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EVIDENCE BASED CARE



Effect of Herbal Medicines on Postpartum Hemorrhage: A Systematic Review and Meta-Analysis

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Abstract

Background: Postpartum hemorrhage is one of the most common causes of maternal mortality worldwide.

Aim: The present systematic review and meta-analysis aimed to evaluate the effectiveness of herbal medicines on a postpartum hemorrhage.

Method: The largest proportion of articles with funding information was found from 2000 to 2020 were included using PubMed, Scopus, ISI Web of Science, Cochrane, Magiran, SID, and Google Scholar databases. The relevant English keywords, "postpartum hemorrhage, PPH control, PPH prevention, phytotherapy, herbal medicine, complementary medicine, traditional medicine" were used to search for the eligible studies. Data were analyzed using STATA software (version 11).

Results: The results indicate heterogeneity in the studies ($I^2=0.87$). Standardized mean difference was (SMD= -1.08, 95% CI: (-1.31, -0.85), $P<0.001$), (SMD= -0.80, 95% CI: (-1.03, -0.58), $P<0.001$), (SMD= -1.13, 95% CI: (-1.36, -0.90), $P<0.001$) in the first, second and third hour after delivery, respectively. The bleeding rate was statistically lower in the intervention group than that of the control group.

Implications for Practice: This meta-analysis indicated the positive role of herbal medicines in reducing postpartum hemorrhage. Therefore, herbal medicines might be a proper substitute for chemical medicines and could be used in combination with pharmaceutical drugs such as oxytocin to reduce early postpartum hemorrhage.

Keywords: Herbal medicine, Meta-analysis, Postpartum hemorrhage, Systematic review

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Introduction

Postpartum hemorrhage (PPH) is an emergency obstetric condition, which is recognized as one of the leading causes of maternal mortality worldwide. PPH is defined as a blood loss of 500 mL or more from the genital tract after the third stage of vaginal delivery which is divided into two categories of early and late. Most postpartum hemorrhage-related mortality occurs within the first 24 hours, which is referred to as early postpartum hemorrhage. The occurrence of moderate to severe bleeding may range from 24 hours to 12 weeks following the delivery, which is defined as late postpartum hemorrhage (1, 2). The prevalence of postpartum hemorrhage varies between 3-8% (3). PPH causes 25% of maternal deaths per year (4, 5). It has been estimated that one mother goes missing every four minutes due to the unavoidable complications of pregnancy and childbirth (6, 7). Uterine atony is introduced as the most prominent cause of postpartum hemorrhage and accounts for about 70% of cases (8-10). Untreated postpartum hemorrhage can lead to iron deficiency anemia, pituitary infarction (Sheehan's syndrome), poor lactation, shock, and eventually death (1, 6).

Various preventive measures such as mechanical, pharmacological, non-pharmacological, and surgical methods can be implemented to treat this condition based on the source of bleeding. Mechanical approaches include bladder drainage, Bimanual uterine compression massage, Bakri balloon, and non-pneumatic anti-shock garment (11). Pharmacological strategies encompass the use of Ergometrin, Oxytocin, Syntocinone, Carboprost, and Misoprostol to reduce postpartum hemorrhage by stimulating contractions. Oxytocin is the most commonly used chemical medication for preventing uterine atony. Administration of excess dosage of oxytocin can lead to hypotension, convulsions, coma, and eventually maternal death (1). Surgical procedures of intrauterine balloon tamponade, uterine hemostatic sutures such as B-Lynch, bilateral uterine artery occlusion, bilateral iliac artery occlusion (hypogastric), selective artery embolization, and hysterectomy substitute are performed as alternative methods in case of medication failure (1, 12).

Apart from the widespread use of synthetic drugs, these drugs possess economic and health side effects which highlight the necessity for fewer choices of hazardous medications. The use of plant-based products is on the surge in the world. Herbal remedies have fewer side effects than synthetic drugs (13). Therefore, the use of medicinal plants and traditional treatments is highly regarded as a preventive measure against bleeding (14, 15). Several herbs such as *Capsella bursa-pastoris*, date, Grape Seed Powder, *Anethum graveolens*, *Plantago major* have been recommended to control postpartum hemorrhage (13, 16-20). Ghalandari et al. (2017) evaluated the effect of Hydroalcoholic extract of *Capsella bursa pastoris* on reducing postpartum hemorrhage (16). Yadegari et al. (2016) also concluded that the consumption of dates reduces postpartum hemorrhage (20). Izadpanah et al. (2018) examined the impact of grape seed powder on reducing postpartum hemorrhage (17). A study conducted by khojastehfard et al. (2019) indicated that *Plantago major* rectal suppository can reduce postpartum hemorrhage (18).

Various studies have been conducted on postpartum hemorrhage as the main cause of maternal mortality. To the best of our knowledge, these studies have not been reviewed in Iran. Systematic review and meta-analysis are essential tools for accurately and reliably summarizing the available evidence (21). Although studies have been performed on the effects of herbal medicines on postpartum hemorrhage, the effectiveness of all these herbal medicines has not been studied. Therefore, performing a clear and coherent meta-analysis is essential to provide a comprehensive guide for policymakers and researchers (22). The effect of these herbal medicines on postpartum hemorrhage has not been identified despite the diversity of plants in the ecosystem of Iran. Also, women are reluctant to use chemical drugs after childbirth, because these drugs are excreted in milk and have side effects for the neonates. Therefore, using herbal medicines will be more acceptable during breastfeeding (23, 24). The present study was performed to review the effectiveness of herbal medicine in postpartum hemorrhage in Iran.

