p$ -value = 0.228). IUV injection of Oxytocin with the active management of the third stage of labor significantly reduced the rate of additional uterotonic agents and duration of third stage of labor. The hemoglobin reduce in the intervention group was lower compared to the control group but this difference was not analytically meaningful. Need to manual removal of the placenta, Hb levels after 24 hours after delivery, and placenta emersion time more than 15 minutes was lower in the group receiving oxytocin but the difference was not significant.

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**Keywords:** Third Stage of Labor; Oxytocin; Intraumbilical Vein Injection

**1. Introduction**

Postpartum hemorrhage as a major cause of maternal death worldwide, and is the cause of approximately half of all maternal deaths in developing countries (Belghiti, 2011) and even in many developed countries, the postpartum hemorrhage is one of the major causes of admission of mothers to intensive care units (Mercier and Van de Velde, 2008). In countries with poor health services, the impact of bleeding in maternal mortality is also higher than this statistics.

The Delivery hemorrhage is the cause of 12% of all maternal mortalities (Rossi and Mullin, 2012) and occurs in its highest rate after delivery.

The common causes of postpartum hemorrhage, includes bleeding from the site of implantation of the placenta, genital and nearby organs trauma or both of them (Cunningham, 2010).

Hemostasis of Placental implantation site is first established with the contraction of myometrium and

thrombosis of the vessel lumens. As a result, parts attached to the placenta or large blood clots which impede efficient contracting of Myometrium, can disrupt hemostasis in the placental implantation site (Cunningham, 2010).

In the third stage of labor due to a partial and transient placental detachment, some degree of bleeding is unavoidable and sometimes the placenta can not be separated the uterus.

Prescribing oxytocin before the passing of placenta reduces the amount of bleeding (Cunningham, 2010). If there is a massive bleeding and placenta can not pass automatically, manually removing of the placenta should be carried out and stunning or anesthesia is required and aseptic surgical techniques must be used (Cunningham, 2010).

By Using of Oxytocin as injection into the umbilical vein, high concentrations of oxytocin reaches the placenta and causes the contraction of uterus, faster

separation of placenta and reducing the time of the third stage of the labor (Harara, 2011).

This method has been used in most studies in the case of residual placentas (Retained Placenta) which has also been beneficial. (Güngördük, 2010).

With regard to the high prevalence of the iron deficiency anemia in our country finding a way to reduce the postpartum bleeding is necessary in the past studies it has been proven that oxytocin injection to the umbilical vein reduces the labor bleeding and prevent the hemoglobin decrease after the delivery and the aim of this study is to evaluate the effect of the oxytocin injection to the umbilical vein in management of the 3<sup>rd</sup> stage of the delivery and reducing the blood loss during this stage of the delivery.

## 2. Material and Methods

In a double blind randomized clinical trial in Ghazvin Kowsar hospital of the Qazvin medical university in 2011 we studied the effect of the oxytocin injection to the umbilical vein in management of the 3<sup>rd</sup> stage of the delivery and reducing the blood loss during this stage of the delivery in the term pregnant women.

We selected 200 pregnant women randomly amongst pregnant women attending to the gynecology ward of Qazvin Kowsar hospital and enrolled them to the study, then we divided them randomly into two equal groups. The patients were blind to the drug which was used for them. Blood sample for checking the baseline hemoglobin was taken in the first stage.

After the second stage of the delivery we injected 20 units of oxytocin solution in 1 liter of Ringer's serum with rate of 10 cc per minute intravenously.

The intervention group received 10 IU oxytocin diluted in 10 ml Ringer's serum for 2 min in the umbilical vein proximal to the site of umbilical cord clamping and 10 cc of Ringer's serum as a placebo in a peripheral vein is injected from angiocath.

The control group received 10 units of oxytocin diluted in 10 ml Ringer's serum in a peripheral vein over 2 min and 10 ml of Ringer's serum as placebo in the umbilical vein proximal to the site of umbilical cord clamping.

If the placenta delivery takes more than 30 minutes or if there is severe bleeding the placenta was removed manually.

In addition, if a patient was suffering from uterine atony, the additional uterotonic drugs were used. These cases are recorded in our study.

If the patient's postpartum hemoglobin decline was sharper or had symptoms of acute anemia, transfusion was performed for the patient.

All patients were monitored for up to one hour after delivery and their vital signs were monitored every

15 minutes. Patients were examined for Oxytocin complications including hypotension and cardiac arrhythmia, bleeding and uterine atony.

