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Review Article

Care technologies to prevent and control hemorrhage in the third stage of labor: a systematic review*

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Objective: to identify evidence concerning the contribution of health technologies used to prevent and control hemorrhaging in the third stage of labor. Method: systematic review with database searches. First, two researchers independently selected the papers and, at a second point in time, held a reconciliation meeting. The Kappa coefficient was used to assess agreement, while the Grading of Recommendations, Assessment, Development and Evaluation was adopted to assess risk of bias and classify level of evidence. Results: in this review, 42 papers were included, 34 of which addressed product technologies, most referred to pharmacological products, while two papers addressed the use of blood transparent plastic bags collector and the contribution of birth spacing and prenatal care. The eight papers addressing process technologies included the active management of the third stage of labor, controlled cord traction, uterine massage, and educational interventions. Conclusion: product and process technologies presented high and moderate evidence confirmed in 61.90% of the papers. The levels of evidence confirm the contribution of technologies to prevent and control hemorrhaging. Clinical nurses should provide scientific-based care and develop protocols addressing nursing care actions.

Descriptors: Postpartum Hemorrhage; Biomedical Technology; Disease Prevention; Diffusion of Innovation; Maternal Death; Nursing Care.

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Introduction

Postpartum hemorrhage (PPH) is one of the main causes of maternal morbidity and mortality worldwide[1-2]. PPH is defined as blood loss above 500 ml, measured up to 24 hours postpartum, while this amount of blood loss after 24 hours is defined as secondary PPH[1,3]. Blood loss up to 500ml among healthy women does not lead to negative consequences; however, uncontrolled blood loss over 500ml can be fatal[1]. Primary PPH occurs in the first 24 hours after birth and is more likely to result in maternal morbidity and mortality, while secondary postpartum hemorrhage refers to bleeding that occurs from 24 hours up to six weeks after birth[1,3].

In general, blood loss is diagnosed as PPH if one or more of the following occur: loss of uterine tone (atony); retention of placental tissue or blood clots; laceration of the genital tract; or coagulopathy[1,3]. Procedures to prevent PPH are initiated by assessing a patient's risk profile and establishing how to respond to complications in order to prevent a small amount of bleeding from becoming a severe hemorrhage with the risk of death. PPH is one of the complications of the third stage of labor and this stage begins after the fetus is expelled; however, with the detaching of the placenta from the uterine wall and its expulsion through the birth canal, greater than expected bleeding may occur. Therefore, it is essential to know the physiology of childbirth and women's clinical conditions, as well as intercurrences that took place during the pregnancy-puerperal period, which might contribute to the emergence of hemorrhaging[1,4].

In order to prevent PPH, the staff needs to be prepared to use protocols with a multidisciplinary approach, which involves maintaining hemodynamic stability while, simultaneously, identifying and treating the cause of bleeding. A combination of prediction and prevention, early identification and rapid coordinated actions is essential to preventing PPH. Consequently, efficient communication among the members of the multidisciplinary obstetrical team is paramount[5].

Prevention and control of PPH demand technologies that support labor and interventions in the event unwanted bleeding occurs. Therefore, health workers should be aware of and implement technologies supported by a higher level of evidence and with positive outcomes, which represent the least harm to women and babies. Additionally, for safe and timely care to be provided, services need to have a well-established capacity to coordinate people, equipment and work processes. Hence, having techniques and technologies as well as protocols does not ensure, by itself, the prevention and control of hemorrhaging; personnel of sufficient quality and number to meet demand is necessary.

Technologies, evidence-based practice, and interventions proposed by workers have grown exponentially in importance from the mid-twentieth century, so much so that providing quality services without such resources is inconceivable currently, with many of them being innovative in nature[6]. All these aspects a service is required to have are known as health technologies – a term that encompasses every intervention used to promote health. "In this sense, health technologies can be conceived as the practical application of knowledge, including machines, clinical and surgical procedures, medications, programs and systems intended to promote health care"[7].

Similarly, the literature presents the elements that integrate health technologies, namely any and all methods/devices used to promote health, prevent death, and treat diseases and improve rehabilitation or the care of individuals or populations[8].

Traditional product technologies (equipment, drugs and material) require intermediate steps with relatively differentiated processes and actors, although these are increasingly connected. Note that product technologies such as diagnostic or therapeutic resources used in healthcare delivery are more effective when combined with process technologies. Process technologies, in turn, include operational procedures, care, education and management techniques. Thus, one should seek a scientific basis to strengthen healthcare delivery and produce evidence to innovate in regard to product and process technologies[9-10].

There are various systematic reviews addressing PPH showing it still accounts for high levels of morbidity and mortality, mainly in developing countries. For this reason, studies need to be conducted regularly, considering that all technologies should be revised and updated over time, especially when we consider the application of technologies in different contexts and populations[6-8,11].

In order to overcome the causes of PPH and its determinants of a sociocultural, technical and technological nature in different geo-economic contexts, the results of systematic reviews should be disseminated among health services in order to contribute to the development of multidisciplinary protocols. In this context, nurses, especially those in the obstetrical field, can propose care processes, among others, such as those associated with patient safety, especially when applying pharmacological products[11].

Given the importance of hemorrhaging, which may be associated with diverse events such as uterine atony, uterine rupture, blood dyscrasia, cephalopelvic

disproportion and placental abruption[1], the need to prepare the staff to intervene appropriately, and lack of information regarding existing technologies in the field, the objective of this study was to identify evidence concerning the contribution of health technologies used to prevent and control hemorrhaging in the third stage of labor.

Method

This Systematic Review adopted the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) checklist[12] to present the results. The entire review process was guided by the question: What is the evidence available concerning the contributions of health technology used to prevent and control hemorrhaging in the third stage of labor?" The PIO (Patient, Intervention and Outcomes) support protocol[13] was used, in which P (population, participants) was represented by women with blood loss in the third stage of labor; I (intervention/procedure) was represented by technologies used to prevent PPH; and O (outcome) was the occurrence of PPH, level of blood loss, or success in managing the decrease of harm to women.

Data were collected from July 10 to 12, 2016 from the following databases: Latin American and Caribbean Health Sciences (LILACS), Database of Nursing (BDENF), Scientific Electronic Library Online – Brazil (SciELO - Brazil), National Library of Medicine (PubMed)/Medical Literature Analysis and Retrieval System on Line (MEDLINE) and Scopus. The period between June 2006 and July 2016 was chosen because we deemed it would contain the most current technologies. Studies, the title or abstract of which addressed the topic and were available in Portuguese, Spanish or English, were identified from July 13th to December 30th 2016. The search strategy included the following descriptors postpartumhemorrhage; hemorrhage; postpartumperiod; labor stage, third, which were adapted for MeSHTerms All Fields - hemorrhage; hemorrhages; hemorrhagic; bleeding; postpartum; puerperal; Third Stage. DeCS terms – postpartumhemorrhage [postpartumhemorrhage]; *Hemorragia Pós-Parto* [Postpartum Hemorrhage]*; Hemorragia Puerperal* [Puerperal Hemorrhage]*; Hemorragia Posparto* [Postpartum Hemorrhage]*; hemorragia* [hemorrhage]*; sangramento* [bleeding]*; Período Pós-Parto* [Post-partum Period]*; pos-parto* [post-partum]*; pós-parto* [post-partum]*; Terceira Fase do Trabalho de Parto* [Third Stage of Labor]. The following key words were used: *Terceiro período* [Third period]*; Terceiro estágio* [Third stage]*; Terceira etapa* [Third stage]. The Boolean expressions "AND", "NOT" and "OR" were used to locate the instances the aforementioned descriptors occurred simultaneously.