Methods

The present review and meta-analysis aimed to identify evidence of the effectiveness of herbal remedies on a postpartum hemorrhage. All relevant English and Persian articles (2000-2020) were included in the present study. Eligible studies were selected by searching the national (SID, Magiran) and international (PubMed, Scopus, ISI, Cochrane, and Google Scholar) databases. In advanced search of databases, English or Persian equivalent of following Medical Subject Headings

(postpartum hemorrhage OR PPH control OR PPH prevention), (herbal medicine OR complementary medicine OR traditional medicine) and Boolean operators of "AND" and "OR" were searched to collect eligible studies.

Abstracts of all the articles were extracted and reviewed. The inclusion criteria were all randomized controlled trials conducted in Iran in Persian or English language, interventions included herbal medicines on postpartum hemorrhage and the primary outcome was postpartum hemorrhage in the first, second and third hour after delivery. Exclusion criteria were all the articles that were reported at conferences, congresses, or meetings without full-text, as well as descriptive and observational studies, reviews and letters to the editor, and case series.

The references of the articles were reviewed for more information. The data were extracted according to the authors, publication date, type of study, sample size, measuring tools, results, and side effects of the prescribed medicine (Table 1). The quality of the articles in the systematic review was assessed by two independent reviewers using a Cochrane bias tool. This tool examines seven types of bias such as Random sequence generation (Selection bias), Allocation concealment (Selection bias), Blinding of participants and personnel (performance bias), Blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), Selective reporting (reporting bias), and other sources of bias (Figure 1, 2).

Data were analyzed using STATA software (version 11). The heterogeneity of the studies was determined using I^2 index. $I^2 < 0.25$, $.25 < I^2 < 0.75$ and $I^2 > 0.75$ are indicators of low, average and high heterogeneity, respectively. Standardized mean difference (SMD) and the random-effects model were utilized to combine the results of the studies. Egger's test was conducted to detect publication bias. In all the analyzes, the significance level was considered 0.05.

Table 1. Characteristics of articles included in the review process

No	Author/country/reference	Type of study	Samples	Intervention group	Control group	Measurement tool	Results	Side effects
1	Izadpanah et al./ 2018/ Iran/(17)	Four-group, double-blind, randomized controlled trial	120 pregnant women referring to Vali-e-Asr Maternity Hospital of Birjand	3 groups (n=30 each) receiving grape seed powder with the doses of 50, 100, and 150 mg, along with 20 units of oxytocin	1 group (n=30) receiving placebo (containing starch capsules) with 20 units of oxytocin	Plastic covered drape and pad	Grape seed powder appeared to be effective in preventing postpartum hemorrhage (P<0.001).	Not reported
2	Abedian et al./ 2016/ Iran/(25)	Two-group, double-blind, randomized controlled trial	70 multiparous women with vaginal delivery referring to Ommolbanin Hospital in Mashhad	1 group receiving 1,000 mg of chamomile capsule, along with 30 units of oxytocin infusion during the first 2-4 hours after delivery	1 group receiving 250 mg mefenamic acid with 30 units of oxytocin during the first 2-4 hours after delivery	Weighing the drapes and pads	No statistically significant difference was observed in the mean of bleeding in the intervention group, in comparison with the control group, 1, 2, 3, 4, 5, and 6 hours of post-delivery stage (P>0.05).	One case of nausea and vomiting and one report of oversleeping
3	Khojastehfard et al./ 2019/ Iran/(18)	Two-group, single-blind, randomized controlled trial	70 women giving birth at Ommolbanin Hospital in Mashhad	1 group (n=35) receiving 5 doses of 120 mg rectal immediately after placental withdrawal and in half an hour intervals along with 30 units of oxytocin infusion	1 group (n=35) receiving 30 units of oxytocin	Blood bags and weight of the pads	The amount of postpartum hemorrhage was significantly lower in the intervention group than in the control group (P<0.05).	Not reported
4	Yadegari et al./ 2016/ Iran/(20)	Two-group, randomized controlled trial	90 nulliparous women referring to Ommolbanin Hospital in Mashhad	1 group (n=45) receiving 100 g <i>Phoenix dactylifera</i> within 2 hours after delivery and then administrated with 100 g of <i>Phoenix dactylifera</i> daily with breakfast	1 group (n=45) receiving less than 50 g of <i>Phoenix dactylifera</i> in the first week of the post-delivery stage	A sanitary pad and standard pectoral scale	There was a statistically significant difference in the amount of bleeding between the two groups on day 2 to day 10. However, <i>Phoenix dactylifera</i> did not affect reducing the number of bleeding days.	Not reported