**Inclusion Criteria:**

37 to 42 weeks gestational age, singleton pregnancy, alive fetus with cephalic presentation, 2500 to 4500 gr birth weight, parity 1 to 3, normal vaginal delivery.

**Exclusion criteria:**

Blood pressure equal to or greater than 140/90, placenta previa, placental abruption, a history of bleeding after delivery in previous pregnancies, history of curettage or cesarean delivery or uterine scar, polyhydramnios, known uterine anomalies, abnormal placental adhesion, coagulation disorders, forceps or vacuum delivery, extensive episiotomy or vaginal and cervical tears that require extensive repairs in the operating room.

We also compared the two groups for During the third stage of labor, percentage of residual placenta after 15 minutes, hemoglobin decrease 24 hours after delivery, the need to manual or instrumental removal of the placenta, the need for transfusion, medical complications and the need to obtain additional uterotonic drugs.

**Ethical considerations:**

A drug used in this study, oxytocin which is used in this study is routinely given to all patients after delivery and there are no complications recorded of its injection till now in the umbilical cord. All injections were through the primary angiocath site. At the beginning of study written consent is obtained from all patients who are enrolled into the study.

**Problems and limitations:**

The best time for hemoglobin check for patients is 48 to 72 hrs after the delivery and since we could not admit the patients for 2 or 3 days all hemoglobin checks were in 24 hrs after the delivery.

The obtained data was coded and then entered into a computer and statistically analyzed by SPSS software. T-Test and chi-square test were used for data analysis. Significance level for tests was determined as 95% ( $P < 0.05$ ).

## 3. Results

In this clinical trial, one patient in the third stage of labor in addition to 20 units of oxytocin injection of Ringer's serum, 10 units of oxytocin was injected into a peripheral vein and diluted to 100 patients and another 20 units of oxytocin in Ringer's injection of serum, 10 units of oxytocin diluted was injected into the cord.

We also compared the two groups for During the third stage of labor, percentage of residual placenta after 15 minutes, hemoglobin decrease 24 hours after delivery, the need to manual or instrumental removal

of the placenta, the need for transfusion, medical complications and the need to obtain additional uterotonic drugs.

Mean age, gestational age, parity, gravidity, first Hemoglobin, the frequency of induction and episiotomy and birth weight in the two groups are shown in Table 1.

Odds ratio of induction compared with control group (95% CI 0.4-1.45) was 1.3, which means the intervention group was under induction 1.3 times more than 1 control groups were equal (Table 1 and Figure 1).

Table 1. Evaluation of parameter between two groups

	Group		P
	Case	Control	
Age	25.28 ± 5.30	25.35 ± 5.57	0.890
Parity	0	40	0.632
	1	32	
	2	28	
Gravidity	1	41	0.732
	2	32	
	3	27	
Gestational age	39.1 ± 1.1	39 ± 1.1	0.455
Infant weight	3303.8 ± 366.3	3288 ± 435.7	0.782
Primary Mother Hb	12.8±0.98	12.6±1.17	0.269
Induction	23%	28%	0.517
Episiotomy	66%	58%	0.244

Table 2. Finding between two groups after intervention

	Group		P
	Case	Control	
Manual separation of the placenta	2(2%)	5(5%)	0.445
Need for transfusion	0	1(1%)	1
Need to additional uterotonic drugs	2(2%)	10(10%)	0.033
Third stage labor time	4.2±4.11	5.53±4.52	0.031
Hemoglobin drop	-1.35±0.94	-1.5±0.96	0.228
placenta emersion time more than 15 minutes	2(2%)	5(5%)	0.445
Drug complication	0	0	-
Hemoglobin 24 hour after labor	11.5±1.2	11.1±1.3	0.065

There were no statistically significant difference in the findings of the two study groups regarding gestational age, parity, gravidity, birth weight, induction and episiotomy rates found no statistically significant difference (p> 0.05) and both groups to review in the study were matched.

Mean delivery time in the control group 4.11 ± 4.2 min (95% CI 3.38-5.02) and 4.52 ± 5.53 minutes in the control group (95% CI 4.63-6.42) which was significantly lower in the intervention group (P=0.031)

In 2% of patients in the intervention group and 5% of control the placental emersion takes more than 15 minutes (p-value = 0.445) (Table 2).

The mean hemoglobin 24 hours after delivery in intervention group was 11.5 ± 1.2 (95% CI 11.2-

11.7) and in the control group was 11.17 ± 1.3 (95% CI 10.9-11.4) (p = 0.065) (Table 2 and Figure 2)

Mean drop in hemoglobin levels in intervention group was 1/5±0/96 (95% CI 1.16-1.53) and in control group was 1/35±0/94 (95% CI 1.3-1.7) and there was significantly difference in this respect in two groups (p-value = 0.228) (Table 2).