Two independent researchers selected the papers, examining each paper's title, abstract and full text according to the following inclusion criteria: studies addressing technologies to prevent hemorrhaging in the third stage of labor; home delivery or hospital delivery; delivery assisted by any birth assistance or traditional birth assistance; randomized clinical trial (RCT) or quasi-randomized, observational studies, or analytic descriptive studies. Exclusion criteria were: theses, dissertations, editorials, integrative or systematic reviews, descriptive observational studies, and qualitative studies.

After selecting the papers, the researchers held a meeting to reconcile agreements and disagreements by carefully consulting the full texts. Of the 48 papers selected, the researchers disagreed in regard to 10. After discussion, they decided to include four of these papers, with 42 papers being included in the final review. The Kappa coefficient[14-18], with a confidence interval of 95%, was applied to assess inter-rater agreement. This coefficient has the following measure levels: less than zero, "insignificant"; between 0 and 0.2, "weak"; between 0.21 and 0.40, "reasonable"; between 0.41 and 0.60, "moderate"; between 0.61 and 0.80, "strong"; and between 0.81 and 1.0, "almost perfect".

The levels of evidence identified in the papers were classified according to Grading of Recommendations Assessment, Development and Evaluation (GRADE)[19-20], a system sensitive to rating the quality of evidence. In this system, quality of evidence is classified as: high, moderate, low, or very low (Figure 1). Evidence originating from randomized clinical trials starts with a high level and evidence from observational studies with a low level.

Level	Definition	Implications
High	There is strong confidence that the true effect is close to what was estimated	Further studies are unlikely to change confidence in the estimate of effect
Moderate	Moderate confidence in the estimated effect	Further studies may change confidence in the estimate of effect, possibly even change the estimate
Low	Confidence is limited	Further studies are likely to have an important impact on our confidence in the estimate of effect
Very low	Confidence in the estimated effect is very limited. There is great uncertainty	Any estimate of effect is uncertain

Source: Adapted by the authors[19].

Figure 1 – Evidence levels. Florianópolis, SC, Brazil, 2018

In this study, the classification used (the GRADE system) to assess the quality of evidence took into account the risk of bias in randomized clinical trials addressing product technologies, in terms of methodological limitations concerning the design or implementation of individual studies. Evidence of randomized clinical trials may be downgraded if allocation is not confidential; absence of blinding; incomplete follow-up; a report of selective outcomes, and other limitations, such as: early interruption of the study due to some benefit or insufficient information to assess whether there is important risk of bias. Risk of bias was assessed for each of these domains and classified as high-risk, uncertain, or low risk of bias[20].

In the third stage of the process, after reading the full texts and excluding those that failed to meet the inclusion criteria, according to two independent researchers, we proceeded to the systematization of studies.

In order to compile and synthetize the results of the different studies included in the review, we organized tables and grouped the technologies into two categories: product technologies and process technologies. Tables are presented in the results.

Results

After applying the search strategies, 6,999 papers were found. Of these, 6,726 were excluded due to the following: the titles and/or abstracts of 5,978 papers did not meet the inclusion criteria; 652 papers were published in more than one database; and 96 were not characterized as papers (e.g., theses, dissertations, integrative literature reviews, descriptive observational studies, papers other than scientific research, and qualitative studies)

The full texts of 273 papers were read and 42 were included (Figure 2). The Kappa coefficient[14-18], which was equal to 0.86 in the first stage and equal to 1.00 in the second, revealed a high level of inter-rater agreement.

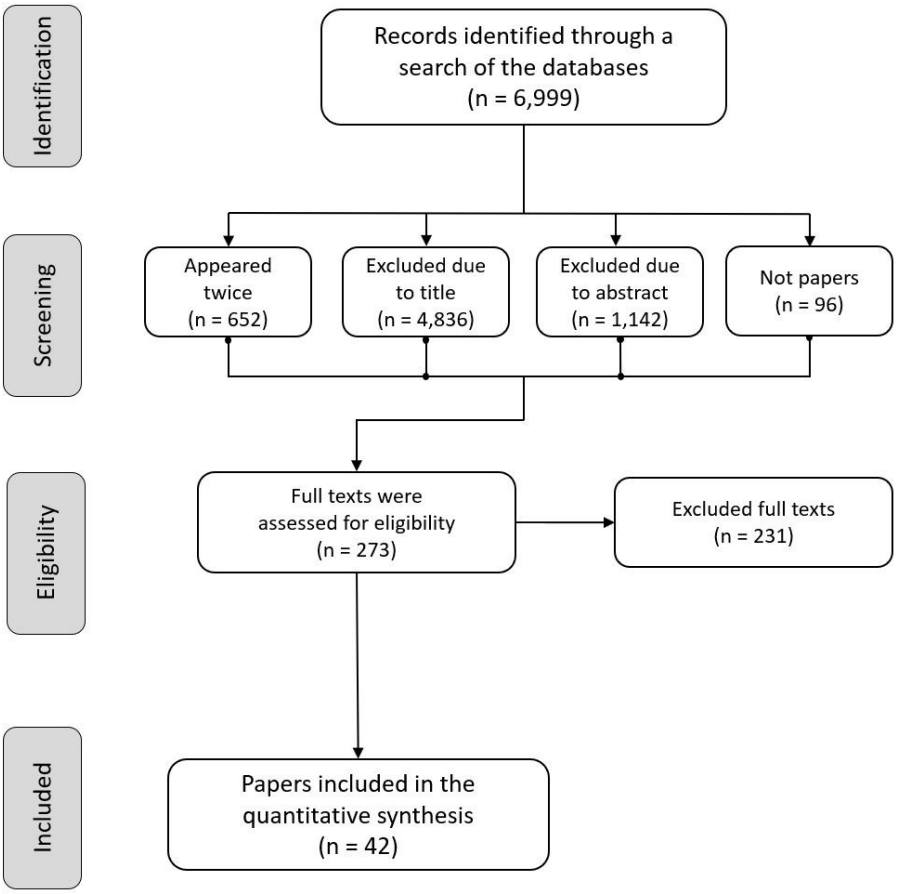

Figure 2 - Flowchart PRISMA concerning the studies' identification and screening process. Florianópolis, SC, Brazil, 2018

Regarding the methods used by the papers under study, 39 are RCTs; one is a quasi-experimental study; one is a retrospective cohort; and one is an observational study. The risk of bias was assessed in the 39 randomized clinical trials addressing technologies to prevent and control hemorrhaging in the third stage of labor using the GRADE system (Figure 3). The findings show that 14 papers present High Level evidence (35.9%), 12 present Moderate Level evidence (30.8%), and 13 present Low Level evidence (33.3%). The remaining studies (quasi-experimental, retrospective cohort and observational studies) maintained the original Low Level evidence (Figures 4 and 5).

