International Journal of Obstetrics and Gynaecology Research (IJOGR)
Vol. 6 (2020) No.6, pp. 839-851
ISSN:2709-1031
http://www.ijogr.com/

Randomized Management of the Third Stage of Labor by Various Protocols in Parturients at Low-Risk of Postpartum Hemorrhage

Afaf Aly Ismail, Doaa Mahmoud Effat, Hanaa AbdlelHamid Ebisy, Amira Mohamed Farahat

Department of Obstetrics and Gynaecology, Al Azhar University, Cairo, Egypt

Email: doaaeffat4560@yahoo.com

ARTICLE INFO

Article history
Received 27 August 2020
Revised 12 October 2020
Accepted 13 October 2020
Available online 15 October 2020

Keywords
Third stage of labor
Maternal mortality
Postpartum hemorrhage
Oxytocin
Misoprostol
Intraumbilical route

ABSTRACT

Introduction: *Prolonged third-stage of labor can be associated with a high risk of serious maternal complications. Nonetheless, active management of the prolonged third stage of labor can effectively reduce the risk of these complications.*

The objective of this study: *To evaluate the efficacy of the following three different protocols on shortening the duration of the third stage of labor and reduction of blood loss during the third and fourth stages of labor using umbilical vein oxytocin injection, umbilical vein misoprostol injection, and placental aspiration.*

Methods: *We recruited one hundred and twenty pregnant women with spontaneous onset of labor, including those who anticipated normal vaginal delivery from the maternity ward of Al- Zahraa University Hospital. Following spontaneous vaginal delivery of the baby, parturients were randomly assigned to one of the following three groups (each included 40 patients): group A that was subjected to intra-umbilical vein injection of 20 IU of oxytocin diluted in 30 ml normal saline; group B that underwent intra-umbilical vein injection of 800 µg of misoprostol diluted in 30 ml normal saline; and*

International Journal of Obstetrics and Gynaecology Research (IJOGR)
Vol. 6 (2020) No.6, pp. 839-851
ISSN:2709-1031
http://www.ijogr.com/

group C that was managed by syringe aspiration of blood from the umbilical vein. The duration of third-stage labor, amount of blood loss, need for manual placental separation, additional uterotonic drugs, blood transfusion, hemoglobin (HB), and hematocrit (HTC) deficits were evaluated. Also, drug-related side effects were monitored.

Result: *The mean duration of the third stage of labor was significantly shorter in the oxytocin group (2.78 min) compared to the misoprostol group (4.78 min) and placental aspiration group (5.19 min; p <0.001). The average blood loss in the third stage was 160.5±17.08ml, 203.5±16.4ml, and 210.50±81.27 ml in groups A, B, and C, respectively (p <0.001). The average blood loss one hour postpartum (fourth stage) was 29±2.88, 33.55±4.02, and 35.05±4.26 ml in groups A, B, and C, respectively, with significant difference (p <0.001). No case of manual separation of placenta or blood transfusion was recorded across the studied groups. The average HB deficit was 0.51±0.14, 0.99±0.29, and 0.99±0.55gm/dl in group A, B, and C, respectively (p<0.001). The average HCT% drop was 1.06±0.27, 1.76±0.36, and 1.39±0.59% in groups A, B, and C, respectively (p <0.001). The need for additional uterotonic drugs was 2.5% in group A, compared to 7.5% in group B and 12.5% in group C, which was statistically insignificant (p>0.05). Concerning the side effects, only two cases (5%) had shivering and pyrexia in group B, which was statistically insignificant (p>0.05).*

Conclusion: *Active management of the third stage of labor decreases postpartum hemorrhage risk and should be offered to all parturients. Intraumbilical oxytocin injection is the best method in the active management of labor. It effectively shortens the duration of the third stage of labor and reduces blood loss compared to the other two strategies. The need for additional uterotonic drugs is also minimal using intraumbilical oxytocin injection; however, we found it statistically insignificant. Intraumbilical injection of misoprostol (800 µg) may be used as an alternative intervention before attempting the manual removal of the placenta. Although placental blood aspiration was comparatively the least effective method in shortening the duration of placental delivery and reducing*

International Journal of Obstetrics and Gynaecology Research (IJOGR)
Vol. 6 (2020) No.6, pp. 839-851
ISSN:2709-1031
http://www.ijogr.com/

blood loss, it can be considered an effective, easy, safe, and cost-effective method with no side effects; particularly, in situations with restricted availability of uterotonic drugs.

