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IMPACT OF GRAPE SEED EXTRACT POWDER TO REDUCE POSTPARTUM HEMORRHAGE

Elham Alahyari[1], Allahyar Shahnavazi[2], Ali Mohammad Izad Panah[3], Khorshid Rigi*[4], Elahe Alahyari[5]

1. *MSc in Nursing, Iran Hospital, Iranshahr University of Medical Sciences, Iranshahr, Iran.*
2. *MSc in Nursing, department of Nursing, Iranshahr University of Medical Sciences, Iranshahr, Iran.*
3. *Instructor, Nursing Department, Faculty of Nursing and Midwifery, Birjand University of Medical Sciences, Birjand, Iran*
4. *MSc in Midwifery, department Of Midwifery, Iranshahr University of Medical Sciences, Iranshahr, Iran.*
5. *Master of Chemical Engineering (Food Technology), Department of Food Sciences and Technology, University of Medical Sciences Zahedan, Zahedan, Iran*

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ABSTRACT

Introduction: The use of herbal products is higher in women. However, their effects on labor and postpartum hemorrhage is unknown. Since the most common cause of maternal mortality, perinatal or post-natal bleeding are numerous studies regarding the effects of chemical and herbal reduce bleeding after delivery is. This study aimed to investigate the grape Tasyrpvdr reduce bleeding after delivery was performed.
Methods: This study was a clinical trial on 120 mothers were eligible for vaginal delivery. The method selected randomly using the cards into 4 groups of 30 each (3 groups receiving powdered grape (doses of 50, 100 and 150 mg) and control group (receiving a capsule placebo within its Pvdrnshasth was filled, Each group based on the card by its mother, Dvzsh after a glass of warm water with a pair of outputs that would be given to the mother to eat. Also 20 IU oxytocin infusion rate of 2 mL salt sugar thousand milliliter per minute were performed according to routine. Bleeding Mother Pads are used to calculate their weight and weight gain equivalent to one gram a milliliter of blood was taken, After 24 hours at a rate of 3 cc of blood from the mother to test HB, HCT was performed on the data entered, After collecting data using SPSS software version 16 was used for analysis.
Results: 4 groups were homogeneous in all the variables In conjunction with the main objective of the study results showed that the mean blood loss at 24 hours after giving birth The Group of 50 mg 9/65 ± 5/310 and the 100 mg 8/94 ± 1/297 and the 150 mg 9/51 ± 3/242 and the control group 68 ± 8/427 which was P <0/001 significant difference.
Conclusions: Considering the effect of grape seed powder in reducing blood loss after delivery is recommended The importance of consuming a variety of ways such as workshops taught by experts, Also, further studies with different doses in single dose containers should be done in this area.

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Introduction

Corresponding Author: Khorshid Rigi, MSc in Midwifery, department Of Midwifery, Iranshahr University of Medical Sciences, Iranshahr, Iran, Email: khorshid.rigi@gmail.com