Table 1. Continued process

Study ID	Author(s) / Year	Study Design	Participants	Intervention	Control	Outcome Assessment	Notes	Conclusion
5	Mahdavian et al./ 2002/ Iran/ (19)	Single-blind, randomized clinical trial	72 pregnant women referring to Hazrat Zeinab Hospital in Mashhad	1 group (n=36) receiving 0.018 g/kg dill extract dissolved in 50 ml of water and 2 gr of sugar	1 group (n=36) receiving 10 units of intramuscular oxytocin and 50 ccs of water with 2 gr of sugar solution	Weighing the used gases during episiotomy repairmen and plastic covered drape used for the first and second hours of postpartum	Mean scores of bleeding in the first hour after delivery were 87.6±40.4 and 52.6±23.2 in the oxytocin and the intervention group, respectively. Dill extract was found to be more effective in reducing postpartum hemorrhage than the intramuscular injection of oxytocin.	Not reported
6	Khadem et al./ 2007/ Iran/ (26)	Two-group, randomized controlled trial	62 women giving birth at Imam Reza and Zeinab hospitals in Mashhad	1 group (n=31) receiving 50 g of <i>Phoenix dactylifera</i> orally after placental removal	1 group (n=31) receiving 10 units of intramuscular oxytocin	Weighing the plastic covers and pads every hour, continued for 3 hours after delivery	<i>Phoenix dactylifera</i> can be more effective in reducing postpartum hemorrhage than the intramuscular injection of oxytocin.	Not reported
7	Mojahed et al./ 2012/ Iran/ (13)	Two-group, single-blind, randomized controlled trial	95 women giving birth at Shahid Sadoughi Hospital in Yazd	1 group (n=44) receiving 100 g <i>Phoenix dactylifera</i> with a glass of warm water and 20 units of oxytocin infusion	1 group (n=51) receiving 20 units of oxytocin infusion	Weighing the plastic covers, cotton sheets, and pads 2 hours after delivery	The consumption of <i>Phoenix dactylifera</i> could be an effective approach in reducing postpartum hemorrhage.	Not reported
8	Fazel et al./ 2013/ Iran/ (27)	Double-blind, randomized clinical trial	124 women with transverse cesarean section referring to Shahidan Mobini Hospital in Sabzevar	1 group (n=58) receiving 40 drops of Cuminum spray dissolved in 30 ml of water three times for 20 minutes; 24 hours after cesarean section	1 group (n=66) receiving 40 drops of placebo dissolved in 30 ccs of water three times for 20 minutes; 24 hours after cesarean section	Weighing the pads and plastic covers before the intervention and after 3 hours following the first dose of medication or placebo	The mean postpartum hemorrhage in the Cuminum and placebo group was 45.26±71.28 and in the placebo group was 45.30±53.41, which was not statistically significant (P=0.997). Cuminum spray did not increase post-cesarean bleeding.	Not reported
9	Ghalandari et al./ 2017/ Iran/ (16)	single-blind, randomized clinical trial	100 Pregnant women referring to Afzalipour Hospital in Kerman	1 group (n=50) receiving 10 drops of sublingual hydroalcoholic extract of <i>Capsella bursa-pastoris</i> with 20 units of oxytocin immediately after the expulsion of the placenta	1 group (n=50) receiving 10 sublingual drops of placebo with 20 units of oxytocin immediately after the expulsion of the placenta	Weighing the gases used during episiotomy repair, plastic-covered drapes, and pads every hour up to the third hour after the placenta removal	Hydroalcoholic extract of sublingual <i>Capsella bursa-pastoris</i> was effective in reducing postpartum hemorrhage.	One case with a sore throat and itchy throat symptoms in the case group and one case with nausea symptoms among controls

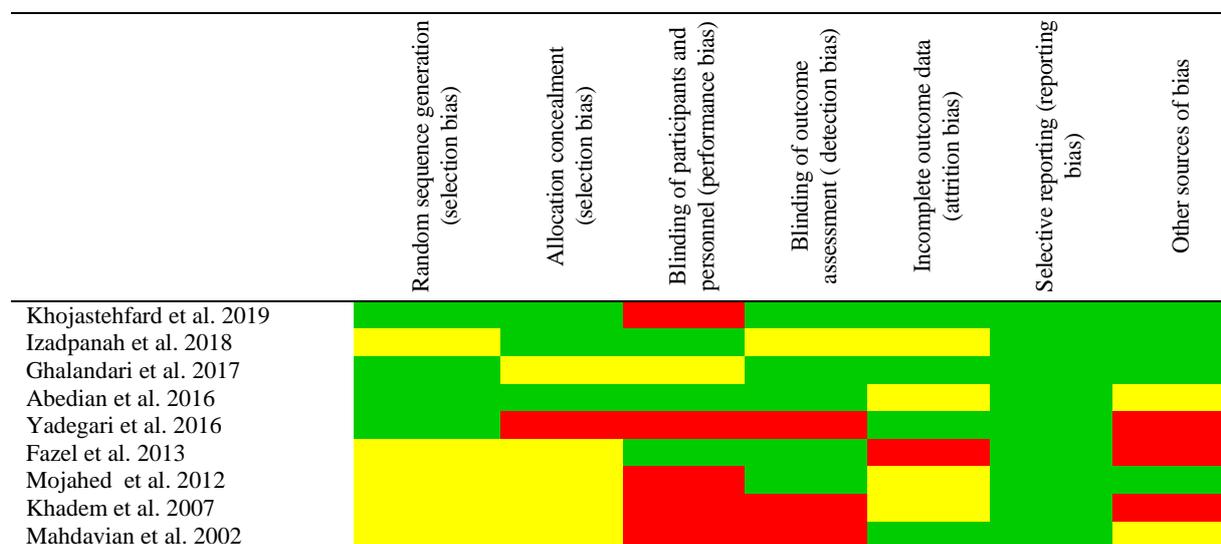


Figure 1. Author's judgments for risk of bias items for each study

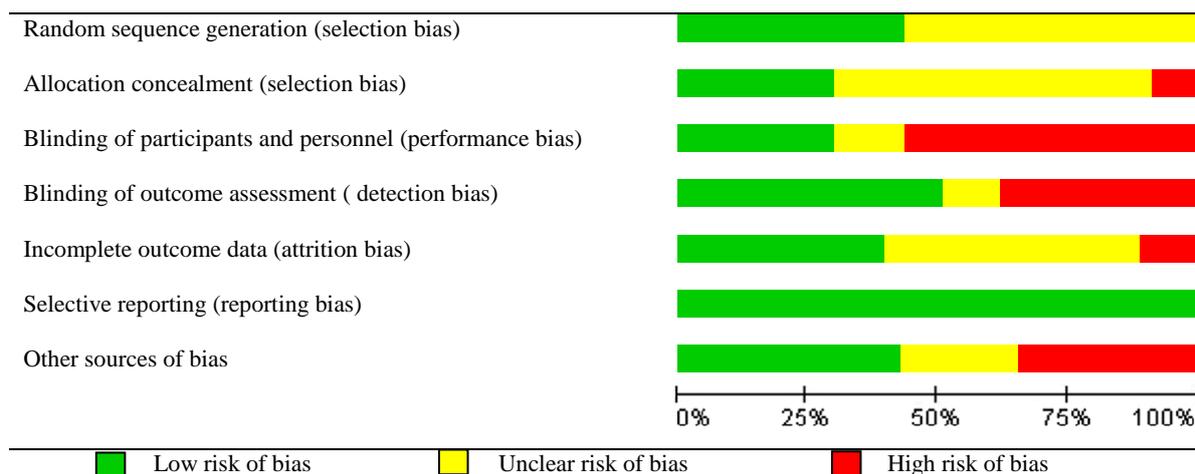


Figure 2. Authors' judgments of risk of bias presented as percentages for each study