Introduction

The third stage of labor begins with the fetus's complete delivery and ends with complete expulsion of the placenta and attached membranes, which generally lasts 5-15 min. The prolonged third-stage of labor is defined as a third-stage extends beyond 30 minutes from the delivery of the fetus.[1, 2] This period is deemed the riskiest labor stage, as a prolonged third stage of labor can lead to maternal complications, such as uterine atony, retained placenta, profuse hemorrhage, shock, and death. Postpartum hemorrhage (PPH) is defined by WHO as a blood loss over 500 ml after childbirth causing hemodynamic compromise. [3] The international federation of gynecology and obstetrics (FIGO) and international confederation of midwives (ICM) recommend using active management of the third stage of labor in all vaginal singleton births. [4] The standard technique of active management of the third stage of labor (AMTSL) involves prophylactic administration of uterotonic drugs immediately upon fetal delivery, controlled cord traction, and massage of the uterine fundus.[5]

Nonetheless**,** PPH is still the first direct leading cause of maternal mortality in developing countries. [6, 7] PPH accounts for about one-third of pregnancy-related mortality in Africa and Asia. In Egypt, it was estimated that PPH accounts for 140,000 deaths each year. [8] PPH's current burden can be attributed to the limited implementation of AMTSL, especially in low resources countries with insufficient training and limited access to uterotonic agents. [4] Although there is a universal agreement about using uterotonic drugs following childbirth to decrease PPH's risk, there is no global consensus about the method of administration of these drugs during the management of the third stage of labor. [4]

Recent reports demonstrated the effective role of umbilical vein oxytocin and misoprostol injections to reduce blood loss during the third stage of labor. [9] On the other hand, one study has suggested that the placental bed blood aspiration is considered an alternative to uterotonic drugs during the management of the third stage of labor, thus preventing PPH. [10]

AIM

This study was conducted to evaluate the efficacy of the following three different protocols on shortening the duration of the third stage of labor and reducing blood loss during the third and fourth stages of labor using: umbilical vein oxytocin injection, umbilical vein misoprostol injection, and placental aspiration.

International Journal of Obstetrics and Gynaecology Research (IJOGR)
Vol. 6 (2020) No.6, pp. 839-851
ISSN:2709-1031
http://www.ijogr.com/

Materials and Methods

This randomized controlled trial was conducted on 120 pregnant women, including women with an active labor phase, and women anticipating spontaneous vaginal delivery. Patients were recruited from Al-zahraa University hospital through the period from March 2018 to February 2019 and approved by the ethical committee of the Faculty of Medicine, Al-Azhar University for girls, Cairo, Egypt. This study's inclusion criteria included primigravida, aged 18-35 years, had average weight, with a singleton pregnancy, with vertex presentation, with the gestational Age 37-41 weeks. Women, who were at risk of PPH (such as an over distended uterus, antepartum hemorrhage, hypertension, bleeding disorders, history of previous PPH, prolonged labor, HB less than 10 gm%) and women who required Cesarean section (CS), were excluded.

Informed consent was taken from each patient before enrollment to this study. All participants underwent full detailed history taking, complete examination, and prepartum complete blood picture (CBC) investigation. Regular observation of labor events was recorded using a partogram starting from the active phase of the first stage of labor.

The second stage of labor was managed without instrumentation. Episiotomy was done if indicated, and the associated incision was compressed with a pack that was discarded to exclude blood loss from an episiotomy.

Vital signs were monitored continuously during delivery, and the duration of the first and second stages of labor was recorded. Once the women delivered vaginally, they were randomized into three groups. Randomization and allocation were performed by using a randomized number table designed by random allocation software. Group A included 40 parturients subjected to intraumbilical vein injection of 20IU of oxytocin diluted in 30 ml saline. Group B included 40 parturients who received intraumbilical injection of 800µg misoprostol dissolved in 30 ml saline. The solution was injected over 30 seconds immediately after cord clamping, and the syringe was removed. The puncture site was compressed between thumb and index fingers to prevent the backflow of injected drugs while the cord was milked with the other hand toward the placenta. Group C included 40 parturients managed by aspiration of blood from the umbilical vein (immediately after the cord was divided) using a 50 ml plastic syringe until the blood stopped drawing into the syringe. All women in each group underwent delayed cord clamping in which two clamps were applied on the umbilical cord; then, the cord was divided at the maternal stump. Subsequently, the studied protocols of management were applied per the allocation results. A basin was placed under the women after clamping of the cord. The collected blood was measured in a graduated cylinder to calculate blood loss.

Once the signs of placental separation were seen, the placentae were delivered by controlled cord traction technique. The duration of the third stage of labor was recorded. All parturients were

International Journal of Obstetrics and Gynaecology Research (IJOGR)
Vol. 6 (2020) No.6, pp. 839-851
ISSN:2709-1031
http://www.ijogr.com/

vitally monitored during the postpartum period (such as pulse, blood pressure, temperature, state of uterus, and blood loss).

