EVIDENCE BASED PRACTICES IN THE PREVENTION OF POSTPARTUM HEMORRHAGE: A SYSTEMATIC REVIEW

Correspondence: **Ayşegül KILIÇLI**[1]Orcid No: 0000-0003-1105-9991

Emine KARACAN[2]Orcid No: 0000-0002-1532-4281

[1, 2] Gaziantep University Institute of Health Sciences, Obstetrics and Gynecology Nursing Department
Post Cod: 27000

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Abstract:

Background: This study was carried out to analyze the studies conducted to investigate evidence basedpractices in preventing postpartum hemorrhage.

Materials and Methods: The literature review was carried out by using the Cochrane database, which was published between 2000-2020, in PDF format with abstract and full text. Screening was performed in English using 12 keywords. As a result of the study, 15 studies were included in the research.

Results: In this study examining evidence-based interventions to prevent postpartum hemorrhage, it was found that oral or sublingual administration of uterotonic agents was less effective than intravenous administration, the use of prophylactic uterotonics in the third stage of labor before and after the removal of the placenta had no effect on the length of the postpartum hemorrhageand the third stage of labor, and misoprostol caused an increase in body temperature, uterine massage reduced postpartum hemorrhage and reduced additional uterotonic need by 80% after delivery of the placenta, evidence of efficacy of breast-feeding and nipple stimulation in reducing postpartum hemorrhage was insufficient, controlled cord traction was found to reduce the placenta manually and slightly decrease postpartum hemorrhage, but there was no significant difference between additional uterotonic use, blood transfusion, maternal mortality / severe morbidity, surgical procedures or maternal satisfaction. It was found that placental cord drainage reduced the length of the third stage of labor by 3 minutes for a period of time and decreased blood loss to an average of 77ml. Early and late clamping time of umbilical cord did not have a significant effect on postpartum hemorrhage.

Conclusions: As a result of this study, more studies with higher level of evidence are needed to prevent postpartum hemorrhage. In particular, studies showing the effects of single or combined administration of uterotonic drugs and randomized controlled trials with higher levels of evidence indicating the efficacy of nonpharmacological applications to prevent postpartum hemorrhage have been identified.

Key words: Postpartum Hemorrhage, Evidence Based Practice, Systematic Review.

INTRODUCTİON

Postpartum hemorrhage (PPH) is defined as 500 ml following normal delivery and blood loss exceeding 1000 ml following cesarean delivery (1). In the systematic analysis report published by the World Health Organization in 2014, it is stated that most of the maternal deaths (27.1%) are due to bleeding. Although obstetric hemorrhages occur during antenatal, intrapartum and postpartum periods, more than 2/3 of them constitute postpartum hemorrhages (2). According to the Ministry of Health (2014) data, the maternal mortality rate in our country is 15.2 per 100,000 live births. PPH is the leading cause of maternal death with a rate of 21% and the most common cause of this health problem is uterine atony and placenta retention (3).

Postpartum hemorrhage is examined in two groups as early and late. Early PPH is within the first 24 hours, and late PPH is bleeding within 6-12 weeks after the first 24 hours following delivery. Estimated blood loss at birth is usually misdiagnosed and less than the current amount of bleeding is reported (4).

In postpartum hemorrhage, hemodynamic instability findings with hypotension, dizziness, pallor and oliguria occur when 10% or more of total blood volume is lost.This situation affects women's health directly and indirectly (5).

Postpartum hemorrhage causes are divided into two groups as primary and secondary. Primary causes; uterine atony, placenta retention, genital lesions or trauma and coagulation disorder is caused by one or more of the causes. These reasons are the 4T rule to keep in mind in English; tonus, tissue (tissue), trauma, thrombin. Among these reasons, uterine atony alone is responsible for 75-90% of post partum hemorrhage.Secondary causes; uterine infection, placental retention and abnormal involution of the placenta (6-8).

Most of the postpartum hemorrhages occur in post partum women with no known risk. In order to minimize maternal mortality with the most important complication, every postpartum woman should be considered as a woman with a potential for bleeding and should be treated primarily with prevention (8,9).

Evidence based practice is defined the most current evidence search, the appropriate resources in the care areas and the preference of patients, clinical expert opinion and evaluation of scientific research evidence, to provide the best care services to the patients (10, 11).Evidence-based practice effects the quality and results of health care. Also evidence based interventions are made possible by standardizing care and increasing patient satisfaction in clinical practice and in patient care outcomes (12).The quality of health services provided in the postpartum period is determined by the fact that the health practices presented in this period are evidence-based, effective and appropriate to the requirements. Knowing the current practices of PPH prevention and treatment by health professionals and using them effectively is very important for preventing maternal deaths due to bleeding (8, 12).