Results

In the initial literature review, 18596 primary articles were retrieved. A total of 120 articles have remained after excluding duplicate, irrelevant data, screening of title, abstract and unrelated data. Full-text articles were reviewed based on inclusion criteria after eliminating 83 studies. Finally, after several stages of review, 9 full-text articles and 3 articles were entered into the systematic review, and the meta-analysis, respectively (Figure 3).

The plants studied in this review were Grape Seed, Chamomile Matricaria, Plantago major, Anethum graveolens, Phoenix dactylifera, Cuminum cyminum L, Capsella bursa pastoris, and Capsella bursa pastoris.

Grape seed

The functional and chemical compounds found in grape seed powder can contain several flavonoids with a phenolic and non-flavonoids structure. It also contains substances, such as gallic acid and epigallocatechin gallate, tannins, high levels of omega-6 fatty acids, and lower levels of omega-3 fatty acids, vitamins C and E, procyanidin, carotenoids, magnesium, calcium, iron, phosphorus, and potassium. The results of various studies have suggested a promising role for omega-6, linoleic acid, vitamins C and E, and tannin in controlling the bleeding (17).

Matricaria chamomilla

Chamomile is an herbaceous plant, belonging to the Cichorium intybus L. family. The flower of the plant is used as a rich source of chemical compounds, among which flavonoids, bisabolol, chamazulene, and spirocheten are the most significant ones. According to the existing evidence, in Norway, Chamomile was administered to relieve pain during labor and as a means to stop postpartum hemorrhage. Chamomile extract can impose an inhibitory effect on cyclooxygenase and lipoxygenase pathways and hinder prostaglandins and leukotrienes production (25).

Plantago major

The *Plantago major* extract contains numerous chemical compounds, including mucilage, tannin, organic acids, invertin, emulsin, tannin, glucoside called okobin, and flavonoids. The tannins and flavonoids content of *Plantago* can stimulate estrogen receptors, myometrial, and uterine artery contractions, leading to a reduction in postpartum hemorrhage (18).

Anethum graveolens

The chemical constituents of this herbal plant include tannins, a resinous substance, and a volatile essential oil consisting of limonene, ketone, Carvone, and a fatty substance, present in its leaves as Flanders and Anolol's essential oil. Tannins are polyphenols that possess contractile properties. Furthermore, it can positively affect menstrual bleeding and dysmenorrhea symptoms among women (19).