The parturients were kept under close observation for the next hour (fourth stage of labor) to detect any complications. Pulse, blood pressure, and temperature were recorded. Blood loss in the first postpartum hour was measured by calculating the difference in pads' weight before and after use (the weight of one gram was taken as one ml blood). [11]

A complete blood picture (CBC) was repeated 24 hours post-partum. The difference between the prepartum and postpartum hemoglobin (HB) and hematocrit (HTC) values was recorded. The need for additional uterotonic drugs, manual removal of the placenta, blood transfusion, and side effects of drugs was recorded. If excessive bleeding occurred in any case due to uterine atony, intravenous drip infusion of 10IU of oxytocin in 500 ml of saline and intramuscular injection of 0.5mg methergine was given. If the uterus was still not sufficiently contracted, 1000µg (misoprostol) was provided by the sublingual route. If bleeding persisted, another active maneuver was performed and recorded. Blood replacement was considered while taking into account its indications.

Sample size calculation

MedCalc® version 12.3.0.0 program "Ostend, Belgium" was designed for the calculation of sample size. The statistical calculator was based on a 95% confidence interval, and the study's power 80% with α error 5%. The sample size calculation demonstrated that 114 cases were sufficient to be included; however, we decided to have 120 women to account for a drop-out rate of 5%.

RESULTS

One hundred and twenty women were recruited, randomized, and divided into three equal groups (n=40 per group). All studied groups were matched well regarding the patient's age, gestational age, BMI, prepartum pulse, blood pressure, temperature, HB, and HTC values (Table 1). The mean duration of the first and second labor stages was comparable among the three groups (p-value>0.05). However, the mean duration of the third stage of labor was significantly shorter in the oxytocin group (2.78 min), compared to misoprostol (4.78 min) and placental aspiration groups (5.19 min) (p <0.001), as shown in Table 2.

The average blood loss in the third stage of labor was 160.5±17.08ml, 203.5±16.4ml, and 210.50±81.27 ml in groups A, B, and C, respectively (p <0.001). The mean blood loss in the

International Journal of Obstetrics and Gynaecology Research (IJOGR)
Vol. 6 (2020) No.6, pp. 839-851
ISSN:2709-1031
http://www.ijogr.com/

fourth stage was 29 ±2.88 ml in group A, 33.55±4.02 ml in group B, and 35.05±4.26 ml in group C; the difference was statistically significant (p<0.001), as shown in Table 3.

Also, there were statistically significant differences in the mean postpartum HB and HCT% among the studied groups (p=0.006 and p<0.001, respectively). The average HB deficit was 0.51±0.14, 0.99±0.29, and 0.99±0.55gm/dl in group A, B, and C, respectively (p<0.001). The average HCT% drop was 1.06±0.27, 1.76±0.36, and 1.39±0.59% in groups A, B, and C, respectively (p <0.001). No case with retained placenta was identified in any studied group. Also, none of the cases needed a blood transfusion. The need for additional uterotonic drugs was 2.5% in group A, compared to 7.5% in group B and 12.5% in group C, which was statistically insignificant (p>0.05). As regards side effects, only 2 cases (5%) in group B (compared to no cases in the other two groups) developed fever >38C and shivering, and this was statistically insignificant (p >0.05) as shown in Table 3.

Discussion

Intraumbilical injection of uterotonic agents such as oxytocin and misoprostol plays an important role in shortening the duration of the third stage of labor. This route directs the drugs fast to the placental bed leading to immediate contraction and early placental separation. This route also avoids the adverse systemic effect of these drugs, and it is useful in women with limited venous access. [12] In some countries, access to certain medications and well-equipped resources are deficient. [13] This evokes some clinicians and researchers to think about other safe and easy maneuvers to overcome such limitations, which can be considered in their clinical practices. Placental blood aspiration aims to induce a decrease in the bulkiness of the placenta, shrinkage of the retroplacental area, thus allowing the uterus to contract and separate the placenta.

The current study revealed no significant difference among studied groups in the duration of the first and second stages of labor. This is because the participants were matched for their clinical characteristics. Women with any risk factor for PPH were excluded from our study. The present study showed a significant difference among the studied group regarding placental delivery time (third stage) with a p-value<0.001. It was found that the intra-umbilical oxytocin injection was the most effective method in shortening the placental delivery time with a mean duration of the third stage of labor of 2.78 min, followed by 4.78 min in the misoprostol group and 5.19 min in the placental aspiration group. No case of retained placenta was observed in any of our study groups.