In 2% of control group and 10 % of intervention group there was a need for using the uterogenic agents that this number patient group was significantly lower in intervention group than control group(p = 0.033) (Table 2).

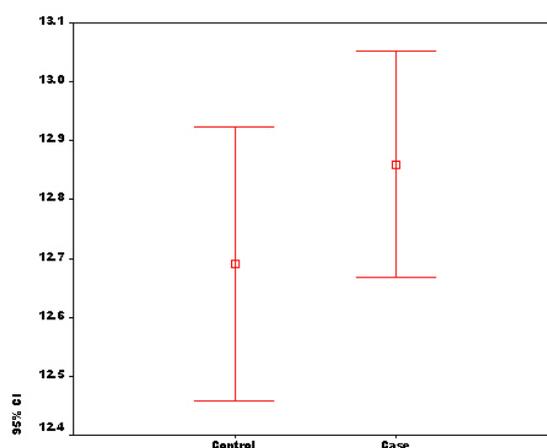


Figure 1. Distribution of patient's hemoglobin before labor

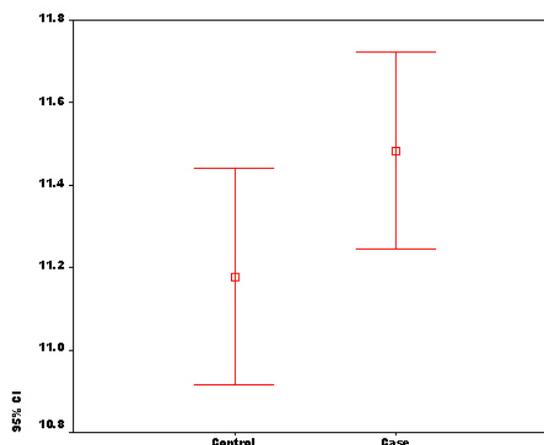


Figure 2. Distribution of patient's hemoglobin 24 hour after labor

#### 4. Discussion

Oxytocin's role in accelerating the third stage of labor and its effect on the placenta and reduce bleeding after delivery is clear. Intravenous and intramuscular use of Uterogenic agents and oxytocin is approved in references.

This study was based upon the hypothesis that injection of oxytocin in the umbilical cord vein can reduce the third stage of delivery and the amount of the bleeding after the delivery

From 1980s, few studies have been performed in this subject these studies have evaluated the uterotonic agents injection in the umbilical cord and they have concluded that "the drug can pass through the placenta and umbilical vein and reach uterine artery. Most of these studies have been cases where the placenta could not separate spontaneously and manual separation of the placenta was done (Belghiti, 2011).

In our study, injection of oxytocin into the umbilical vein compared with peripheral intravenous injection and its results in the third stage of labor. The aim of this study was to compare the drug injection to umbilical cord with its injection to umbilical vein.

In past studies, the drug is injected only in the cord and its effect was compared with placebo (Güngördük, 2010).

If we assume that even a small percentage of the drug can reach the placenta from the cord, in any case much more uterotonic drugs is received by the intervention group to improve the results.

Approximately all patients admitted for delivery has an intravenously open way to receive the drug, whether is it necessary to examine the effect of injection on the cord? In urgent situations where delivery is made and there is not an intravenous way to inject the drugs can we use umbilical cord vein as a way to access the placenta and injection of uterotonic agents to prevent uterine atony, bleeding and residual placenta.

In our study, there was no statistically significant difference between two groups regarding gestational age, number of pregnancies, number of previous birth weight infants, episiotomy performed and results were similar for both groups.

In our study and in the intervention group the time of the third stage of the delivery was  $4.2 \pm 4.11$  and in control group was  $5.53 \pm 4.52$  minutes which was meaningfully lower in intervention group, as a result the oxytocin injection to the umbilical cord can increase the speed of placental emersion This result probably reflects the higher speed access to the uterine oxytocin in the intervention group.

In a study by Reddy and et al study, the third stage time of the delivery was 4.1 minutes in the group with oxytocin injection to the umbilical vein and 9.4

minutes in the group with injection of normal saline in umbilical vein (Reddy and Carey, 1989).

Weeks and colleagues injected 50 units of oxytocin in the umbilical vein which this injection precipitate the placental separation (Weeks, 2010).