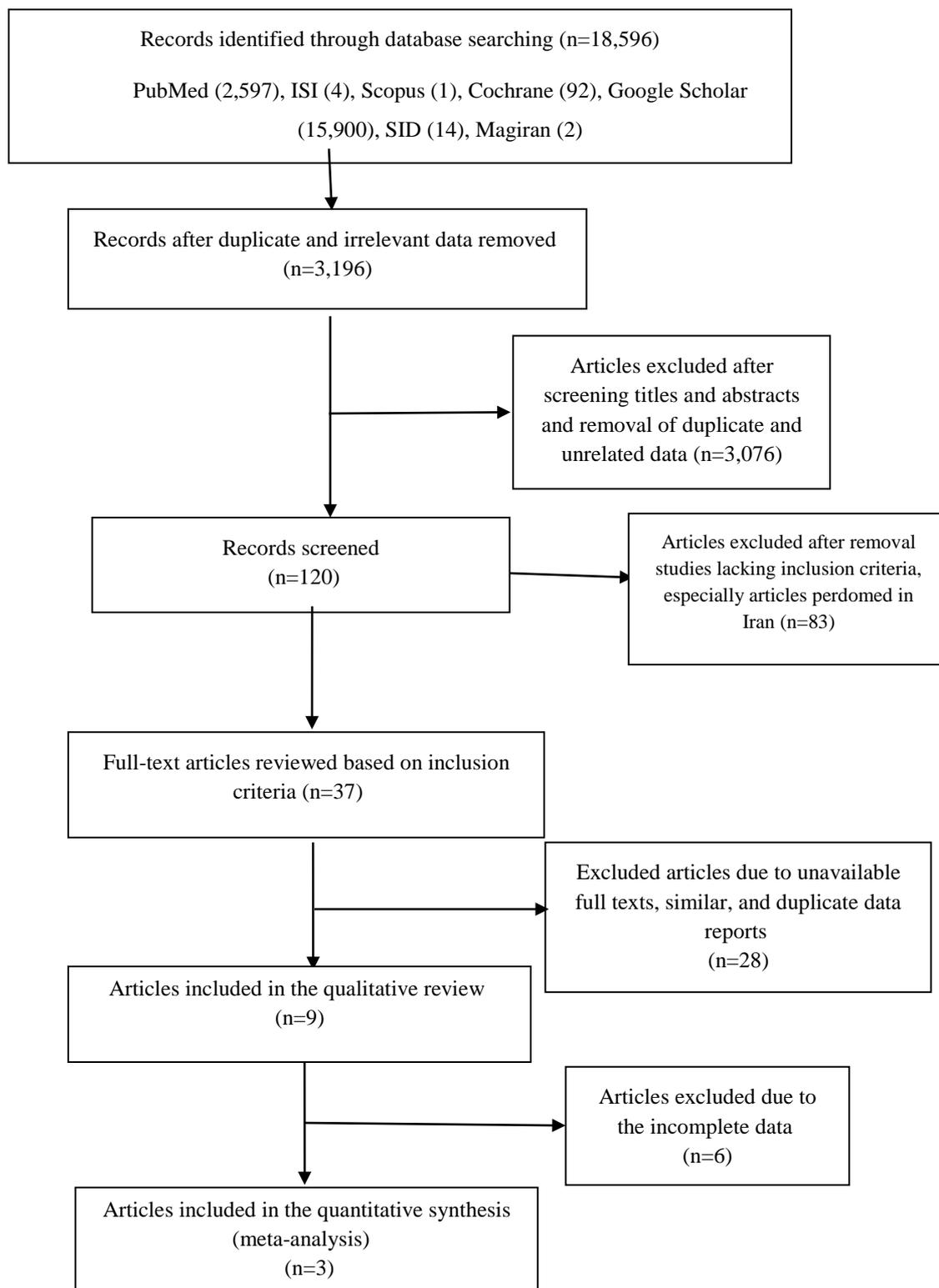


Figure 3. The PRISMA flowchart of the study's selection process

Phoenix dactylifera

Dates, by the scientific name of *Phoenix dactylifera*, are known as a disinfectant tropical fruit, containing various compounds, such as carbohydrate, fat, protein, vitamins, and fibers. This fruit has also demonstrated natural oxytocin properties due to the existing oxytocin-like substances. The laxative effect of dates, along with other constituents of date (namely serotonin, tannins, calcium,

and oxytocin-like substances) can contribute to uterine smooth muscle contraction. In addition, the tannin content of date palm fruit can act as a constrictor and cause the uterus and myometrium to constrict. Furthermore, these fatty acids are claimed to be involved in prostaglandins production pathways. As a result, dates can positively improve the energy levels and the muscles' strength of the uterus (13, 20, 26).

Cuminum cyminum L.

Cuminum cyminum is a member of the Apiaceous family. It is known as a therapeutic herb with medical properties, such as stomach strengthening, intestinal anti-spasmodic, anti-flatulence, diaphoretic, and diuretic. Trace quantities of Flandrone, Carun, and alcohol have also been found in cumin. Additionally, tannin and resin oil are among other constituents of cumin (15). Furthermore, evidence indicates a role for cumin in curing anemia and menstrual disorder (27).

Capsella bursa-pastoris

This herbal plant from the family of Brassicaceae contains various substances, such as tannins, choline, acetylcholine, flavonoids, amino acids, fatty acids, sterols, thiamine, ascorbic acid, calcium, potassium, beta-carotene, vitamin K, niacin, and iron. According to recent studies, this herb can act as a wound-healing agent with oxytocic, anti-inflammatory, and anti-coagulation properties. To add, *Capsella bursa-pastoris* can increase uterus contraction through the stimulation of the uterine's smooth muscles. Oral administration of *Capsella* is effective in the treatment of heavy menstrual bleeding or intermenstrual bleedings. Moreover, this plant can be used as a preventive measure for postpartum hemorrhage (15, 16).

The results of the meta-analysis showed that based on the I^2 index, there was heterogeneity in the studies ($I^2=0.87$). According to the meta-analysis, in the first hour after delivery, there was a statistically significant difference between the control and intervention (receiving herbal medicine) groups ($P<0.001$); as a result, SMD was estimated at -1.08 with a 95% confidence interval (CI; -1.31, -0.85). The forest plot of postpartum hemorrhage in the first hour is shown in Figure 4. Based on the results of the Egger test, there was no publication bias in the studies ($P=0.27$).

In the second hour following the delivery, a statistically significant difference was observed between the intervention and control groups ($P<0.001$); accordingly, SMD was obtained at -0.80 with 95% CI