***Güngördük et al.* [14] *and Zaher et al.* [15]** reported that the women who received 20 IU intraumbilical vein oxytocin had a shorter third stage of labor than those managed expectantly, i.e., 4.5 min vs. 7.9 min, and 2.8 min vs. 4.7 min, respectively. According to ***Lim et al.* [16],** there was a significant reduction in the rate of manual removal of the placenta in the intraumbilical

International Journal of Obstetrics and Gynaecology Research (IJOGR)
Vol. 6 (2020) No.6, pp. 839-851
ISSN:2709-1031
http://www.ijogr.com/

oxytocin group due to shortening the third stage's duration in this compared to the cord traction group. ***Leduc et al.*** [17] reported that intraumbilical cord injection of oxytocin (10-30IU) or misoprostol(800ug) shortened the third stage duration and can be considered an alternative intervention before attempting the manual removal of the placenta. On the other hand, ***Harara et al.*** [18] disagree with our results as the authors reported that misoprostol is slightly more effective than oxytocin and ergometrine when given through the umbilical route in patients with *retained placenta* and the duration of placental delivery significantly is shorter in the misoprostol group than oxytocin and ergometrine groups (7.0 min vs. 13.14 min, and 22.5 min respectively) with p-value (<0.001). The authors also mentioned that misoprostol reduces the need for manual removal of the placenta, thus avoiding the side effects associated with manual removal of the placenta. Moreover, ***Mori et al. .***[19] found that intra-umbilical oxytocin injection was not effective in shortening the third stage's duration. This variation may be attributed to different doses of oxytocin injected intraumbilical, or maybe the clinicians didn't apply milking of the cord after drug injection (as it may facilitate reaching the drug to placental beds).

Although we found the placental blood aspiration method is the least effective strategy in shortening the third stage's duration. However, it was still useful (the mean duration was 5.19 min). Therefore, it may be considered a helpful method in such clinical scenarios, particularly in countries with insufficient resources. ***El-Sharaky*** [10] studied 148 Parturient women to manage the third stage of labor and divided them randomly into three groups. Group I included 48 parturients subjected to placental drainage (defined as clamping and cutting the umbilical cord following delivery of the infant and then, immediately, unclamping the maternal side of the umbilical cord, allowing the blood from the placenta to drain freely into a container), group II included 50 parturients who underwent placental blood aspiration and group III with 50 parturients categorized as control (expectant management). The author found that the third stage's duration was shorter in the placental aspiration group than placental drainage (3.45min vs. 4.5min) and control groups (3.45min vs. 6.5min), respectively.

There were no cases in our study regarding blood loss that suffered from PPH (>500cc blood loss). Our study revealed that intraumbilical oxytocin was the most effective method in reducing blood loss during the third stage, followed by the misoprostol and placental aspiration method. This finding is per ***Güngördük et al.*** [14] , who reported a significant reduction in blood loss in the third stage of labor in women who received intra-umbilical oxytocin injection compared with those managed with placebo (195.3 ml vs. 288.3 ml) p<0.001. ***Rajab and Alalaf*** [20] reported that median blood loss in patients with the retained placenta in the misoprostol group (100 ml) was significantly lesser than the saline group (210 ml) from the time of injection until delivery of the placenta. Similarly, our study results are close to the findings by ***Tehseen et al.*** [21] , who studied the role of intraumbilical vein oxytocin in the active management of the third stage of labor by enrolling 500 low-risk singleton parturients and randomly assigning them to 2 groups, i.e., study

International Journal of Obstetrics and Gynaecology Research (IJOGR)
Vol. 6 (2020) No.6, pp. 839-851
ISSN:2709-1031
http://www.ijogr.com/

group and control group where each group comprised of 250 women. Both groups received intravenous 5 IU oxytocin and 0.5mg ergometrine at the delivery of the baby's shoulder while women in the study group received intraumbilical vein oxytocin 10 IU. This study's authors noticed a marked reduction in blood loss in women in the study group who received intraumbilical vein oxytocin (234.03ml in the study group vs. 276.51ml in the control group; p-value =0.001). On the contrary, ***Mori et al.*** [19]reported that routine injection of oxytocin or other uterotonic drugs into the umbilical vein is not recommended in managing the third stage of labor until the availability of further evidence.