Evidence based practices in prevention of PPH include the most current evidence-based practices for prevention of PPH in guidelines prepared by World Health Organization (WHO), The International Confederation of Midwives (ICM) and The International Federation of Gynecology and Obstetrics (FIGO) taking into account research results and expert opinions in 2012. Evidence-based interventions for PPH preventions are; use of uterotonics (oxytocin, ergometrin, misoprostol / prostaglandin, carbetocin, combined drugs, tranexamic acid), controlled cord traction, uterine massage, interventions for the placenta, use of health protocols, interventions for uterus (13, 14).

The purpose of this study is to analyzethe evidencebased practices in preventing postpartum hemorrhage

MATERIAL AND METHOD

A review of the literature was carried out using the Cochrane database, covering the period between 2000 and 2020, reviewing the abstracts (only the abstract of full text restricted ones) or full-text PDF format. Scanning was performed using 12 key words in English. Keywords used in scanning; postpartum haemorrhage, uterotonic agents, controlled cord traction, uterine massage, oxytocin, ergometry, misoprostol, prostaglandine, carbetocin, tranexamic acid, the third stage of labor and nursing.

Inclusion criteria for the studies reviewed are meta-analysis, systematic review, cohort studies and randomized controlled studies. Exclusion criteria; qualitative and descriptive studies.

At the end of the screening, a total of 55 articles were reached. 55 articles were first examined according to the headings and 33 articles that are not related to the research are excluded. Abstracts and full texts of the remaining 22 studies were evaluated in terms of inclusion and exclusion criteria and 7 studies were excluded from the study because they did not meet the inclusion criteria. Thus, a total of 15 studies was chosen in accordance with the inclusion and exclusion criteria. This study included 15 studies for the whole universe. This systematic review was prepared to PRISMA 2009 flow diagram.

RESULTS

In this systematic review, 15 systematic reviews that examined evidence-based practices in preventing PPH were examined in detail and the time / amount of administration / use of uterotonic agents, controlled cord traction, uterine massage, clamping time of umbilical cord, placental cord drainage, effects of breastfeeding and nipple stimulation on PPHwas investigated (Table 1).

Using of Uterotonic Drugs:

In a systematic review examining the effect of uterotonic agents used to prevent PPH; in the treatment of primary PPH, oxytocin infusion is more effective and cause fewer side effects when used as the first choice compared to misoprostol. After the use of prophylactic uterotonics, misoprostol and oxytocin infusion were found to work similarly. It has been proposed that the co-administration of misoprostol does not provide any additional advantage among women receiving oxytocin for primary PPH treatment (15).

In another systematic review, it has been reported that the use of prophylactic oxytocin at any dose reduces PPH of more than 500 mL (risk ratio (RR) 0.53; 95% confidence interval (CI) 0.38-0.74; in six studies 4203 women, T^2 = 0.11, İ2 = 78%) and (RR 0.56, 95% CI 0.36 - 0.87, four trials, 3174 women; T^2 = 0.10, I^2 = 58%)and reduces the need for therapeutic uterotonics compared to placebo alone.

Prophylactic oxytocin was found to be superior to ergot alkaloids in preventing PPH greater than 500 mL. It has been identified limited number of high-quality evidence supporting the benefit of prophylactic oxytocin on ergot alkaloids. The use of prophylactic oxytocin was found to have fewer side effects than ergot alkaloids (especially less nausea and vomiting). There was no evidence that prophylactic oxytocin increased the risk of retained placentas compared to placebo or ergot alkaloids. In order to prevent PPH, more placebo-controlled, randomized and double-blind studies were needed to evaluate the effective dose, timing and route of administration of prophylactic oxytocin and to improve the quality of the data used (16).

In order to prevent PPH, more placebo-controlled randomized and double-blind studies were needed to evaluate the effective dose, timing and route of administration of prophylactic oxytocin and to improve the quality of the data used (oral: seven studies, total 6225 women due to significant heterogeneity, sublingual: risk ratio (RR) 0.66; 95% confidence interval (CI) 0.45-0.98; 661 women) and blood transfusion (oral: RR 0.31; 95% CI 0.10 0.94; four trials, 3519 women).Compared with injectable uterotonics, oral misoprostol was found to be associated with severe PPH(RR 1.33; 95% CI 1.16 to 1.52, 17 trials, 29.797 women) risk and additional uterotonic use, but was found to be less prone to blood transfusion(RR 0.84 95% CI 0.66 to 1.06, 15 trials; 28.213 women) (17).