Gungorduk and et al. conducted a study in 2010 in Turkey, with the aim of evaluating effect of injecting the oxytocin in the umbilical cord and stated that the duration of stage 3 in the group receiving oxytocin into the umbilical vein was  $4.5 \pm 1.6$  minutes and in placebo group,  $9.7 \pm 4.3$  minutes which was significantly lower in the intervention group ( $P < 0.001$ ). (Güngördük, 2010)

In our study, approving the above results the third stage of labor in the intervention group was significantly lower than control indicating greater impact of umbilical vein injection of oxytocin in the third stage of labor is accelerating.

In our study the need to use additional uterotonic agents was 2% in intervention group 10% in control group which was significantly lower in in the intervention group as a result the injection of oxytocin in umbilical vein in the third stage of delivery reduces the uterine atony, need for using the additional uterotonic drugs to prevent the bleeding.

In the study of Gungorduk and colleagues the need for uterotonic agents in the oxytocin receiving group was 1 person(0/5%) and in the placebo group was 7 persons(3.4%) that was significantly lower in the oxytocin group ( $p=0.03$ ) (Güngördük, 2010).

Reddy and colleagues stated 373 cc blood loss in the intervention group 135 cc in control group (8).

In the study of Gungorduk and colleagues the amount of bleeding in the administration of oxytocin group was  $195.3 \pm 81$  cc and in placebo group,  $288.3 \pm 134$  cc, which was significantly lower in the group receiving oxytocin. ( $P < 0.001$ ) (Güngördük, 2010).

In the study conducted by Gungorduk and colleagues (Güngördük, 2010) the oxytocin injection to umbilical vein has been compared with the placebo injection to the umbilical cord but we compared oxytocin injection to umbilical cord with the injection of oxytocin to a peripheral vein to determine if reaching to the placenta in peripheral vein is faster or by the umbilical vein.

In our study the prescription of oxytocin was equal for both groups and the difference was only in the route of administration but the in the Gungorduk et al study (Güngördük, 2010), the intervention group received oxytocin while the control group did not receive oxytocin. We can conclude that in their study the intervention group receives more uterotonic agents than the control group and the uterine also receive more uterotonic agents and this improves the results in the point of bleeding and the hemoglobin loss.

We also should consider the laboratory faults in the measurement of the Hb and its better to use a method with the fewest faults after the delivery.

Our study reveals that oxytocin injection to umbilical cord has no advantages to its injection to the peripheral vein in reducing bleeding the third stage of the labor.

The need to manual removal of the placenta in our study and in the control group was in 5 patients (but there were not significant difference between the two groups ( $p=0.445$ )).

The rate of placenta remaining in the study by Gungorduk after 15 minutes and the need for curettage was 1 person in placebo group and there were not case like that in the oxytocin receiving group that the difference was not meaningful between the two groups ( $p=0.49$ ).

In our study there was only one case who needed the transfusion in the control group and there were not significantly difference between two groups ( $p=1$ ).

In the study by Gungorduk and colleagues there also was just 1 case of transfusion requirement in the placebo group and two groups was not different analytically ( $p=0.49$ ) (Güngördük, 2010).

### Conclusion

With regards to the findings of this study we can conclude that the oxytocin injection to the umbilical cord comparing with its injection to a peripheral vein has no advantages in reducing the postpartum hemorrhage whereas it can reduce the need for the use of other uterotonic agents and the time of the 3<sup>rd</sup> stage of delivery. The hemoglobin reduce in the intervention group was lower compared to the control group but this difference was not analytically meaningful.

Need to manual removal of the placenta, Hb levels after 24 hours after delivery, and placenta emersion time more than 15 minutes was lower in the group receiving oxytocin but the difference was not significant.

### Recommendations

With regards to the findings of this study we can conclude that the oxytocin injection to the umbilical cord comparing with its injection to a peripheral vein has no advantages in reducing the postpartum hemorrhage whereas it can reduce the need for the use of other uterotonic agents and the time of the 3<sup>rd</sup> stage of delivery and these findings shows the advantages of this methods. So performing other similar studies with the population more than this study to evaluate the volume of the hemorrhage in the oxytocin receiving group and in the control group to eliminate the Hb measurement faults is recommended.

In addition if the results of oxytocin injection to the umbilical cord can be comparable with its injection to a peripheral vein and in the cases which there is need for injecting the uterotonic agents and the peripheral vein is not available the umbilical cord can be used for injection and preventing the delivery hemorrhage and to facilitate the placental removal.

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