Our study showed that the intraumbilical oxytocin injection was the most effective method in the reduction of the amount of blood loss in 4th stage of labor, where the mean blood loss was 29 ml with intraumbilical oxytocin injection, followed by intraumbilical misoprostol injection with mean blood loss of 33.55 ml, followed by placental aspiration with mean blood loss of 35.05ml and this difference was statistically significant ($p<0.001$). None of the cases in our study needed a blood transfusion as there were no reports of severe bleeding, i.e., more than 500 cc or unstable vital signs. ***Zaher et al.*** [15] findings were consistent with our study findings. Authors found that intraumbilical oxytocin resulted in a shorter duration of the third stage and less blood loss and hemoglobin concentration reduction. In contrast, ***Nardin et al.*** [22] conducted a Cochrane systematic review (published on 11 May 2011) on the use of umbilical vein injection (UVI) of the uterotonic agent or alternative solution or expectant management versus saline solution (with or without oxytocin) for management of retained placenta. This review reported that the umbilical vein injection of prostaglandin resulted in a statistical difference in manual removal of the placenta compared to both umbilical vein injection of saline and oxytocin solution.
Furthermore, UVI of prostaglandin solution did not show any difference in blood loss compared to UVI of saline alone. The authors advised adopting a guarded approach while interpreting these findings. This review concluded that considering UVI of oxytocin solution as a cost-effective and simple intervention; it could be performed while awaiting the placental delivery; however, this approach has little or no effect, as shown by high-quality randomized trials.

Regarding the HB deficit, we found that umbilical vein oxytocin injection is the most effective method in reducing the postpartum HB drop (0.51±0.14), followed by intraumbilical misoprostol injection (0.99±0.29) and placental aspiration (0.99±0.55) gm/dl. Our study was consistent with ***Zaher et al***. [15]**,** who found that intraumbilical oxytocin significantly reduced the postpartum HB deficit (0.31 gm/dl) compared to controls (0.59 gm/dl). Similarly, ***Tehseen et al.*** [21] mentioned that postpartum HB drop was found lower in parturients who received umbilical vein injection of 10 U oxytocin in addition to intravenous injection of 5 IU oxytocin and 0.5mg ergometrine, i.e., study group when compared to parturients who received intravenous 5 IU oxytocin and 0.5mg ergometrine only, i.e., control group (0.413 in the study group vs. 1.051gm/dl in the control group). In contrast, ***Najafian et al.*** [12] reported that umbilical vein injection of misoprostol is

International Journal of Obstetrics and Gynaecology Research (IJOGR)
Vol. 6 (2020) No.6, pp. 839-851
ISSN:2709-1031
http://www.ijogr.com/

more effective in treating the prolonged third stage of labor (i.e., retained placenta after 30 min), particularly in cases without the previous scar, abortion, and curettage compared to the umbilical vein injection of oxytocin. The same study also observed less HB drop in the misoprostol group. We postulate that the published literature's heterogeneity stems from various drugs used across the published studies. Many of the previous studies were performed to evaluate uterotonics' role in cases with retained placenta. In contrast, our study was designed to assess these drugs' role in the active management of the third stage of labor. This, in turn, prevents the retained placenta and PPH.

The current study found that the intraumbilical oxytocin group had the least frequency of the need for additional uterotonic drugs (2.5%), followed by umbilical vein misoprostol injection (7.5%), and placental aspiration (12.5%) groups. This is consistent with ***Lim et al.*** [16] **,**which reported that the intra-umbilical oxytocin group needed less additional uterotonic agents than the control group to manage a retained placenta.

Regarding side effects, our study found only two parturients (5%) in the misoprostol group who developed chills and pyrexia (more than 38C), which lasted a few minutes and resolved spontaneously. ***Rajab and Alalaf*** [20]reported the development of shivering in only one case of the 23 women who received intraumbilical misoprostol for the treatment of retained placenta. From our results, we observed a relatively lower rate of shivering and fever with the administration of 800µg of misoprostol (which is considered somewhat a large dose) via umbilical vein compared with other routes as used in other studies focusing on the management of the third stage of labor. ***Sreelatha et al.*** [23] conducted a comparative study to evaluate the efficacy of oral, sublingual, and rectal routes administration of 400 µg of misoprostol in the management of the third stage of labor with associated maternal side effects. As regards side effects, ***Sreelatha et al.*** [23] found that the maximum side effects of misoprostol were observed with the oral route (32%) followed by sublingual (30%) and rectal route (14%).

Furthermore, ***Sreelatha et al.*** [23] reported shivering, which was more common in the oral group (12%), whereas fever was more common in sublingual routes (12%) and rectal route (6%). ***Soltan et al.***[24] evaluated sublingual misoprostol using doses of 600µg, 800µg, and 1000µg in the management of the third stage of labor for the prevention of atonic PPH. And found the dose-related adverse effects of misoprostol, such as an increased incidence of side effects including shivering, fever, and vomiting with a higher dosage of sublingual misoprostol. Side effects of misoprostol, such as nausea, vomiting, and diarrhea, were not reported in our study.