Compared with oxytocin and ergometrin-oxytocin in the third stage of labor, the use of ergometrin-oxytocin compared to oxytocin for 500 ml or more blood loss has been found to cause a small but statistically significant reduction in PPH risk(risk ratio 0.82, 95% CI 0.71-0.95). Although the use of ergometrin-oxytocin in the study resulted in a reduction in the risk of PPH between 500 and 1000 ml compared with oxytocin use, adverse side effects associated with the use of ergometrin-oxytocin (maternal side effects such as increased diastolic blood pressure, vomiting and nausea) were detected (18).

In a review examining the effect of postpartum misoprostol use in preventing maternal mortality and morbidity, there was no statistically significant difference in misoprostol use in maternal mortality compared to all control groups.(31 studies: 11 / 19.715 versus 4 / 20.076 death, risk ratio (RR) 2.08, 95% confidence interval (CI) 0.82 - 5.28); or for placebo trials with misoprostol: 10 studies, 1/4706 versus 6/4626; RR 2.70; 95% CI 0.72 to 10.11; or for other misoprostol with other uterotonics:21 studies, 5 / 15,089 versus 3 / 15,369 (19 / 100,000); RR 1.54; 95% CI 0.40 to 5.92).In patients used misoprostol, all 11 deaths, it has been reported that it occurs in studies using over misoprostol 600 µg(micrograms). Pyrexia> 38 ° C was seen more common in patients used misoprostol compared to controls (56 studies, 2776 / 25,647 (10.8%) versus 614 / 26,800 (2.3%); mean RR 3.97, 95% CI 3.13 to 5.04; Tau^2 = 0.47, I^2 = 80%).When misoprostol was used to prevent or treat PPH, it was determined that it did not increase or decrease severe maternal mortality and morbidity (excluding hyperpyrexia). It was determined that it causes maternal hyperpirexia when taken in especially 600 µg or more doses (19).

In a systematic review, prostaglandins compared with placebo were not found to be effective in manual removal of the placenta (mean risk ratio (RR) 0.82; 95% confidence interval (CI) 0.54 to 1.27), postpartum hemorrhage (RR 0.80, 95% CI 0.55-1.15), need for blood transfusions (RR 0.72; 95% CI 0.43-1.22), and lowering the mean blood loss rate (mean difference (MD) -205.26 mL; 95.7% CI -536.31 with 125.79 random effects).It has been determined that the use of prostaglandins leads to the need for manual removal of the placenta and less need for blood transfusion in severe postpartum hemorrhage, but statistically significant difference was not found.In average blood loss, there was no difference in the mean time (minutes) from the injection of prostaglandins to placental removal between prostaglandins and placebo. No significant difference was found between the groups in terms of side effects such as vomiting, headache, pain and nausea during lactation, except for more frequent shivering in women

receiving prostaglandin (RR 10.00; 95% CI 1.40-71).Tremor was more common in women receiving prostaglandin compared to placebo, but there were no significant differences in vomiting, headache, maternal pain or nausea (20).

In another review, there was no clear evidence that prophylactic oral metlergometrin was effective in reducing postpartum hemorrhage after delivery of the placenta to reduce bleeding in the postpartum period. It was seen also uncertainty about the efficacy of prophylactic use of herbal medicine or homeopathic remedies for PPH (21).

In another review, intramuscular or intravenous injections of injected prophylactic ergot alkaloids in the third stage of labor were found to reduce postpartum hemorrhage and mean blood loss by at least 500 ml (risk ratio (RR)) 0.38,% 95 CI 0.21 - 0.69) and it was seen to have reduced significantly the use of therapeutic uterotonic (RR 0.25, 95% CI 0.10 to 0.66). However, its effect on the risk of placental involvement or manual removal was unclear.In the studyespecially intravenous administration of ergot alkaloids after birth was found to cause a significant increase in blood pressure (RR 2.60, 95% CI 1.03 to 6.57)and pain requiring analgesia after delivery(RR 2.53, 95% CI 1.34 to 4.78). However, it was defined that it did not cause symptoms such as vomiting, nausea and headache.When the evidence for the application of ergometry as oral, intramuscular or intravenous is considered, the oral route is not very effective, but it has been found to cause high blood pressure and pain due to uterine contraction despite the reduction of blood loss in the intravenous tract. Intramuscular administration of ergometry was found to be beneficial in reducing blood loss. In addition, it was seen that intramuscular administration according to intravenous administration had less side effects (22).