Study	Randomization	Allocation concealment	Levels of blinding	Follow-up loss	Other sources of bias
Musa et al.[21]	Systematic random sampling. Participants were assigned according to double-blind randomization, using computer-generated random numbers prepared by an independent statistician, and concealed for data analysis.	Opaque envelopes containing random numbers were opened in the third stage of labor.	The participants, caregivers and evaluators of outcomes were blind in regard to the groups' allocation	5.66% oxytocin group and 3.84% misoprostol group	--
Rajaei et al.[22]	Simple randomization using computer-generated random numbers.	Uncertain	Reported as double blind	Uncertain/does not report	--
Atukunda et al.[23]	A biostatistician generated a random list of 570 participants in each group.	The MRA* received opaque envelopes were labeled with study codes	Participants and assessors were blind	There was none	The participation of eligible participants decreased (54.9%)
Bellad et al.[24]	Simple randomization using computer-generated random numbers.	Packaged in properly encoded envelopes	Reported as double blind	There was none	Used misoprostol instead of a placebo
Vagge et al.[25]	Simple randomization.	Does not report	Uncertain	Uncertain/does not report	--
Firouzbakht et al.[26]	Patients were randomly assigned to two groups.	Does not report	Does not report	Uncertain/does not report	Small sample
Tita et al.[27]	Women were randomly assigned to one of the study's three groups according to confidential computer-generated block randomization algorithm	Bags numbered according to a randomization scheme	Reported as double blind	none	Sample was insufficient to respond to the primary outcome
Gutarra-Vilchez et al.[28]	Systematic randomization	Uncertain/does not report	Patients and those involved in the investigation were blind	Uncertain/does not report	A physician assigned the patients to the groups
Shrestha et al.[29]	Randomization was performed when vaginal delivery was imminent. Women were randomly assigned according to lottery technique.	Uncertain/does not report	Uncertain/does not report	Uncertain/does not report	--
Güngördük et al.[30]	Simple randomization using a random numbers list.	Oxytocin infusions were prepared and labeled as randomization bags	Patients and providers were blind	8.00% in the oxytocin group and 8.48% in the placebo group	--
Nasr et al.[31]	Randomization to each group through a computer-generated random allocation system.	Sealed envelopes pre-prepared with computer-generated numbers	Reported as double blind	There was none	--
Caveda Gil et al.[32]	Randomization into 3 groups of 200 members each, according to type of treatment.	Opaque and encoded envelopes	Patients and workers were blind	Uncertain/does not report	--
Samimi et al.[33]	Randomization was performed using a random number list.	Both drugs were encoded and packaged before recruiting.	Patients and physicians were blind	9.00% in the carbetocin and 7.00% follow-up loss in the syntometrine group	--
Singh et al.[34]	Randomization using computer-generated random numbers.	Drug packages were sealed and encoded using a computer-generated random number graph	The head nurse not involved in the study opened the assigned package; the researcher was blind for the package's content	There was none	--
Orji et al.[35]	Randomly assigned to the oxytocin and ergometrine groups	Sealed envelopes were used in the allocation	None	Uncertain/does not report	--
Uthman et al.[36]	Prospective, randomized study.	Uncertain	Uncertain/there was none	Uncertain/does not report	--
Ugwu et al.[37]	The method of blocked randomization was used and the participants were randomly assigned.	Opaque and sealed envelopes containing details of allocation were used	Researchers and data analysts were blind in regard to assignment	There was none	Small sample
Zachariah et al.[38]	All women who experienced vaginal births were randomly assigned to one of the three groups using computer-generated random numbers.	Medication was given according to randomization	None	Uncertain/does not report	--

(the Figure 3 continue in the next page...)

Study	Randomization	Allocation concealment	Levels of blinding	Follow-up loss	Other sources of bias
Stanton et al.[39]	Randomization was determined using Stata†, which generated the sequence of allocation	Packaged in bags	Uncertain/Not reported	There was none	--
Diop et al.[40]	Computer-generated random allocation was supervised by the Gynuity Health Projects, clusters	Medications were packaged in single-dose envelopes with individual numbering	None	27.54% misoprostol group and 22.54% oxytocin group	Cannot report on uterotonic coverage at the community level.
Zuberi et al.[41]	The sample was randomized into blocks of ten and stratified by site using a computer-generated random sequence.	Envelopes contained three misoprostol or placebo tablets	All women, providers, and researchers were blind in regard to the treatment assignment	Uncertain/does not report	Small sample
Patil[42]	Each of the patients was assigned to one of the groups using the colored coin method (random sampling method)	Not reported	None	Uncertain/does not report	--
Ononge et al.[43]	Randomization was obtained using a computer-generated numeric sequence	Not reported	None	19.90% in the control group and 12.00% in the intervention group	--
Mobeen et al.[44]	Randomization was obtained using a computer-generated random code	Medication was packaged in numbered boxes encoded by colors to identify randomization sequence	All women and midwives were blind in regard to the study's task	3.53% misoprostol group and 4.28% in the placebo group	--
Derman et al.[45]	Randomization was obtained using a computer-generated random block size	Envelopes were numbered and each envelop had a five-digit code number assigned to it	Uncertain	0.36% in the misoprostol group and 0.12% in the placebo group	--
Harriott et al.[46]	Patients were randomly assigned	Uncertain	None	Uncertain	--
Bajwa et al.[47]	Patients were randomly assigned into three groups with 100 people each	Encoded envelopes: O‡ group, S§ group, and R‖ group.	The nursing staff was blind: the nature of the medications were not reported	Uncertain/does not report	--
Widmer et al.[48]	Randomization was computer generated and stratified by country	To conceal the allocation, treatment boxes were sealed and numbered.	The workers and participants were blind in regard to the assignment of treatment	There was none	--
Hofmeyr et al.[49]	A sequence of random numbers generated by computer was used for random allocation and stratified by country	Medications were placed in identical packages in terms of form, color, weight and feeling.	Reported as double blind	0.18% in the misoprostol group and 0.54% in the placebo group	--
Miller et al.[50]	Computer-generated random list	Packages tested in approved random sample	Reported as double blind	0.84% misoprostol group and 0.61% in the ZB11¶ group	--
Su et al.[51]	The randomization list with intervention mode allocation was sent to the Hospital Pharmacy	Both medications were packaged and encoded.	Midwives, obstetricians and participants were blind	There was none	--
Ducloy-Bouthors et al.[52]	Computer-generated random sequence	Uncertain	Assessment of each endpoint was performed with researchers blind in regard to assignment of treatment	6.49% in the tranexamic and 2.70% in the placebo group	Small sample
Zhang et al.[53]	The maternities were randomly assigned to groups using collector bags after vaginal delivery and not using collector bags	Not reported	Reported as double blind	There was none	--
Jangsten et al.[54]	Women were assigned to active or expectant management using computer-generated randomization	Sealed envelopes were prepared in consecutive order	The pregnant women were blind	1.69% in the active management group and 2.38% in the expectant management group	--