Conclusion

International Journal of Obstetrics and Gynaecology Research (IJOGR)
Vol. 6 (2020) No.6, pp. 839-851
ISSN:2709-1031
http://www.ijogr.com/

Active management of the third stage of labor decreases postpartum hemorrhage risk and should be offered to all parturients. Intraumbilical oxytocin injection is the best method in the active management of labor. It effectively shortens the duration of the third stage of labor and reduces the amount of blood loss. The need for additional uterotonic drugs is also minimal using intraumbilical oxytocin injection; however, we found it statistically insignificant. Intraumbilical injection of misoprostol (800 μg) may be used as an alternative intervention before attempting the manual removal of the placenta. However, placental blood aspiration was the least effective method for shortening the placental delivery duration and reducing blood loss. It can be considered an effective, easy, safe, and cost-effective method with no side effects; particularly, in situations with restricted availability of uterotonic drugs.

Limitation

This study does not discuss intraumbilical misoprostol injection's effectiveness in preventing PPH in cases with retained placenta. None of the participants of our study experienced a prolonged third stage of labor or retained placenta. This may be attributed to two factors; (i) Participants were healthy and had a low risk of the retained placenta or PPH, and (ii) Small sample size. Therefore, more studies are needed to investigate the role of umbilical vein injection of misoprostol in parturients, including the high-risk group. The other limitation of this study was the unavailability of sufficient previous researches to support or disclaim our results about the role of placental blood aspiration in shortening the duration of the third stage of labor and the associated reduction of the blood loss. We emphasize that more studies should be conducted to evaluate this regimen's role in managing the third labor stage.

Conflict of interest: Authors declare no conflict of interest

Funding: Authors declare that this study received no financial support.

International Journal of Obstetrics and Gynaecology Research (IJOGR)
Vol. 6 (2020) No.6, pp. 839-851
ISSN:2709-1031
http://www.ijogr.com/

References

1. **Baig FS, Shahzad N, Khurshid HN, Malik A (2015):** Postpartum haemorrhage; comparison of intraumbilical and intra venous injection of oxytocin on blood loss in third stage of labor: The Professional Medical Journal; 22(06):793-7. (Google scholar)
2. **Helmy ME, Sayyed TM, Abdo AA (2018):** The effect of the duration of the third stage of labor on the amount of maternal blood loss. Menoufia Medical Journal; 31(4):1244. Doi:10.4103/mmj-135-17
3. **Begley CM, Gyte GM, Devane D, McGuire W, Weeks A, Biesty LM (2019):** Active versus expectant management for women in the third stage of labour. Cochrane database systematic reviews. (2).CD007412DOI:10.1002/14651858.cd00 7412.Pub5.
4. **Stanton C, Armbruster D, Knight R, Ariawan I, Gbangbade S, Getachew A, Portillo JA, Jarquin D, Marin F, Mfinanga S, Vallecillo J, Johnson H, Sintasath D (2009):** Use of active management of the third stage of labour in seven developing countries. Bull World Health Organ; 87(3): 207-15. doi:10.2471/BLT.08.052597
5. **Güngördük K, Olgaç Y, Gülseren V, Kocaer M.(2018)** Active management of the third stage of labor: A brief overview of key issues. Turkish Journal of Obstetrics and Gynecology; 15(3):188. doi:10.4274/tjod.39049(Google scholar)
6. **Shamshirsaz AA, Fox KA, Salmanian B, Diaz-Arrastia CR, Lee W, Baker BW, Ballas J, Chen Q, Van Veen TR, Javadian P, Sangi-Haghpeykar H (2015):** Maternal morbidity in patients with morbidly adherent placenta treated with and without a standardized multidisciplinary approach. American Journal of Obstetrics and Gynecology; 212(2):218-e1-218.e2189.doi:10.1016/j.ajog.2014.08.019
7. **Dahlke JD, Mendez-Figueroa H, Maggio L, Hauspurg AK, Sperling JD, Chauhan SP, Rouse DJ (2015):** Prevention and management of postpartum hemorrhage: a comparison of 4 national guidelines. American Journal of Obstetrics and Gynecology; 213(1).doi1016/i.aiog.2.15.2.023.PubMed.
8. **Elgzar WT, Ibrahim TA, ElKhateeb HM (2020):** Effect of placental cord drainage on third stage of labor progress and incidence of PPH: Randomized controlled trial. South Asian research Journal of Nursing and Health Care; 2: 155-1.doi:10.36346/sarjnhc.2020.v020io1.001
9. **Katheria AC, Truong G, Cousins L, Oshiro B, Finer NN (2015):** Umbilical cord milking versus delayed cord clamping in preterm infants. Pediatrics; 136(1):61-9.doi:1010.1542/peds.2015-0368
10. **El-Sharaky HF (2006):** Evaluation of placental aspiration as new method for placental delivery. Ain Shams Medical Journal 2006; 57(4:6):50-57.