In another systematic review of the use of prophylactic uterotonics in the third stage of vaginal delivery, oxytocin was used as the sole uterotonic drug. Among the studies included in the review, oxytocin was found to differ as dose and route of administration.Before exiting the placenta and after exiting the placenta it was determined that oxytocin administration did not have a significant effect on the amount of postpartum hemorrhage(blood loss greater than 500 ml) (risk ratio (RR) 0.81, 95% confidence interval (CI) 0.62 to 1.04; n = 1667, three trials); (RR 1.54, 95% CI 0.76-3.11, n = 1667, three trials), the length of the third stage of delivery(minutes) (mean difference (MD) -0.30, 95% CI -0.95 to 0.36; n = 1667, three studies),postpartum blood loss (ml) (MD 22.32, 95% CI -58.21 with 102.86; n = 181 in two trials),hemoglobin changes(g / dL) (MD 0.06, 95% CI -0.60 to 0.72; n = 51, a trial), blood transfusion(RR 0.79, 95% CI 0.23 to 2.73; n = 1667, three trials), additional uterotonic use(RR 1.10, 95% CI 0.80 with 1.52, n = 1667, three trials), incidence of maternal hypotension(RR 2.48, 95% CI 0.23 - 26.70, n = 130, as an assay) and the incidence of severe postpartum hemorrhage(blood loss 1000 ml or more) (RR 0.98, 95% CI 0.48-1.19; n = 130, an experiment).The administration of oxytocin before and after the excretion of the placenta was determined to have no significant effect on many clinically important results such as the incidence of postpartum hemorrhage, the rate of placental retention and the duration of the third stage of labor (23).

In a systematic review called the effect of the use of tranexamic acid (TA) in the third phase of labor or during cesarean section (CS);blood loss of more than 500 mL is more pronounced in women who have vaginal delivery than women who have cesarean section and mean blood loss(up to two hours after delivery)was found to be lower in patients who received tranexamide acid (TA) than in patients who had placebo or who had no any other intervention(mean difference MD 77.79 mL, 95% CI -97.95, -57.64, five trials, 1186 women).Additional medical intervention and blood transfusion were less frequent in women receiving tranexamide acid than placebo or control groups. Mild side effects including diarrhea, nausea and vomiting were more common in women with TA compared to placebo. In addition, two different doses of TA were found to be unremarkable in blood loss and side effects. The effect of TA on maternal mortality, severe morbidity and thromboembolic events has been found to be unclear (24).

Uterine Massage:

In a systematic review examining the effect of uterine massage on post partum hemorrhage (2 randomized controls consisted of experimental study); in the first study involving 200 women, it was found that uterine massage after placental delivery reduced blood loss and additional uterotonic need by 80%. The number of women with blood loss greater than 500 mL was found to be small without a statistically significant difference. (risk ratio (RR) 0.52, 95% confidence interval (CI) 0.16 to 1.67). Mean blood loss was found to be 41.60 mL after 30 minutes (mean difference (MD) -41.60 mL, 95% CI-75.16 to -8.04) and 77.40 mL after 60 minutes (MD-77.40 mL, 95% CI-118.71 to -36.09).The need for additional uterotonic use in the uterus massage group decreased significantly (RR 0.20, 95% CI 0.08-0.50).In the second study which included 1964 women in Egypt and South Africa it was investigated the effect of uterine massage on PPH before and after the placenta.After the birth of the fetus and

before the birth of the placenta, this study involved oxytocin, uterine massage, and co-administration of both. When oxytocin was used in the study, it was determined that uterine massage did not provide an additional advantage in PPH. The need to use additional uterotonics (RR 1.02 ,% 95 CI 0.56 ile 1.85) in blood loss equal to or greater than 500 mL (mean RR 1.56, 95% CI 0.44, 5.49; random effects) did not provide an additional advantage in PPH. Two studies were combined to examine the effect of uterine massage before or after the birth of the placenta, and no statistically significant difference was found between the groups (mean RR 1.14, 95% CI 0.39-3.32; random effects) (25). It should be done more randomized controlled trials showing the effect of uterine massage on reducing PPH.

Breastfeeding and Nipple Stimulation:

In a systematic review examining the effect of breastfeeding and nipple stimulation on PPH; due to factors such as maternal mortality, PPH incidence(≥ 500 mL), blood loss in the third stage of labor, retained placenta, perinatal deaths, or hospitalized mother, thre was no significant difference between which was applied nipple stimulation (suction) group and control group.Studies showing the effect of breastfeeding or nipple stimulation to reduce PPH in the third phase of labor were found to be small and insufficient, and more high quality / randomized controlled studies are needed.It has been determined that the stimulation of the nipple should be evaluated in comparison with uterotonic agents such as cetometrin and oxytocin (26).