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Study	Randomization	Allocation concealment	Levels of blinding	Follow-up loss	Other sources of bias
Yildirim et al.[55]	Randomization was done by using standardized forms assigned to each group	Allocation was concealed by using sealed opaque envelopes.	Uncertain, not reported	1.80% active management group and 2.67% expectant management group	--
Gülmezoglu et al.[56]	Computer-generated random sequence obtained at the WHO**¶	A computer was programmed with a random sequence of allocation developed with the women's information, which were entered in the computer by local researchers. In Egypt and Kenya, sealed opaque envelopes had to be used instead, due to breach and theft in the middle of the process.	Neither the researchers nor the participants could be blinded for the interventions or outcomes	5.12% active simplified management group and 3.50% active complete group	--
Althabe et al.[57]	Randomization was stratified per hospital and the sequence generated in the coordinating center with computer-generated random block numbers	Women were assigned using sequence numbers and sealed opaque envelopes.	When childbirth was imminent, a midwife registered the patient on the next numbered envelope and communicated the intervention assigned to the assistant	1.94% CCT†† group and 2.97% control group	--
Chen et al.[58]	The participants were assigned according to computer-generated random allocation	Numbered opaque envelopes containing random allocations were kept in the delivery room at each study site.	No blinding was used due to the nature of the intervention.	There was none	--
Deneux-Tharaux et al.[59]	Cluster randomization was obtained using a random number generator available at SAS‡‡	Uncertain	Uncertain	There was none	The control group did not receive any intervention

*MRA - Midwife Research Assistants; †Stata - Statistical Software for Data Science, ‡O - Oral; §S - Sublingual; ‖R - Rectal; ¶ZB11 - Zhi Byed 11; **WHO – World Health Organization; ††CCT – Controlled Cord Traction; ‡‡SAS – Statistical Analysis Software.

Figure 3 – Risk of bias in randomized clinical trials classified as technologies to prevent and control hemorrhage in the third stage of labor. Florianópolis, SC, Brazil, 2018

Authors and years	Settings and country of study	Objectives	Type of study	Participants	Outcomes	EL*
Musa et al.[21]	Department of Obstetrics and Gynecology, University Hospital at Ilorin, Nigeria	Compare the efficacy of oral misoprostol with oxytocin in AMTSL†	RCT‡ controlled double-blind	200	The third stage of labor was longer in the oxytocin group, while blood loss and drop in hemoglobin was greater in the misoprostol group, though differences were not significant. Thus, both drugs are efficacious to be used in AMTSL†	High
Rajaei et al.[22]	Hospital at Shariati, Bandar Abbas, Iran	Compare the safety and efficacy of 20UI§ of oxytocin and 400µg‖of oral misoprostol for PPH¶ prevention	RCT‡ controlled double-blind	400	The amount of blood loss was greater in the oxytocin group. Hemorrhaging decreased significantly when misoprostol was used to prevent PPH¶	Moderate
Atukunda et al.[23]	Regional Referral Hospital Mbarara, Uganda	Compare the use of SL** misoprostol with IM†† oxytocin to prevent PPH¶	RCT‡ controlled double-blind non-inferiority	1,140	SL** misoprostol is inferior to oxytocin in the prevention of primary PPH¶ among women who underwent vaginal births without complications	High
Bellad et al.[24]	University Hospital in Belgaum, India	Assess the efficacy of one dose of 400µg‖ of SL** misoprostol with 10UI§ of IM†† oxytocin to decrease post-partum hemorrhage and blood loss	RCT‡ controlled double-blind	652	This study verified that SL** misoprostol is more efficacious in decreasing PPH¶ than IM†† oxytocin. The SL** or powder form of misoprostol may increase its efficacy in the prevention of PPH¶, making it superior to the injectable oxytocin	High
Vagge et al.[25]	Hospital of Vanivila, India	Compare the efficacy and safety of rectal misoprostol with IV‡‡ oxytocin to prevent primary PPH¶	RCT‡ controlled prospective	200	There was no significant difference between groups in terms of the occurrence of PPH¶. Thus, both drugs are equally efficacious and safe.	Low

(the Figure 4 continue in the next page...)

Authors and years	Settings and country of study	Objectives	Type of study	Participants	Outcomes	EL*
Firouzbakht et al.[26]	Hospital Imam Ali, in Amol, Iran	Assess and compare the efficacy and safety of rectal misoprostol and oxytocin to prevent PPH¶	RCT‡	100	Rectal misoprostol was as efficacious as IV‡‡ oxytocin to prevent PPH¶, presenting the same incidence of side effects. For this reason, the routine use of misoprostol as an uterotonic agent in AMTSL† is recommended.	Low
Tita et al.[27]	University Hospital in Birmingham, Alabama, USA	Compare the efficacy of two higher dosages of oxytocin (80 and 40UI§) with the routine dosage (10UI§) among women who underwent vaginal childbirth	RCT‡ controlled double-blinded	1,798	Comparison between 10, 80 and 40UI§ of prophylactic oxytocin shows that it does not decrease the need for PPH¶ treatment in general. The group that received 80 units presented a decreased need for additional oxytocin and also a decrease of 6% or more in the risk of falling hematocrit	Moderate
Gutarra-Vilchez et al.[28]	Gynecology and Obstetrics Service of the Vitarte Hospital in Lima, Peru	Assess the efficacy and safety of childbirth using intra-umbilical oxytocin and expectant management with partial clamping compared to traditional childbirth without these interventions.	RCT‡ controlled	180	Labor assisted with intra-umbilical oxytocin and labor assisted with expectant management were more efficacious than routine labor	Low
Shrestha et al.[29]	Department of Obstetrics and Gynecology at the Dhulkhel Hospital, Nepal	Compare the efficacy of rectal misoprostol with IM†† oxytocin to prevent PPH ¶	RCT‡ prospective and analytical	200	Rectal misoprostol is as efficacious as oxytocin in the prevention of postpartum hemorrhage, with a similar incidence of side effects	Low
Güngördük et al.[30]	Department of Obstetrics and Gynecology of Bakirkoy and Maternal and Children's University Hospital in Istanbul, Turkey	Estimate the efficacy of intra-umbilical oxytocin as a routine in the AMTSL† to decrease blood loss and its duration in the third stage of labor	RCT‡ prospective double-blind	412	Estimated mean blood loss was significantly lower among women treated with oxytocin compared to women in the placebo group. The third stage of labor was significantly shorter in the oxytocin group than in the placebo group.	High
Nasr et al.[31]	Department of Obstetrics and Gynecology at the University Assiut, Egypt	Assess the effect of 800µg‖ of rectal misoprostol and 5UI§ of IV‡‡ oxytocin as prophylaxis for PPH¶	RCT‡ Controlled prospective double-blind	514	Misoprostol was as effective as oxytocin in decreasing the incidence of PPH ¶. Even though women who used misoprostol needed uterotonics and blood transfusion more frequently in comparison to those who used oxytocin, differences were not significant	High
Caveda Gil et al.[32]	Delivery Service at the Gynecological Obstetrical Hospital Mariana Grajales Coello, in Santiago, Cuba	Establish a new indication for the obstetrical practice: active childbirth with SL** prostaglandin and show its efficacy and safety when compared to the standard procedure.	RCT‡ controlled double blind concealed	600	SL** misoprostol in the two dosages proposed was more efficacious and safer in the active management of labor than IM†† oxytocin	Moderate
Samimi et al.[33]	Shabih Khani Maternity Center in Kashan, Iran	Compare the efficacy of carbetocin and syntometrine in the prevention of PPH ¶	RCT‡ double blind	200	Carbetocin is more effective than syntometrine in the prevention of postpartum hemorrhage	High
Singh et al.[34]	Guru Teg Bahadur Hospital, India	Compare the efficacy and adverse effects of SL** misoprostol, IV‡‡ oxytocin and IV‡‡ methyl ergometrine in the AMTSL†	RCT‡ double-blind	300	The administration of 600µg‖ of SL** misoprostol was more effective than 400µg‖ of SL** misoprostol, IV‡‡ oxytocin, and methyl ergometrine in the active management of the third stage of labor	High
Orji et al.[35]	Obafemi Awolowo University Hospital, Ile-Ife, Nigeria	To compare the use of oxytocin and ergometrine in the active course of the third stage of labor	RCT‡ Prospective	600	Oxytocin is as effective as ergometrine in decreasing the incidence of PPH¶, but side effects such as nausea, vomiting, and high blood pressure were more frequently associated with ergometrine	Low
Uthman et al.[36]	Maiduguri University Hospital, Specialized Hospital of Maiduguri and Yerwa Maternal and Child Health Center in Maiduguri, Nigeria	Compare the contribution of birth spacing and prenatal care in the occurrence of PPH¶ and verify how these factors interfere in preventive actions using oxytocin and misoprostol	RCT‡ Prospective, comparative and multicenter	1,140	Inadequate birth spacing and inadequate prenatal care are risk factors for PPH¶. The relative efficacy of oral misoprostol and IV‡‡ oxytocin varies significantly when associated with different levels of prenatal care and birth spacing.	Very low