International Journal of Obstetrics and Gynaecology Research (IJOGR)
Vol. 6 (2020) No.6, pp. 839-851
ISSN:2709-1031
http://www.ijogr.com/

11. **Spahn DR, Casutt M (2000):** Eliminating Blood Transfusions: new Aspects and Perspectives. Anesthesiology: The Journal of the American Society of Anesthesiologists; 93(1):242-55.doi:10.109700000542-200007000-00035
12. **Najafian A, Ghasemi M, Hajiha-Esfahani N (2018):** Umbilical Vein Injection of Misoprostol Versus Oxytocin for Managing Retained Placenta After Parturition: A Randomized Clinical Trial. International Journal of Women Health and Reproduction Sciences; 6(3):297-301. doi;10.15296/ijwhr.2018.49
13. **Sharavage JC, Silpa P(2007).** Randomized controlled trial of placental blood drainage for the prevention of postpartum haemorrhage. J Obstet Gynaecol India. 2007;57(3):213-5. (Google Scholar)
14. **Güngördük K, Asicioglu O, Besimoglu B, Güngördük OC, Yildirm G, Ark C, Tekirdag AI (2010):** Using intraumbilical vein injection of oxytocin in routine practice with active management of the third stage of labor: a randomized controlled trial.Obstetrics&Gynecology116(3):619-24**.**doi;10.1097/AOG.0b013e3181edac6b
15. **Zaher SM, El MashadAI, El Sherbiny MF, Mohammed ME (2018):** Study of the effect of intraumbilical vein oxytocin injection on third stage of labor. Al-Azhar Journal of Pharmaceutical Sciences; 58(2):81-92. (Google Scholar)
16. **Lim PS, Singh S, Lee A, Yassin MA (2011):** Umbilical vein oxytocin in the management of retained placenta: an alternative to manual removal of placenta?. Archives of Gynecology and Obstetrics; 284(5):1073-9.doi.org/10.1007/s00404-010-1785-6
17. **Leduc D**, **Senikas V, Lalonde AB (2009):** Active management of the third stage of labor: prevention and treatment of postpartum hemorrhage. Journal of Obstetrics and Gynecology Canada: JOGC;31(10):980-93.doi:10.1016/S1701-2163(16)34329-8
18. **Harara R, Hanafy S, Zidan MSA**, **Alberry M**. **(2011):** Intraumbilical injection of three different uterotonics in the management of retained placenta. Journal of Obstetrics and Gynecology Research. 37(9):1203-7. doi;10.1111/j.1417-0756.2010.01499.x
19. **Mori R, Nardin JM, Yamamoto N, Carroli G, Weeks A (2012):** Umbilical vein injection for the routine management of third stage of labour. Cochrane Database of Systematic Reviews.201214;(3);CD006176.doi:10.1002/14651858.CD006176.pub2
20. **Rajab SS, Alalaf SK (2014):** Umbilical vein injection of misoprostol versus normal saline for the treatment of retained placenta: intrapartum placebo-controlled trial. BMC Pregnancy and Childbirth; 14(1):37.doi;186/1471-2393-14-37
21. **Tehseen F, Anwar A, Arfat Y (2008**): Intraumbilical venous injection oxytocin in the active management of third stage of labor. J Coll Physicians Surg Pak; 18(9):551-4. (PubMed)(Google Scholar)
22. **Nardin JM**, **Weeks A**, **Carroli G**. (**2011**): umbilical vein injection for management of retained placenta. Cochrane Database Sys Rev:(5):CD0013337.

International Journal of Obstetrics and Gynaecology Research (IJOGR)
Vol. 6 (2020) No.6, pp. 839-851
ISSN:2709-1031
http://www.ijogr.com/

23. **Sreelatha S, Nethra HS, Seema N, Vandana A, Rajeshwari (2017):** A comparative study of different route of administration of misoprostol in the management of third stage of labor: IJRCOG;6(9):3865-3871.
24. **Soltan** M**H**, **El Gendi E, Imam H, Fathi O**.(**2007**): Different doses of sublingual misoprostol versus methylergometrine for the prevention of atonic postpartum hemorrhage. Int.J Health Sci Jul;1(2):229-236. (Google Scholar)

Table (1): Comparison of three groups as regards the general characteristics of the studied groups (n=120).