Controlled Cord Traction (CCT):

In a systematic review, it was found that CCT application reduced the manual removal of the placenta (two trials, 27.665 women, RR 0.69, 95% Cl0.57-0.83).There was no significant difference between CCT and mean blood loss ≥ 500 mL (three studies, 27.454 women; RR 0.93, 95% CI 0.88-0.99), (two studies, 27.255 women; mean difference (MD) -10.85 mL, 95% CI-16.73 to -4.98), duration of the third stage of labor(two trials, 27,360 women, standardized MD -0.57, -0.59 to -0.54),additional uterotonic drug use(three studies, 27,829 women, mean RR 0.95, 95% CI 0.88 to 1.02), blood transfusion, maternal mortality / severe morbidity, surgical procedures, and maternal satisfaction.In the third stage of labor, ıt was found that CCT did not clearly reduce severe PPH (blood loss> 1000 mL), but resulted in a small reduction in PPH (blood loss> 500 mL), resulting in mean blood loss. It was also found that CCT reduced the risk of manual delivery of the placenta. When the caregiver has the ability to manage the CCT safely, it has been determined that CCT is recommended (27).

Placental Cord Drainage:

In a systematic review, it was found that the application of placental cord drainage in the third phase of labor reduced the length of the third stage of labor (mean difference -2.85 minutes, 95% confidence interval -4.04 to -1.66, three studies, 1257 women (heterogeneity: $T^2 = 0.87$; $Chi^2P = 17.19$, $I^2 = 88\%$)) and the amount of mean blood loss (MD-77.00 ml, 95% CI-113.33, -40.27; an experiment, 200 women).It was found that the third stage of labor was reduced by an average of three minutes and blood loss decreased by 77 ml. There was no significant difference between placental cord drainage and PPH, manual removal of the placenta and the need for blood transfusion (28).

Clamping Time of Umblikal Cord:

Although early umbilical cord clamping method is thought to reduce PPH risk, in a systematic review reviewing 15 randomized controlled trials including 3911 women and infant pairs, there was no significant difference between early and late cord clamping (comparison between one to three minutes) and postpartum bleeding rates.However, in healthy infants, such as high birth weight, early hemoglobin concentration and increased iron reserves up to six months after birth, it was found that delayed cord clamping had had been potentially some significant advantages (29).

DISCUSSION

In this systematic review, 15 systematic review studies aimed at examining evidence-based practices in preventing postpartum hemorrhage (PPH) have been discussed. Although there are traditional reviews about evidence-based practices aimed at preventing postpartum hemorrhage in our country and throughout the world, there is no systematic review study in this area. This study is the first systematic review which was carried out for the purpose of examining evidence-based nursing practices in preventing postpartum hemorrhage, unlike the literature.This systematic review showed that evidence-based nursing studies were insufficient to prevent PPH.Therefore, more

randomized controlled / evidence based nursing studies are needed for the prevention of PPH.Uterotonic drugs (ergometrin, oxytocin, prostaglandins, etc.) which is used in the third stage of labor cause contraction of the uterus and used in the active management of the third phase.In our study, it was determined that uterotonic agents used to prevent PPH reduce bleeding.Especially it was seen that oxytocin was used as the first choice in the treatment of primary PPH and less side effective.It was seen taht the use of prophylactic oxytocin reduced therapeutic uterotonic need compared to placebo. But it was found that there were differences between studies related to dose of oxytocin given, route of administration and time of administration (23). Oxytocin is more effective in reducing PPH than misoprostol (prostaglandin) and ergot alkaloids, however, more placebo-controlled, randomized and double-blind studies are needed to improve the quality of the data used in order to evaluate the effective dose, timing and route of administration of oxytocin (15. 16). Although it has been determined that ergometrin-oxytocin, which is the combined uterotonic, is more effective on PPH than only oxytocin use, it has been determined that there are negative side effects associated with its use (such as increased diastolic blood pressure, maternal side effects such as vomiting and nausea) (18).It is reported that oral administration of ergometry is not very effective with respect to IV or IM administration, but despite decreasing blood loss, IV administration causes pain and high blood pressure due to uterin contraction. Furthermore, IM administration of ergometry has been shown to reduce blood loss, reduce the need for therapeutic uterotanics, and have fewer side effects than IV administration, but its effect on the risk of placental involvement or hand removal is reported to be unclear (22). The effect of the use of tranexamic acid (TA) in the third phase of vaginal delivery or during cesarean section (CS) was more pronounced in women with vaginal delivery than in caesarean deliveries, and mean blood loss was found lower in patients with TA than placebo or women without any intervention. In addition, use of TA has been reported to reduce additional medical intervention and blood transfusion (24). When the studies are examined, it is seen that uterotonic agents decrease the risk of PPH, but there are uncertainties regarding the amount of administration, route of administration, time of administration and side effects further high-quality evidence and randomized controlled trials are needed.