(the Figure 4 continue in the next page...)

Authors and years	Settings and country of study	Objectives	Type of study	Participants	Outcomes	EL*
Ugwu et al.[37]	Obstetrics Unit of the University Hospital, Ibadan, State of Oyo, Nigeria	Compare the efficacy and adverse effects of 200μg‖ and 400μg‖ of misoprostol to prevent PPH¶	RCT‡ Controlled	124	Blood loss and the occurrence of PPH¶ did not differ according to the dosage of misoprostol. The dosage of 200μg‖, however, was associated with decreased levels of adverse effects.	Moderate
Zachariah et al.[38]	Medical College Christian Hospital, Vellore, India	Compare the efficacy of IV‡ ergometrine, IM†† oxytocin and oral misoprostol in the AMTSL†	RCT‡ Controlled, prospective	2,023	400μg‖ of oral misoprostol is as well-tolerated and effective as oxytocin or ergometrine, used in the AMTSL† to prevent PPH¶. The drug is stable at an ambient temperature, easy to administer, thus, its routine use is recommended in low-resource settings.	Low
Stanton et al.[39]	Brong-Ahafo region, Ghana	Assess the efficacy, safety and viability of injectable oxytocin administered by unskilled caregivers in home childbirth to prevent PPH¶	RCT‡ cluster population based	1,586	Prophylactic oxytocin applied by people without obstetrical skills decreased the risk of PPH¶ caused by blood loss greater or equal to 500ml§§	Moderate
Diop et al.[40]	Studies conducted in 28 mobile maternity tents in three health districts in Senegal	Compare the efficacy of oxytocin and misoprostol distributed by auxiliaries midwives in tent maternity hospitals	RCT‡ cluster controlled	1,049	Both drugs can be offered by auxiliary midwives to prevent PPH. The results suggest that misoprostol might present some advantages over the single-dose oxytocin used in communities	Moderate
Zuberi et al.[41]	Four hospitals in Karachi, Pakistan	Determine the auxiliary benefit of misoprostol when combined with conventional oocytes to treat PPH¶	RCT‡	61	Adding 600μg‖ of SL** misoprostol to the PPH¶ standard treatment suggest a tendency to decrease postpartum blood loss, a smaller drop in postpartum hemoglobin and a lower need for additional interventions	Low
Patil[42]	Department of Obstetrics and Gynecology of University Hospitals in Basaveshwar and Sangmeshwar, India	Compare the efficacy and adverse effects of rectal misoprostol with PGF2α‖‖ in the prevention of PPH¶	RCT‡	200	PPH¶ occurred in a smaller number in the group that received PGF2α‖‖ IM†† in comparison with the group that received rectal misoprostol	Low
Ononge et al.[43]	The studies were conducted in 31 health units in Mpigi, Uganda	Determine whether the distribution of misoprostol during prenatal care for self-administration at home decreases PPH¶	RCT‡ stepped-wedge cluster	2,057	The study did not report a significant decrease of PPH¶ between the groups, though the prenatal distribution of misoprostol increased the use of uterotonics at birth	Low
Mobeen et al.[44]	Chitral, Khyber Pakhtunkhwa province, Pakistan	Determine whether misoprostol administered in home childbirth by traditional trained midwives is safe and efficacious to prevent PPH¶	RCT‡ double blind, controlled, placebo	1,119	The administration of 600μg‖ of oral misoprostol by trained traditional midwives in home births decreased the rate of PPH¶. Considered easy to use and low-cost, misoprostol might decrease the number of PPH¶ cases	High
Derman et al.[45]	Four Primary Health Care Centers, in the Belgaum District, India	Investigate whether oral misoprostol is a potential alternative to oxytocin to prevent PPH¶ in home births in the community	RCT‡ controlled, placebo	1,620	Oral misoprostol was associated with a significant decrease in the rate of acute PPH¶ and severe acute PPH¶. One case of PPH was prevented for every 18 women treated. Women who received misoprostol experienced a higher rate of transient symptoms, such as chills and fever, compared to the women in the control group	Moderate
Harriott et al.[46]	University Hospital of West Indies, Jamaica	Compare the clinical effect of rectal misoprostol with IM†† syntometrine to decrease blood loss in the third stage of labor		140	There were no significant differences in the duration of the third stage of labor or blood loss in the active management groups with misoprostol and syntometrine. The treatment with syntometrine was associated with an increase in systemic blood pressure in the postpartum. Rectal misoprostol was well-tolerated in 88.5% of the participants	Low
Bajwa et al.[47]	University Hospital of a medical school, India	Compare the effects of oral, rectal and sublingual misoprostol in AMTSL†	RCT‡ prospective	300	The administration of 400μg‖ of oral, sublingual and rectal misoprostol was equally efficacious in AMTSL†, however the administration of rectal misoprostol was better accepted, presented comparable efficacy and a minimum incidence of side effects	Moderate
Widmer et al.[48]	Hospitals in Argentina, Egypt, South Africa, Thailand and Vietnam	Assess the efficacy of misoprostol as a complement for standard uterotonics in comparison with standard uterotonics alone to treat PPH¶	RCT‡ double- blind multicenter	1,422	The analysis did not show significant differences between the misoprostol and the placebo groups associated with routine uterotonics. Although, for every three women treated with misoprostol, an additional episode of tremors was recorded in comparison to placebo. The results did not suggest the clinical use of 600μg‖ SL** misoprostol in addition to standard uterotonics to treat PPH¶	High

(the Figure 4 continue in the next page...)