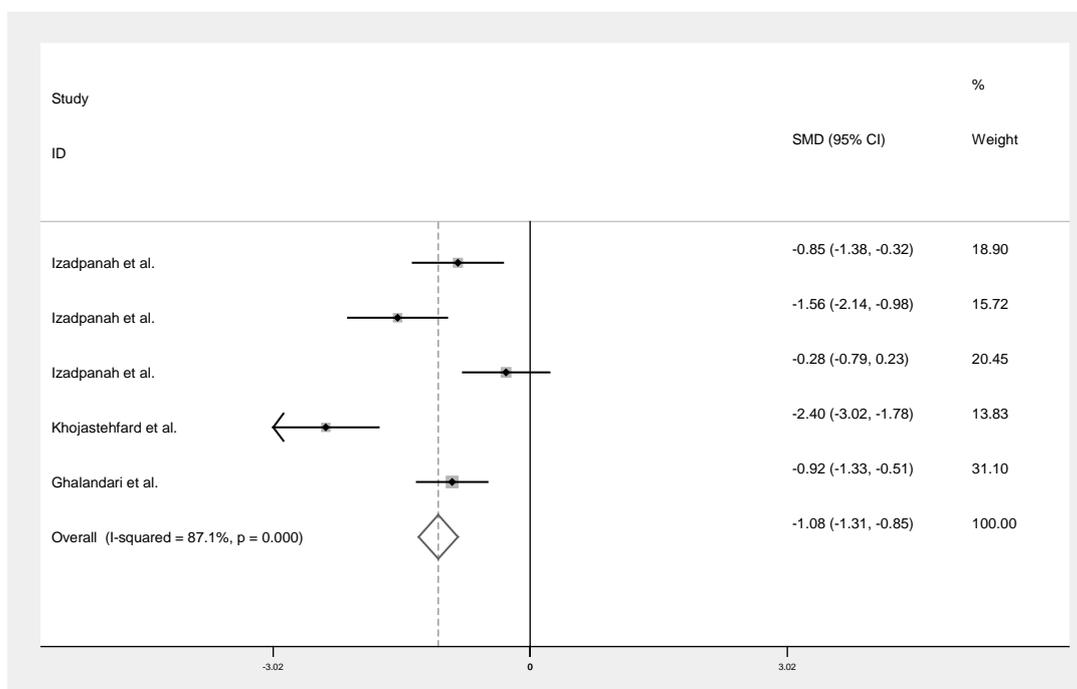


Figure 4. Herbal medicines effect on postpartum hemorrhage in the first hour

The horizontal lines denote the 95% CI, the square (■) shows the point estimate (the size of the square corresponds to its weight), the diamond (◇) shows the combined overall effects of treatment.

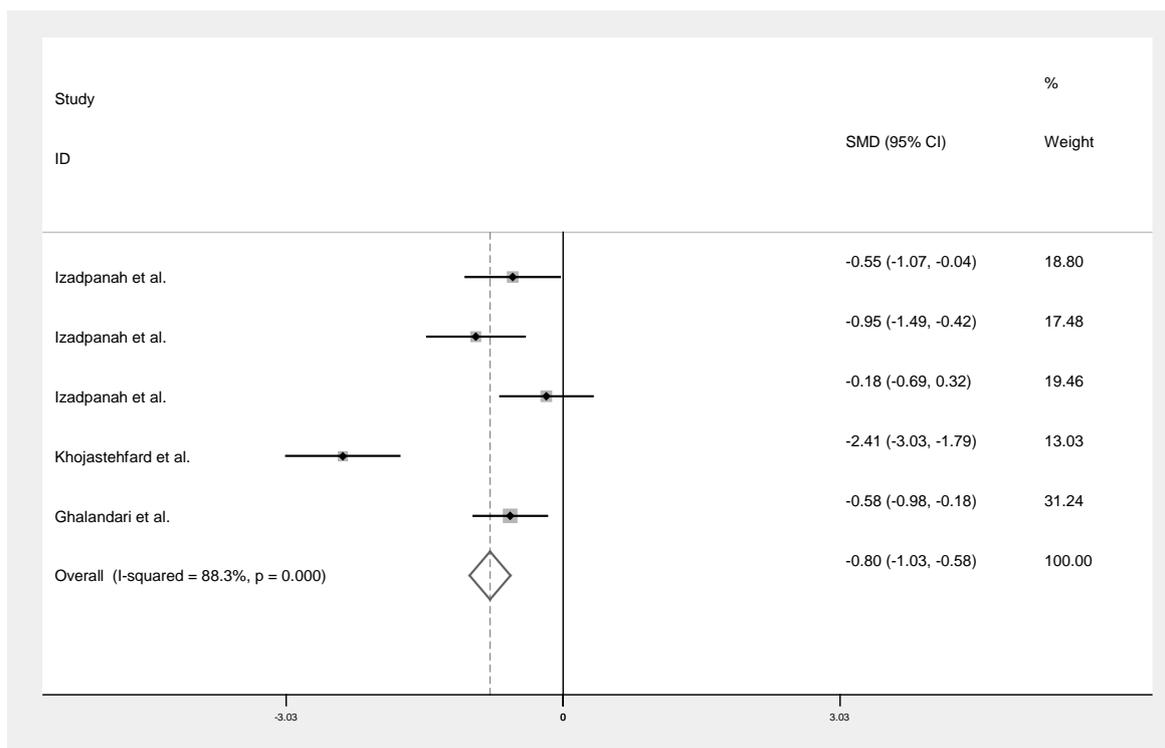
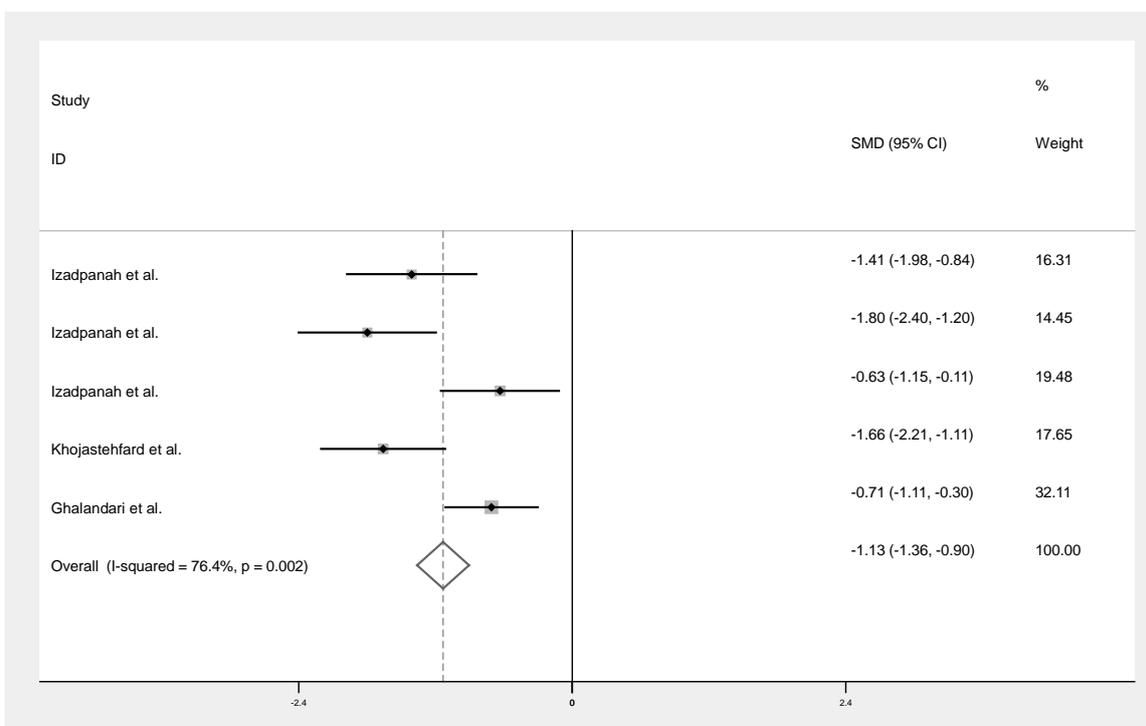