Although uterine massage after delivery is thought to decrease PPH, in a Cochrane systematic review included in our study, in women who was not applied uterotonic drug, because of the lack of studies evaluating the effectiveness of uterine massage on PPH and current study results insufficient, continuous uterine massage is not recommended to women who are applied prophylactic oxytocin women (14, 25).More randomized controlled experimental studies showing the effect of uterine massage on reducing PPH are needed.

In a Cochrane systematic review covering a limited number of studies examining the effect of breast-feeding and nipple stimulation in preventing PPH; according to maternal mortality, incidence of PPH (≥ 500 mL), blood loss in the third stage of labor, placental retention, perinatal deaths or mother who was hospitalized, there was no clear difference between nipple stimulation (absorption) group and who was not treated, In addition, it was found that there was insufficient number of evidence indicating the effect of breast-feeding or nipple stimulation to reduce PPH in the third stage of delivery and there was a need for high-quality studies. It has been reported that stimulation of the nipple should be evaluated comparatively with uterotonic agents such as syntimethrin and oxytocin (26).

In studies conducted, in the third stage of labor, it is reported that the effect of Controlled Cord Traction (CCT) on PPH is controversial. In a study it has been found that CCT has little effect on PPH prevention. Especially at birth happening outside the hospital, It was emphasized that oxytocin use was important to prevent bleeding (30). In another study, it was found that CCT did not have a significant effect on PPH reduction and other postpartum blood loss values, and for the prevention of PPH there is not enough evidence which recommend routine CCT application (31). In a Cochrane systematic review included in our study, manual removal of the placenta with CCT decreased and led to a slight decrease in PPH. In addition, it was determined that there was no significant difference between CCT and the third phase of delivery, additional uterotonic drug use, blood transfusion, maternal mortality / serious morbidity, surgical procedures or maternal satisfaction. It is stated that CCT should be performed by experienced health workers and also there are research gaps in the application of CCT in the absence of uterotonics (8, 27).

In a systematic review showing that placental cord drainage reduces the amount of PPH, it was found that placental cord drainage reduced the length of the third stage of labor by 3 minutes and the mean amount of blood loss decreased by 77 ml. However, there was no significant difference between placental cord drainage and manual removal of the placenta and the need for blood transfusion (28). Although placental cord drainage in the third stage of labor has positive effects on fetal blood values, there is a need for more studies with higher level of evidence examining the effect of preventing PPH.

Immediately after the birth of the umbilical cord, there are various applications related to clamping such as after stopping pulse on the umblical cord or within the first 60 seconds and the benefits and harms of each application are discussed. In a Cochrane systematic review, early (within the first 1 min after birth) and late (at least 1 min after birth or after the cord pulse stops) maternal and neonatal results of cord clamping were evaluated. In the study, while there was no statistically significant difference in terms of neonatal and maternal morbidity and mortality, there have been several benefits of neonatal late cord clamping. These results were statistically significant; was found that neonatal weights (mean 101 g) were higher, needed less phototherapy, and hemoglobin concentrations were higher in the first 24-48 hours and iron reserves were higher (29). In this direction, it has been recommended that the umbilical cord is clamped late (after at least 1 min after birth, in about 1-3 minutes after stopping the cord) (14, 29).

CONCLUSION and RECOMMENDATIONS

It was determined that oral or sublingual administration of uterotonic agents in preventing PPH is more effective and less side-effectly than IV administration, uterine massage reduces PPH and additional uterotonic need.More evidence is needed to demonstrate the efficacy of breastfeeding and nipple stimulation in reducing PPH. it was found that controlled cord traction reduced manual removal of the placenta and decreased PPH slightly. Placental cord drainage was found to reduce PPH and the length of the third stage of delivery. It was determined that the clamping time of the umbilical cord had no significant effect on PPH. However, it was found that late clamping of the cord had positive effects on fetal health. As a result of this work Randomized controlled trials with higher levels of evidence to prevent PPH appear to be needed. In particular, there is a need for more randomized controlled trials showing the efficacy of single and combined administration of uterotonic drugs and the effectiveness of nonpharmacological applications to prevent PPH.