Authors and years	Settings and country of study	Objectives	Type of study	Participants	Outcomes	EL*
Hofmeyr et al.[49]	Hospitals in South Africa, Uganda and Nigeria	Assess the efficacy and safety of oral misoprostol associated with uterotonic therapy in AMTSL†	RCT‡ double-blind, multicenter, controlled placebo	1,103	The results did not confirm the beneficial effect of administering 400µg‖ of SL** misoprostol in addition to the routine uterotonic therapy during the third stage of labor; only superficial benefits. The benefit of adding misoprostol may not outweigh the likelihood of adverse effects	High
Miller et al.[50]	Three obstetrical units in Lhasa, Tibet, People's Republic of China	Compare the traditional Tibetan medicine (uterotonic *ZB11*¶¶) with oral misoprostol to the prophylaxis of PPH¶	RCT‡ Double-blind controlled placebo	960	The results show that if oral misoprostol were available and accessible, it could have decreased rates of PPH¶ (equal to or greater than 500mL§§) than o *ZB11*¶¶, though no significant differences were found in regard to severe PPH¶ and mean/median blood loss	High
Su et al.[51]	Hospital of the National University, Singapore	Compare IM†† carbetocin with IM†† syntometrine to prevent PPH¶ among women who underwent normal childbirth	RCT‡ controlled double-blind, prospective	370	The women in the carbetocin group (13.5%) and the syntometrine group (16.8%) had PPH¶ and required additional uterotonics. Tremors, sweating, nausea, vomiting and uterine pain were more common among the syntometrine group than in the carbetocin group. The drugs present similar efficacy in preventing PPH¶, but carbetocin is associated with fewer adverse effects	High
Ducloy-Bouthors et al.[52]	Eight obstetrical centers, France	Determine whether the administration of one high dosage of tranexamic acid used to treat PPH¶ can decrease blood loss	RCT‡ controlled, open, multicenter	144	High dosages of tranexamic acid might decrease blood loss and morbidity among women with a diagnosis of PPH¶. Even though the study was not properly designed to address safety issues, side effects were rapid and transient	Moderate
Zhang et al.[53]	Studies were conducted in 78 maternity hospitals of 13 European countries	Assess the efficacy of the systematic use of a transparent plastic collector bag to measure blood loss after vaginal birth in decreasing the incidence of severe PPH	RCT‡ cluster	25,381	Severe PPH¶ occurred in 1.71% of the intervention group using collector bags and 2.06% of the control group. This difference was not statistically significant. For this reason when intervention is compared with visual estimate of postpartum blood loss, the use of a collector bag after vaginal birth does not decrease the rate of severe PPH¶	Moderate
Irshad et al.[60]	Allied Hospital, Faisalabad, Pakistan	Determine the efficacy and the adverse effects of misoprostol in the management of primary PPH¶ due to uterine atony	Quasi-experimental intervention study	100	Misoprostol was shown to be an effective drug in the treatment of primary PPH¶ caused by uterine atony	Low

*EL – Evidence Level; †AMTSL - Active Management of the Third Stage of Labor; ‡RCT – Randomized Clinical Trial; §IU – International Units; ‖µg - Microgram; ¶PPH - Postpartum Hemorrhage; **SL - Sublingual; ††IM - Intramuscular; ‡‡IV - Intravenous; §§mL - Milliliter; ‖‖PGF2α - Prostaglandin F2α; ¶¶ZB11 - *ZhiByed 11*.

Figure 4 – Distribution of papers classified as product technologies. Florianópolis, SC, Brazil, 2018

Study	Settings and country of study	Objectives	Type of study	Participants	Results	EL*
Jangsten et al.[54]	Two units in a University Hospital, Swede	Compare blood loss in women in active management and expectant management in the third stage of labor	RCT†	1,802	Active management of the third stage of labor was associated with decreased blood loss and a lower rate of severe PPH‡ compared to expectant management	High
Yildirim et al.[55]	Maternal-Child Hospital Istanbul Bakirkoy, Turkey	Compare the protocol of active management among women at low-risk of PPH using the protocol of expectant management in regard to changes in hematological parameters, uterotonics, blood transfusions or additional interventions.	RCT† controlled prospective	654	Even though the active management of the third stage of labor was associated with higher levels of postpartum hemoglobin, it did not influence the risk for severe PPH‡ among women at low risk for PPH‡	Moderate
Gülmezoglu et al.[56]	16 hospitals and two health centers in Argentina, Egypt, India, Kenya, Philippines, South Africa, Thailand and Uganda	Investigate whether the simplified approach of AMTSL§ without CCT‖ is less efficacious than the complete set of actions	RCT† controlled, multicenter of noninferiority	23,681	The study shows that CCT‖ presents a superficial benefit to the complete set of actions for the third stage of labor, especially when compared to oxytocin, which appears as the main component of this set	Moderate
Althabe et al.[57]	Two public maternity hospitals in Montevideo, Uruguay	Assess whether CCT‖ in the third stage of labor decreases postpartum blood loss in comparison to the physiological management of labor protocol (hands-off)	RCT† controlled	204	The difference of blood loss between the two groups was not significant, however, delay in collecting blood in the hands-off group was greater, which may have influenced the result. The study suggests that controlled cord traction may decrease postpartum blood loss	High
Chen et al.[58]	Four university hospitals, China	Assess whether trans-abdominal uterine massage decreases blood loss after vaginal birth	RCT† controlled, multicenter	2,340	Uterine massage following placental deconditioning, accompanied by oxytocin, among patients who underwent vaginal birth, did not decrease blood loss when compared with the administration of oxytocin only	Moderate
Deneux-Tharaux et al.[59]	Six perinatal networks, France	Test a multifaceted intervention to facilitate the implementation of a protocol for the early management of PPH‡	RCT† cluster	106	The mean rate of severe PPH‡ was 1.64% in intervention units and 1.65% in control units; the difference was not significant. Therefore, this educational intervention did not change the rates of severe PPH‡ when compared to the control group	Low
Segura Fernández et al.[61]	Central Military Hospital Dr. Luis Díaz Soto in La Habana, Cuba	Determine the utility of active management of the third stage of labor in maternal morbidity caused by PPH‡	Observational, analytical, cross-sectional study	2,523	AMTSL§ was associated with a lower need for blood transfusion, shorter duration of the third stage of labor, lower rates of puerperal hysterectomy and fewer admissions to the intensive care unit. These results show that the AMTSL§ is a protective factor against PPH‡ , according to the variables under study.	Low
Saxton et al.[62]	Three hospitals, Australia	Investigate whether two physiological elements (skin-to-skin contact and breastfeeding) implemented after birth present benefits decreasing the rates of PPH‡	Cohort retrospective study	7,548	The risk of PPH‡ decreased four times among women who practiced skin-to-skin contact and breastfed. This study suggests that these practices implemented immediately after birth can be efficacious to decrease the rates of PPH‡	Low

*EL – Evidence Level; †RCT – Randomized Clinical Trial; ‡PPH – Postpartum Hemorrhage; §AMTSL - Active Management of the Third Stage of Labor; ‖CCT – Controlled Cord Traction.

Figure 5 – Distribution of papers classified as process technologies. Florianópolis, SC, Brazil, 2018

The papers were classified as product and process technologies[9]. Among the 34 papers classified as product technologies (Figure 4), most were represented by pharmacological products and only two papers refer to another type of product, that is, plastic collector bag and the contribution of birth spacing and prenatal care.

Thirty, out of the 34 papers classified as product technologies addressed technologies directed to the prevention of PPH, including eight papers that accessed the isolated use of misoprostol; four addressed the use of oxytocin through different routes and dosages; 12 studies compared misoprostol to oxytocin; two studies compared carbetocin to syntometrine; one analyzed ergometrine *versus* oxytocin; one ergometrine *versus* oxytocin *versus* misoprostol; one addressed PGF2α (Prostaglandin F2α) *versus* misoprostol; and one compared ZB11 *(ZhiByed 11* – Tibetan traditional medicine) to misoprostol. Product technologies to prevent PPH encompassed studies that presented interventions using uterotonic drugs and transparent plastic collector bag.