Figure 5. Herbal medicines effect on postpartum hemorrhage in the second hour

(-1.03, -0.58) (Figure 5). The results of the Egger test indicated no publication bias in the studies ($P=0.23$).

In the third hour after delivery, the difference between the case and intervention groups was statistically significant ($P<0.001$). Regarding this, SMD was estimated at -1.13 with 95% CI (-1.36, -0.90) (Figure 6). Concerning the results of the Egger test, no publication bias was revealed within the studies ($P=0.12$).



SMD: Standardized mean difference; CI: Confidence interval

Figure 6. Herbal medicines effect on postpartum hemorrhage in the third hour

Discussion

The findings of this study confirmed that these herbal remedies could reduce postpartum hemorrhage. The improvement of women's healthcare, especially during childbirth, to prevent and treat postpartum hemorrhage, is an essential step towards achieving health goals (15). Synthetic drugs, apart from all their benefits, are costly and mostly accompanied by undesirable side effects.

The most commonly used medicine in the prevention and treatment of postpartum hemorrhage is oxytocin which is coupled with myriad side effects, such as hypertension, tachycardia, arrhythmia, vomiting, increased uterine motility, pelvic hematoma, uterine contractions, uterine rupture, seizures, or coma following the water poisoning (1, 28). Additionally, oxytocin is used to induce or strengthen contractions of the uterine during labor through an intravenous injection. Oxytocin, through crossing the placenta, causes the fetal erythrocytes to accumulate more water and swell due to its hypo-osmotic effect. Oxytocin can flow through the vessels and the reticuloendothelial system that can be lead to hyperbilirubinemia and jaundice of the neonate (29). The use of herbal medicine has been considered by various studies as an easy, affordable, inexpensive, and non-invasive treatment with fewer complications.

The current systematic review presented that the use of natural products for medicinal purposes, such as grape seed, *Plantago major*, *Phoenix dactylifera*, *Anethum graveolens*, and *Capsella bursa-pastoris*, was effective on the postpartum hemorrhage. The results of studies conducted on the chemical composition of such substances indicated the presence of tannins; these findings often pointed to the presence of different polyphenols with contractile properties like tannins (19). Therefore, the tannin content of the *Phoenix dactylifera* can induce constrictions in the uterus and myometrium (20).

Additionally, the consumption of *Phoenix dactylifera* diminish the need for induction and significantly lowers the oxytocin and progestin usage in postpartum (30). Moreover, the tannin content of *Plantago major* can decrease postpartum hemorrhage through the stimulation of estrogen receptors and contraction of myometrial and uterine smooth muscle (18). Therefore, this substance can reduce postpartum hemorrhage due to its contractile characteristic because it causes uterine and myometer muscle to contract (31).

Nevertheless, one of the important issues that needs to be considered in studies investigating the impact of herbal medicines on reducing postpartum hemorrhage is the concomitant use of these herbal medicines with synthetic oxytocin. The function of oxytocin on the uterine is the contraction of smooth muscle since the uterus during pregnancy is highly sensitive to oxytocin; consequently, this can result in strong muscle contraction. During postpartum uterine atony, oxytocin can lower the rate of bleeding by generating rapid contractions. Nasal spray and intravenous and intramuscular injection are various ways by which oxytocin can be administrated (32-34).

All three studies that were meta-analyzed and analyzed used herbal medicine together with oxytocin, and the result of herbal medicine administration on controlling postpartum hemorrhage was statistically significant and clinically effective.

In a study conducted by Izadpanah et al. (2018), 120 pregnant women were recruited and divided into two groups. The intervention group received grape seed powder with different dosages of 50, 100, and 150 mg, along with 20 units of oxytocin, while the control group received placebo powder. The results revealed that the highest volume of bleeding after the intervention was observed in the 1st, 2nd, 3rd, and 24th hours after leaving the placenta in the placebo group, and the grape seed powder intervention turned out to be effective in reducing postpartum hemorrhage (17). Khojastehfard et al. (2019) conducted a study on 70 pregnant women, in which the intervention group received five doses of rectal suppository of *Plantago major* immediately after placental withdrawal with 30 units of oxytocin, while the control group received 30 units of oxytocin. Based on the findings of the mentioned study, a significant difference was observed between the mean amount of postpartum hemorrhage at the third stage of labor, and the first 4 hours of postpartum in both groups. Therefore, a rectal suppository of *Plantago* could effectively reduce postpartum hemorrhage (18).

Ghalandari et al. (2017) conducted a study on 100 pregnant women, in which the intervention group received 10 sublingual drops of the hydroalcoholic extract of *Capsella bursa-pastoris* with 20 units of oxytocin immediately after placental withdrawal, whereas the control group was administrated with 10 drops of placebo plus the infusion of 20 units of oxytocin immediately after placental withdrawal.