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Table 1. Characteristics of the studies included in the research

Author	Date	Method	Sampling	Results
Mousa HA, Blum J, Abou El Senoun G, Shakur H, Alfirevic Z	2017	Systematic Rewiew	10 randomized experimental trials covering 4052 women	Oxytocin infusion was found to be more effective and less side effective when used as the first choice in the treatment of primary PPH compared to misoprostol. It was found that misoprostol and oxytocin infusion were working similarly after prophylactic uterotonic use. It has been suggested that the co-administration of misoprostol does not provide any additional advantage for the treatment of primary PPH among women receiving oxytocin.
Hofmeyr GJ,	2016	Systematic Rewiew	Total 2164 women 2 randomized controlled	In the first study including 200 women, after the birth of the placenta, the uterine massage effectively reduced blood loss and reduced the need for additional uterotonics by

Abdel-Aleem H, Abdel-Aleem MA			experimental studies	80%. The number of women who lost more than 500 mL of blood was found to be too small for a significant comparison. The second study consisted of 1964 women who received oxytocin, uterine massage or both before delivery and after the birth of the placenta. When oxytocin was used, it was found that there was no additional advantage for uterine massage. This two studies were combined to examine the effect of uterine massage before or after the birth of the placenta and there was no statistically significant difference between the groups.
Abedi P, Jahanfar S, Namvar F, LeeJ	2016	Systematic Rewiew	4472 women Randomized and semi-randomized controlled experimental 2 studies	In order to reduce PPH in the third stage of labor, there is insufficient evidence to assess the effect of breast-feeding or nipple stimulation, and more high-quality studies are needed. Nipple stimulation should be evaluated comparatively with uterotonic agents such as syntimethrin and oxytocin
Hofmeyr GJ, Mshweshwe NT, Gülmezoglu AM	2017	Systematic Rewiew	27 873 women randomized controlled 3 experimental study	In the third phase of labor Controlled cord traction (CCT) was found to decrease the manual removal of the placenta. There was no significant difference between controlled cord traction and mean blood loss ≥ 500 mL, the duration of the third stage of labor, additional uterotonic drug use, blood transfusion, maternal mortality / serious morbidity, surgical procedures or maternal satisfaction. In the third stage of labor, it was seen that CCT did not clearly reduce severe PPH (blood loss> 1000 mL), but caused a small reduction in PPH (blood loss> 500 mL), and reduced the risk of manual removal of the placenta.
Soltani H, Poulose TA, Hutchon DR	2011	Systematic Rewiew	1257 women Randomized controlled three experimental studies	In the management of the third stage of labor, it was seen that placental cord drainage reduced the third stage of labor by a mean of three minutes as time and reduced blood loss by an average of 77 ml. There was no significant difference between placental cord drainage, manual removal of the placenta, postpartum hemorrhage or the risk of blood transfusion.
McDonald SJ, Middleton P, Dowswell T, Morris PS	2013	Systematic Rewiew	15 randomized controlled experimental studies involving 3911 women and infant pairs	Although early umbilical cord clamping method is thought to reduce PPH risk, in a study reviewing a total of 15 randomized controlled trials, It was determined that there was no significant difference in early and late cord clamping postpartum bleeding rates. Also in healthy term infants delayed cord clamping has been found to have some potentially significant advantages such as high birth weight, early hemoglobin concentration and increased iron reserves up to six months after birth.
Westhoff G, Cotter AM, Tolosa JE	2013	Systematic Rewiew	10806 women randomized controlled and semi-experimental controlled 20 trials	It was determined that prophylactic oxytocin at any dose is superior to ergot alkaloids in preventing PPH greater than 500 mL and there is a limited number of high quality evidence supporting the benefit of prophylactic oxytocin on ergot alkaloids. It was seen that the use of prophylactic oxytocin was reported to have fewer side effects than ergot alkaloids, and was less likely to cause nausea and vomiting. There was no evidence that prophylactic oxytocin