Eight papers were classified as process technologies (Figure 5), which included: active management of the third stage of labor; controlled cord traction; skin-to-skin contact and breastfeeding; sustained trans-abdominal uterine massage; and educational intervention.

Discussion

The evidence supports decision-making concerning clinical practice and gives rise to new ways to approach a problem over time. Changes in care practice, however, are slow considering that the production of knowledge and its incorporation require qualified personnel, as the application of evidence in care practice is a responsibility of not only one profession but of the entire care system; thus, it is a responsibility of all the professionals in institutions and of society itself. Therefore, one has to consider the sociocultural and educational context, as well as safety culture and the innovation taking place in health services concerning practice, intervention and outcomes. Otherwise, evidence may become innocuous if professionals are mobilized by repetition rather than innovation, commitment and responsibility to life.

It is, therefore, based on this assumption that we present evidence reported by the 42 studies that make up this systematic review: 33 of these analyzed the efficacy of uterotonic drugs to prevent/treat PPH, including studies addressing oxytocin, misoprostol, ergometrine, syntometrine, carbetocin, PGF2α and ZB11. Oxytocin and misoprostol appear as the most studied drugs, with results for them being presented in a larger number of publications.

In regard to the product technologies, most papers addressed the use of uterotonics during the third period of labor and recommend them to prevent PPH. The studies addressing the efficacy of different dosages of synthetic oxytocin, report a shorter duration of the third stage of labor[21-31], when compared to other drugs, regardless of the dosage and route of administration, with the exception of one study[32].

In regard to blood loss, six studies[22,24,32-35] report that oxytocin presented a mean blood loss. Birth spacing influences this result; that is, greater blood loss in found among childbirths with intervals of less than two years[36]. Other studies[21,25-26,28,30] did not report significant differences in regard to this aspect.

Significant differences were not reported by the studies addressing oxytocin in the third stage of labor in regard to the occurrence of PHH and/or severe PPH and drop in the concentration of hematocrit/hemoglobin[21-23,25-27,31,37-38]. Other studies[22,24], however, presented a greater occurrence of PPH in the oxytocin group, requiring a greater use of additional uterotonics in this group. The employment of oxytocin in intervals shorter than two years between births determined a greater occurrence of PPH[36]. Additionally, a drop in the concentration of hematocrit in the oxytocin group was significant in the postpartum[24,32].

The administration of oxytocin, even by unskilled individuals, was efficacious to control PPH and also to decrease blood loss, as well as the need to refer patients to referral units[39]. One study[40], however, reports greater amounts of blood loss in the oxytocin group.

The use of misoprostol was analyzed in studies with different compositions and administration routes to prevent PPH[21-26,29,31-32,37,41]. These studies show that, regardless of the dosage of misoprostol, the duration of the third stage of the labor did not present significant differences, nor did the drop in the concentration of hematocrit/hemoglobin, except in those papers[24,32] that found a decrease in the concentration of these hematological components.

Studies report that both that the duration of the third period of labor and mean loss of blood were significantly longer and greater[23,29,42-43] and shorter and lower[22,24,32,34,37,41].The occurrence of PPH and/or severe PPH was greater among women who received misoprostol[22,43-44]. The RCTs[21,26,32,36,46] report that misoprostol was more efficacious in preventing PPH among women with inadequate birth spacing, that is, less than two years. This drug/dosage/route was

effective when used in the treatment of primary PPH caused by uterine atony[59].

When considering the route of administration, sublingual misoprostol was more efficacious, decreasing the duration of the third stage of labor and mean blood loss in comparison to the rectal and oral routes. Conversely, side effects like fever and tremors were more frequent when the sublingual route was used. The group who received the medication through the oral route presented a greater need for additional uterotonics. In terms of acceptability, rectal misoprostol was better accepted by women and was the one with fewer side effects[46-47].

Side effects were common in all women who received misoprostol. Most studies comparing oxytocin to misoprostol report significant differences in which groups treated with misoprostol experienced more side effects, especially tremors and fever[21-26,29,31,34,37-38,42,44-45,47-50], with the exception of one study[32] that did not report significant differences. Other symptoms like nausea, vomiting and diarrhea were found, but no significant differences were found between groups [21-26,29,31,38,43,50].

Seven studies[21,23,25,31,43-45] recommend misoprostol be adopted in areas where routine uterotonics are not available, as it is the best option to prevent PPH, given its ease of application, stability at ambient temperature and low cost. This is a safe and efficacious alternative to be used by midwives and auxiliaries in home births. Misoprostol is the most viable choice in communities[40] and is easy to store[42]. In areas where there are routine uterotonics available, however, the benefits of misoprostol might not outweigh the discomfort of side effects[49].

In regard to the viability of using misoprostol in communities, a study that distributed it during prenatal care for women to self-administer it at home, no significant decrease of PPH was found. Nonetheless, the use of uterotonics increased as did the return visits of women to the health service. The self-administration of misoprostol with little monitoring and supervision was considered safe[43], though women need to be better educated on when to use misoprostol in regard to placental deconditioning.

In regard to misoprostol, RCTs present a high level of evidence[21,24,31,34,40,44,50] recommending the use of this uterotonic via the oral, sublingual and rectal routes in different dosages, indicating it is efficacious, economically viable and easy to administer. Therefore, the use of misoprostol in areas with few resources is a good alternative to oxytocin. Analysis of bias indicated there were no methodological limitations regarding the design or implementation of the individual papers presented. The RCTs[43,59] with moderate evidence indicate that oral misoprostol is the only pharmacological option available in areas with few resources to prevent postpartum hemorrhaging and bleeding. Other studies[25-26,29,41-43,46] addressed in this review and that address the use of misoprostol also make similar recommendations but, in accordance with GRADE (Figure 3), present methodological limitations. Further studies need to focus on the potential efficacy of misoprostol in areas where standard uterotonics are not available.

In regard to the use of oxytocin, RCTs with moderate level of evidence[35,39] recommend the prophylactic use of misoprostol to prevent PPH, while this is an essential intervention. Thus, oxytocin is the drug of choice whenever available and with a 10UI dosage; it is as efficacious as ergometrine in decreasing the incidence of PPH, though without the undesirable side effects associated with ergometrine. These studies present methodological limitations regarding the blinding of participants.

As noted in the previous paragraph, in addition to misoprostol and oxytocin, the efficacy of ergometrine, syntometrine and PGF2α in preventing PPH was also compared. Studies addressing ergometrine[33-35,38] report no significant differences in regard to the remaining uterotonics assessed in terms of blood loss, drop in hematocrit, duration of the third stage of labor, or the additional need of other drugs. The risk of side effects (nausea, high blood pressure, headaches and vomiting), however, was greater in the group receiving ergometrine. For this reason, the recommendation to use ergometrine depends on the relevance of risks[35].

In regard to syntometrine, the studies intending to determine the severity and incidence of this drug's side effects report no significant differences in terms of the duration of the third stage of labor, amount of blood loss, and use of additional uterotonics[33,46]. Significant differences, however, were reported by another study[51], in regard to nausea, tremors, vomiting, uterine pain, and sweating.