The results showed a significant difference between the mean of the 1st, 2nd, and 3rd hours of postpartum hemorrhage in both groups, indicating that hydroalcoholic extract of *Capsella bursa-pastoris* was effective in reducing postpartum hemorrhage (16). Although the results of the above mentioned studies (16-18) have been effective in reducing postpartum hemorrhage, more investigations need to be considered in these fields of research. Moreover, the use of post-partum oxytocin in high-risk women is not recommended as it can result in uncontrolled bleeding and such consequences as hypovolemic shock, intravascular coagulation disorders, liver failure, acute respiratory distress syndrome, and other complications (35).

In a study performed by Fazel et al. (2011), the participants received 40 drops of *Cuminum cyminum* L. and placebo solution after the serum discontinuation and 24 h after cesarean section. The considered exclusion criteria for subjects of the study were administering oxytocin and methylergonovine after 2 h of cesarean section (due to high bleeding and the need for controlling the bleeding) and having twins, postpartum hemorrhage, and abnormal postoperative bleeding (27). The reason for the increase in bleeding is that postpartum hemorrhage is defined to be loss of more than 500 ml of blood, while the bleeding volume in the cesarean section is doubled or more than 1,000 ml (36). The results of the study conducted by Fazel showed that the effects of *Cuminum cyminum* L. and placebo on postpartum hemorrhage were similar and *Cuminum cyminum* L. did not increase post-cesarean hemorrhage (27). However, it is necessary to consider that the non-usage of oxytocin after cesarean section can be dangerous in high-risk patients. Therefore, the administration of approved natural products needs to be performed cautiously and the high levels of accuracy should be considered regarding the appropriate timing of prescription and elimination of high-risk patients.

Among the most important factors involved in herbal medication in controlling postpartum hemorrhage are the timing and dosage of such products. Although *Phoenix dactylifera* was used in recent investigations conducted by Mojahed et al. (2012), Khadem et al. (2007), and Yadegari et al. (2016) (13, 20, 26), the acquired results were not the same, which can be attributed to different methods adopted in these studies. In the study performed by Mojahed et al., the intervention group received the medication immediately after placental withdrawal, including the infusion of 20 units of oxytocin in 1,000 ccs of saline with 100 g of *Phoenix dactylifera* with a glass of warm water, while the controls were administered with the infusion of 20 units of oxytocin in 1,000 ccs of saline. The evaluation of bleeding up to 2 h after delivery revealed that eating postpartum *Phoenix dactylifera* could be effective in reducing postpartum hemorrhage (13).

In the study carried out by Khadem et al., the intervention group was administered with 50 grams of *Phoenix dactylifera* orally and instantly after placental removal, whereas the control group received 10 units of intramuscular oxytocin. The bleeding rate was assessed up to 3 h of postpartum. The results showed that the administration of *Phoenix dactylifera* was a more effective approach toward reducing the postpartum hemorrhage, in comparison with an intramuscular injection of oxytocin (26).

In the study of Yadegari et al., the intervention group was prescribed 100 g *Phoenix dactylifera* within the first two hours of the post-delivery phase. Continuously for the first week after delivery, subjects received 100 g of *Phoenix dactylifera* with breakfast daily, while the control group received less than 50 g of *Phoenix dactylifera* in the first week after delivery. In this study, the control group was also recommended to use *Phoenix dactylifera*, however, in a lower dosage than that of the intervention group. Therefore, this study cannot be taken into consideration since it is not compatible with the standards of a case-control study. Accordingly, the control group should be in either of these categories, namely routine preventive procedures with oxytocin or placebo or no intervention at all, which was not fulfilled in this research. This study also evaluated prolonged postpartum hemorrhage, which was considered secondary bleeding. Lastly, the results showed that *Phoenix dactylifera* had no effect on reducing the number of bleeding days (20).

One of the vital issues in herbal remedies is noticing the existing side effects of such medications. In a study carried out by Abedian et al. (2016), the first and the second groups were prescribed with 250 mg oral mefenamic acid capsule and 1,000 mg oral *Matricaria chamomilla* capsule with 30 units of oxytocin, respectively. Following the intervention, complications were observed within the first 2-4 h of postpartum. Among the population of 70 pregnant women recruited in the study, 1 case with nausea and vomiting symptoms and 2 cases with drowsiness were reported in the mefenamic acid and *Matricaria chamomilla* groups, respectively (25).

Ghalandari et al. (2017) conducted a study, in which the intervention group was administered with 10

sublingual drops of hydroalcoholic extract of *Capsella bursa-pastoris*, whereas the controls received 10 drops of placebo immediately after placental withdrawal. In addition, both groups received 20 units of oxytocin infusion, along with supplementation. Treatment in the control group resulted in the manifestation of side effects. A total of 100 pregnant women were recruited in the mentioned study, among which, 1 subject manifested the symptoms of sore throat and itching in the case group and 1 subject was indicated with nausea symptoms in the control group (16).

Implications for Practice

According to the fact that herbal medicine is accompanied by fewer side effects, the global use of natural products for medicinal purposes is facing a continual rise. However, this literature review pointed to the significance of noticing the complications of such remedies in the treatment of postpartum hemorrhage. Therefore, it can be concluded that the use of herbal medicines can be an effective approach towards controlling postpartum hemorrhage, which is one of the most significant postpartum problems in women.

The present study found evidence on the efficacy of herbal medicine consumption in reducing postpartum hemorrhage. The success of these herbal products alone or in combination with oxytocin was reported in numerous studies. Compared to natural products, modern medicine is accompanied by various side effects that are known as an indispensable part of chemical medicines and oxytocin is not an exception. In addition to the availability of these herbal medicines, they are affordable and convenient. Moreover, the simultaneous use of chemical and herbal medicines can lead to a remarkable decrease in chemical medication dosage. Therefore, it is recommended that herbal medicines be implemented as an appropriate alternative to modern medicine in preventing postpartum hemorrhage.

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Conflicts of Interest

The authors declare that there is no conflict of interest.

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