General characteristics of groups		Group A (No.=40)	Group B (No.=40)	Group C (No.=40)	One way ANOVA	
					F	P-value
Age (years)	Mean±SD	23.6±2.5	24.5±2.1	22.8±2.4	1.922	0.126
Gestational Age (weeks)	Mean±SD	38.43±0.54	38.87±0.61	38.61±0.61	2.147	0.195
BMI(kg/m2)	Mean±SD	23.5±5	24.5±6.4	24.9±4.4	0.428	0.813
Prepartum Pulse	Mean±SD	79.25±4.47	79.0±2.36	78.85±5.30	2.184	0.178
Prepartum systolic blood pressure	Mean±SD	121.25±7.59	113.5±11.37	114.50±8.87	0.502	0.596
Prepartum diastolic blood pressure	Mean±SD	77.75±4.72	74.50±5.10	76.0±5.03	1.057	0.249
Prepartum temperature	Mean±SD	37.05±0.10	37.03±0.09	37.05±0.12	1.583	0.452
Prepartum HB (gm/dl)	Mean±SD	10.93±0.56	11.13±0.48	11.42±1.37	1.831	0.097
Prepartum HCT%	Mean±SD	39.28±1.62	40.55±1.57	38.30±1.95	1.658	0.127

Using: One Way Analysis of Variance; P-value >0.05 was considered insignificant.
Abbreviations: Hemoglobin =HB, Hematocrit=HCT

International Journal of Obstetrics and Gynaecology Research (IJOGR)
Vol. 6 (2020) No.6, pp. 839-851
ISSN:2709-1031
http://www.ijogr.com/

Table (2): Comparison of the studied groups as regards the 1st stage, 2nd stage, and 3rd stage of labor.

		Group A (No.=40)	Group B (No.=40)	Group C (No.=40)	One-way ANOVA	
					F	P-value
1st stage (hr)	Mean±SD	10.18±3.31	10.7±1.7	9.98±1.7	0.495	0.612
2nd stage (min)	Mean±SD	31.05±2.61	30.15±2.25	30.20±2.5	0.847	0.434
3rd stage (min)	Mean±SD	2.78±0.43	4.78±0.49#	5.19±3.6#¥	7.453	<0.001

p-value <0.05 was considered significant
Using: One Way Analysis of Variance;
Post HOC: #: significant difference with group A,¥: significant difference with group B

International Journal of Obstetrics and Gynaecology Research (IJOGR)
Vol. 6 (2020) No.6, pp. 839-851
ISSN:2709-1031
http://www.ijogr.com/

Table (3): Comparison of three groups as regards the postpartum outcome

		Group A (No.=40)	Group B (No.=40)	Group C (No.=40)	Test	p-value
Blood loss (3rd)	Mean±SD	160.5±17.08	203.5±16.4#	210.50±81.27#¥	F= 5.768	<0.001**
Blood loss (4th)	Mean±SD	29±2.88	33.55±4.02#	35.05±4.26#¥	F= 4.779	<0.001**
Retained placenta	Yes	0 (0%)	0 (0%)	0 (0%)	NA	NA
	No	40 (100%)	40 (100%)	40 (100%)		
State of uterus	Contracted	39 (97.5%)	37 (92.5%)	35(87.5%)	x^2= 2.883	0.237
	Atonic	1 (2.5%)	3 (7.5%)	5 (12.5%)		
Postpartum pulse	Mean±SD	81.8±2.84	81.15±3.15	82.2±3.11	F=1.386	0.219
Postpartum systolic blood pressure	Mean±SD	106.75±8.32	107.50±10.51	104.68±9.38	F=0.893	0.591
Postpartum Diastolic blood pressure	Mean±SD	68.50±6.71	70.0±7.95	68.0±6.16	F=1.243	0.681
Postpartum temperature	Mean±SD	37.06±0.14	37.11±0.29	37.04±0.10	F=0.927	0.382
Post-partum HB	Mean±SD	10.42± 0.55#	10.14±0.47#	10.43±0.37¥	F=2.751	0.006
Post-partum HCT%	Mean±SD	38.22±1.55	38.79±1.42	36.91±1.95#¥	F=3.326	<0.001
HCT deficit	Mean±SD	1.06±0.27	1.76±0.36#	1.39±0.59#¥	F=9.6447	<0.001
HB deficit	Mean±SD	0.51±0.14	0.99±0.29#	0.99±0.55#	F= 6.29	<0.001
Additional utertonic drugs	Yes	1 (2.5%)	3 (7.5%)	5 (12.5%)	x^2= 2.883	0.237
	No	39 (97.5%)	37 (92.5%)	35 (87.5%)		
Need for blood transfusion	Yes	0 (0%)	0 (0%)	0 (0%)	NA	NA
	No	40 (100%)	40 (100%)	40 (100%)		
Drug side effects	Fever	0 (0%)	2 (5%)	0 (0%)	x^2= 0.513	0.474
	Shivering	0 (0%)	2 (5%)	0 (0%)		

p-value <0.05 was considered significant
Using: F-One Way Analysis of Variance; x^2Chi-square test
Post HOC: #: significant difference with group A,¥: significant difference with group B.

Abbreviations: Hematocrit=HCT, Hemoglobin=HB.