In the comparison performed between syntometrine and carbetocin in the prevention of PPH[33,51], carbetocin was more efficacious than syntometrine, though one of the studies[51] does not report relevant differences between the efficacies of both. The study with carbetocin identified fewer side effects and, even though an analysis of cost/efficacy was not performed, the author reports that the cost of carbetocin is ten times greater than the cost of syntometrine, while emphasizing that carbetocin was associated with fewer side effects, so that its use can contribute to reduced costs and time required for professionals.

PGF2α in one RCT[42] was more efficacious than misoprostol in decreasing mean blood loss and the duration of the third stage of labor and the drop in hemoglobin levels. The associated gastrointestinal side effects, however, were significantly greater and included nausea, vomiting, diarrhea and abdominal cramps.

One RCT[50] conducted in China addressed the ZB11 uterotonic, used in Tibetan traditional medicine to prevent PPH. The results show higher rates of PPH in the ZB11 group in comparison to the misoprostol group. No significant differences were found in terms of blood loss. Side effects such as diarrhea, tremors, and fever were less recurrent. The authors[50] suggest that other studies be undertaken in that geographic area because home births performed by the pregnant women themselves, or without the assistance of qualified workers, is not uncommon. Thus, research addressing efficacious uterotonics with accessible prices is especially relevant in areas with these characteristics and can contribute to women's easier access to safe technologies[50]. This specific RCT was assessed using the GRADE system and was considered to have a high level of evidence, presenting no methodological limitations.

Another drug that was addressed in order to verify its efficacy and safety in preventing and treating PPH was tranexamic acid (TA)[52]. The authors covering this drug report that high dosages of TA can decrease blood loss and maternal morbidity among women with PPH. Due to moderate quality evidence, this drug is recommended only in cases in which oxytocin and other uterotonics are not able to stop hemorrhaging.

Another product technology that was assessed in European countries was the transparent plastic collection bag. A multicenter RCT assessed its efficacy in preventing severe PPH, based on the measurement of blood lost after vaginal birth. The results reveal no significant differences when blood loss was measured using a collector bag or only visually verified. The authors note that more studies are needed to develop strategies able to decrease severe PPH by improving care management[53].

In regard to process technologies, we initially verified that some authors conducted RCTs[54,60] and an observational study[61] to verify changes in hematological parameters caused by blood loss among women who received AMTSL (Active Management of the Third Stage of Labor) and the expectant management of the third stage of labor. They concluded that blood loss was greater and the level of hemoglobin was lower in the group with expectant management.

Active management of the third stage of labor is especially indicated for primiparous women, but the findings of a systematic review[54,60] did not find valid and relevant evidence regarding the efficacy of physiological care in the third stage of labor among women at a low risk for PPH.

Decreased blood loss has a greater impact on the health of women in low-income countries[54,60]; however, if active management is the preferred option for AMTSL among low-risk women in high-level hospitals in developed countries, the only benefit will be to decrease drops in hemoglobin caused by childbirth[54].

Another technology used to prevent PPH is the controlled cord traction (CCT) adopted in vaginal births to superficially decrease blood loss and reduce the duration of the third stage of labor. A multicenter RCT investigated the simplified approach of AMTSL without CCT and its results show that the risk of PPH, rate of manual removal of placenta, mean blood loss, and duration of the third stage of labor were greater in the group in which CCT was not performed[56]. Not performing CCT led to an increase in the risk of severe hemorrhaging, especially when compared to the effect of oxytocin, which is the main component of AMTSL. In regard to this process technology, more clinical studies are needed to verify whether CCT decreases blood loss and prevents PPH among women who received prophylactic oxytocin in the third stage of labor[56].

Still in regard to the prevention of PPH, the efficacy of skin-to-skin contact and breastfeeding after birth in decreasing PPH rates were also investigated. Risk for PPH decreased by almost four times among women practicing these. The highest effect in this study was among women at a lower risk of PPH. Both practices, when implemented immediately after birth, might be efficacious in decreasing PPH rates, regardless of the already existing risk factors for PPH [62].

According to the authors, these practices promote the release of endogenous oxytocin, and they emphasize that pregnant women should be educated and supported in the implementation of these practices during the third and fourth stage of labor[62]. Note, however, these that the application of such practices should include a rigorous assessment of the clinical conditions of the women, because such a resource is not viable for those with at-risk pregnancies.

In regard to technology intended to prevent and control severe PPH and maternal morbidity and mortality, one paper addressed here focuses on sustained trans-abdominal uterine massage. The multicenter RCT[57] verified whether this technology can decrease blood loss after vaginal birth. The results show that patients who underwent vaginal birth, having received uterine massage combined with uterotonics, did not experience a decrease in blood loss when compared to the administration of uterotonics only. The group of women who received uterine massage reported pain and/or discomfort when

receiving the massage and asked for it to be stopped[57]. Routine uterine massage is not a technology indicated for the prevention of PPH after vaginal childbirth. It is a time-consuming and painful procedure and eliminating this practice from AMTSL benefits the obstetrical team because, in addition to saving effort, the time used in its application can be directed to other tasks[57].

Another technology addressed is an educational intervention. Whether the implementation of a protocol of early PPH prevention decreased the incidence of severe PPH was assessed. The pregnant women involved were randomly assigned to the educational intervention (where sensitization meetings were held and the protocol was discussed) or only received the protocol without interventions. The results show that the mean rate of severe PPH did not differ in the units that received the educational intervention. Some elements of the PPH prevention protocol, however, were more frequently used in the units that received the intervention, such as asking for the help of specialized personnel and asking for specialized service within 15 minutes of PPH being diagnosed[58]. The authors emphasize that educational interventions are increasingly necessary to improve clinical practices in the face of new technologies and changes implemented in care components.

Some limitations were identified in this systematic review. A total of 39 RCTs were found and, *a priori*, one assumes these present equivalent scientific rigor and evidence. After applying the GRADE system, however, a lack of methodological rigor was identified in 13 studies, which were classified as presenting low level evidence. Additionally, among the 34 papers classified as product technology, most is represented by pharmacological products.

Still, the knowledge gathered here regarding the health technologies used to prevent and control hemorrhaging in the third stage of labor contributes to the development of evidence-based instruments and protocols intended to prevent and control PPH. Moreover, studies conducted by nurses in the context of clinical practice can lead to new technological developments, whether product or process technologies, in order to meet the needs of women and to reduce avoidable deaths.

Cross-referencing with other descriptors should also be considered in future studies.

Conclusion

Product technologies of a pharmacological nature, especially uterotonics such as misoprostol and oxytocin, the studies of which compose the body of analysis, presented high and moderate evidence on the prevention and control PPH in the third stage of labor, in addition to contributing to decreased blood loss, shorter duration of the third stage of labor, improved concentration of hematocrit/hemoglobin and a reduced need for additional uterotonics.

Among the studies addressing process technologies, the active management of the third stage of labor presented high, moderate and low evidence level, while controlled cord traction presented a high level of evidence. When product technology (oxytocin) was associated with process technology (uterine massage), the level of evidence was moderate.

Therefore, the prevention and control of hemorrhaging in the third stage of labor requires studies addressing the association of product and process technologies, considering the evidence found so far concerning the contributions of these technologies. Clinical nurses should incorporate scientific evidence, conduct new systematic reviews and develop nursing protocols to provide women with the best possible care practices.

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