				increased the risk of retained placentas compared to placebo or ergot alkaloids. In order to prevent PPH, it was determined that prophylactic oxytocin should be evaluated the effective dose, timing and route of administration and more placebo-controlled, randomized and double-blinded studies were needed to improve the quality of the data used.
Tunçalp Ö, Hofmeyr GJ, Gülmezoglu AM	2012	Systematic Rewiew	52.678 women 72 randomized experimental studies	Oral or sublingual misoprostol (prostaglandin) was found to be more effective when compared with placebo in reducing serious blood loss after delivery and reducing the need for blood transfusions. Oral misoprostol was found to be associated with severe PPH risk and additional uterotonic use compared to injectable uterotonics, but was found to be less prone to blood transfusion.
McDonald SJ, Abbott JM, Higgins SP	2009	Systematic Rewiew	9332 women Randomized controlled 6 experimental studies	The use of oxytocin and ergometrin-oxytocin in the third stage of labor was compared. In case of blood loss of 500 ml or more, It was determined that the use of ergometrin-oxytocin compared to oxytocin resulted in a small but statistically significant decrease in PPH risk. Although the use of ergometrin-oxytocin provides a reduction in the risk of PPH compared to the use of oxytocin, it has been identified negative side effects associated with the use of ergometrin-oxytocin (such as increased diastolic blood pressure, maternal side effects, vomiting and nausea).
Novikova N, Hofmeyr GJ, Cluver C	2015	Systematic Rewiew	3285 women 20 experimental studies with published, unpublished, ongoing randomized control	In this review which was investigated the effect of the use of tranexamic acid (TA) on the PPH during the third stage or during cesarean section (CS); blood loss of more than 500 mL is more pronounced in women who have vaginal delivery than women who have cesarean section. Mean blood loss (up to two hours after delivery) was lower in patients to be used TA than in placebo or in women without doing any intervention. Additional medical interventions and blood transfusion were less frequent in women receiving TA than placebo or control groups. Mild side effects including diarrhea, nausea and vomiting were more frequent in women who received TA compared to placebo. Also there were no significant differences in terms of blood loss and side effects when two different doses of TA were evaluated, and the effect of the use of TA on maternal mortality, serious morbidity and thromboembolic events is unclear.
Hofmeyr GJ, Gülmezoglu AM, Novikova N, Lawrie TA	2013	Systematic Rewiew	59.216 women Randomized experimental 78 study	When misoprostol is used to prevent or treat PPH It was determined that misoprostol did not increase or decrease severe maternal morbidity (excluding hyperpyrexia) and maternal mortality. In particular, the use of misoprostol at doses of 600 µg or more was associated with an increased risk of fever.

Grillo-Ardila CF,Ruiz-Parra AI,Gaitán HG, Rodriguez-Malagon N	2014	Systematic Rewiew	244 women Randomized controlled 3 experimental studies	It has been determined that the use of prostaglandins leads to the need for manual removal of the placenta and less need for blood transfusion in severe postpartum hemorrhage, but no statistically significant difference was not found. In average blood loss, there was no difference in the mean time (minutes) from the injection of prostaglandins to placental removal between prostaglandins and placebo. No significant difference was found between the groups in terms of side effects such as vomiting, headache, pain and nausea during lactation, except for more frequent shivering in women receiving prostaglandin Tremor was more common in women receiving prostaglandin compared to placebo, but there were no significant differences in vomiting, headache, maternal pain or nausea
Yaju Y, Kataoka Y,Eto H, Horiuchi S, Mori R	2013	Systematic Rewiew	1466 women Randomized controlled and quasi-experimental 5 studies	To reduce bleeding in postpartum period, there is no clear evidence that prophylactic oral metlergometrin use after placenta birth is effective in reducing postpartum hemorrhage, there is also uncertainty about the efficacy of prophylactic use of herbal medicine or homeopathic remedies for PPH.
Liabsuetrakul T, Choobun T, Peeyananjarassri K, Islam QM	2011	Systematic Rewiew	Total: 3941 women 6 randomized controlled and semi-experimental studies Experimental group: 1996 Control group: 1945	It was identified that prophylactic intramuscular or intravenous injections of ergot alkaloids in the third phase of labor significantly reduced mean blood loss, postpartum hemorrhage at least 500 ml and therapeutic uterotonic use significantly, however, its effect on the risk of placental involvement or manual removal was unclear. Especially intravenous administration of ergot alkaloids after deliveryn was significantly caused pain that requires analgesia after birth and rise in blood pressure. However, it was found not to cause symptoms such as vomiting, nausea and headache. When we look at the evidence of oral, intramuscular or intravenous administration of ergometry, oral route was found not to be very effective. Although the IV route reduces blood loss, it was determined that it caused high blood pressure and pain due to uterine contraction. Intramuscular administration was found to be beneficial in reducing blood loss and had fewer side effects than IV administration.
Soltani H, Hutchon DR, Poulose TA	2010	Systematic Rewiew	1671 women 3 Randomized controlled experimental study	It was found that the only uterotonic drug used in the studies was oxytocin and the dose and route of administration of oxytocin changed. Also it was determined that the administration of oxytocin before and after the birth of the placenta did not significantly affect the condition of postpartum hemorrhage (blood loss greater than 500 ml), the length of the third stage of birth (minutes), amount of postpartum blood loss (ml), hemoglobin changes (g / dL), blood transfusion, additional uterotonic use, the incidence of maternal hypotension and the incidence of severe PPH (blood loss of 1000 ml or more), placental retantion ratio.

Figure 1. Study flow diagram using the PRISMA 2009 flow diagram