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Postpartum hemorrhage is one of three most common causes of maternal morbidity and mortality in developed and developing countries which is preventable and the highest rates are nearly found in less developed countries, and its prevalence is different in approximately 1 to 5 percent of deliveries in terms of the bleeding criteria (1). Postpartum hemorrhage refers to the loss of blood volume of 500 ml or more after the completion of the third stage of vaginal delivery (2 and 3,4,5,), which causes some complications such as low blood pressure, chest pain, respiratory failure, high blood pressure, uterus weakness, hysterectomy, hypovolemic shock, disseminated intravascular coagulation, maternal anemia and results in reduced ability to work and child care(1). More bleeding occurs during the first 24 hours after childbirth, which has a major share of maternal mortality; prevention is thus an important objective of the prevention of maternal mortality after birth (4). At present, oxytocin and methergine are the most common treatments among proposed ones in most labor and delivery wards in order to reduce postpartum hemorrhage. The use synthetic drugs in the labor management reduces the amount of blood loss but causes some side effects such as nausea, vomiting, hypertension and hypotension due to syntocinon (oxytocin)(6). So far, different treatment protocols are used to prevent bleeding after childbirth, and these protocols are constantly being revised and improved to achieve an acceptable success rate and to reduce the problems of patients;therefore, identification of the most effective and less dangerous medication to control bleeding after childbirth can have an important role in reducing the incidence of postpartum hemorrhage as well as the prevention of maternal mortality (7). With all efficiency, synthetic medications have their own adverse effects which have been resulted in finding safer alternatives for less dangerous drugs and the use of medicinal herbs (8). World Health Organization recognizes herbal medicine as part of complementary medicine which has been accepted by a large number of the population and 40% of the current common drugs are derived from plants and natural resources (9 and 10). In addition, studies in the field showed that 80 percent of the world's population depends on herbal medical aspects (11). In several studies of some medicinal plants, including Xuesaitony (12) and Xiaoyanzhixue ,dill seed extract, Chan Lyba , cumin , dates (13 and 14) were effective in reducing postpartum bleeding which each of theminclude compounds such as a Caron, tannins, amino acids such as linoleic acid. Grape (vitisvinifera) is one of the herbal remedies that have attracted much attention and has many uses; it has been proved effective in various diseases more than 6,000 years ago (15). Pedanius Dioscorides(1st century AD)also used it to treat bleeding and bloody sputum (16). In traditional Iranian medicine, grape seed has a cold and dry nature and is regarded as excellent for its astringent and tonic properties because of the high tannin contentand is also effective in treating uterine and menstrual bleeding (17).Grape seed accounted for about 5.2 percent of the weight of grape (18).Functional and chemical ingredients in grape seed powder contain flavonoid with a phenolic structure (phenolic compounds include monomeric flavonols such as catechin, epicatechin, dimmer flavonols, trimmer flavonoid, procyanidin polymer,non-flavonoids (non-flavonoid compounds phenolic including resveratrol, fatty tartaric acids, phenolacrylic acid compounds) and materials such as gallic acid and epigallic acid, tannins, high levels of linoleic acid, high levels of omega-6 and less omega-3, vitamin E and C, Peru anthocyaninand Karoonas well as magnesium, calcium, iron, phosphorus and potassium (19). Several studies have considered the effects of omega-6, linoleic acid, vitamin E and C and tannins in the control of bleeding (20). Protective and beneficial effects of grape seed against diseases such as breast and colon cancers, increased plasma antioxidant power, strength and stabilization of collagen, regeneration of blood vessels and restoring tissue blood flow, ulcers, inhibition of oxidative stress, myocardial infarctions and ischemic have been recognized (21). So far, grape seed powder is produced through extraction and combination with alcohol and no single study was conducted to measure the impact of grape seed powder on various diseases and bleeding especially postpartum hemorrhage. As various studies have documented that the compounds of plantsby extracts or separately have different or contrasting propertiesas well as considering the fact that grape seeds contain tannin and fatty acids, linoleic acid and omega-6 and active compounds and has long attracted the attention of local midwives in South Khorasan province, and used it to reduce bleeding after childbirth;therefore, in order to find a natural, safe and effective product for bleeding after delivery and given the importance of postpartum hemorrhage and prevention of excessive bleeding and increased promotion of physiologic delivery in the current era without venipuncture and serum therapy during deliveries, we do need a way to control bleeding after childbirth without intravenous drug administration,I decided to conduct the present study in order to academically and scientifically determine the impact of grape seed powder in reducing postpartum hemorrhage due to lack of scientific support; it is hoped that the results of the present study would be an important step in making decision regarding routine use of medication after delivery which in addition to maintaining the health of women after childbirth, can lead to cost savings as well.

Method:

Corresponding Author: Khorshid Rigi, MSc in Midwifery, department Of Midwifery, Iranshahr University of Medical Sciences, Iranshahr, Iran, Email: khorshid.rigi@gmail.com

This is a controlled clinical trial with a single-blind intervention which was carried out on 120 women with vaginal delivery in 4 groups of 30 patients treated at doses of 50, 100 and 150 mg by black grape extract and a control group (receiving placebo capsules). The procedure is as follows:

Preparation of capsules: At this stage, after approval of the project and the necessary coordination with authorities, graduate Committee, research affairs of university, the ethics committee and the necessary coordination with head of laboratory of physiology at the University of Medical Sciences, researchers purchased red grape from the market and rural areas of Birjand.After grape seeds were manually separated,they were washed and dried under the sun for 72 hours.Then they were manually milled to a fine powder by researcher and it was shown to the professors of pharmacology and physiology at the university for confirming its quality status.Then, according to the Ethics Committee and Chang and Guidelinesstudy (2011) in using California grape seed powder, doses of grape seed powder in the formulation of the extract (8 grams extract is obtained per hundred grams of seed grape powder) were measuredand prepared and packaged in the form of capsules 50,150,100at the physiology laboratory of Birjand University by researcher and stored in the refrigerator.Placebo capsules were filled with starch powder by researcher and were placed in the refrigerator.

625 mg of grape seed powder = 50 mg capsules

1250 mg of grape seed powder = 100 mg capsules

1875 mg of grape seed powder = 150 mg capsules

Sampling: In this stage, after approval of the project and the necessary coordination with authorities, graduate Committee, research affairs of university, president and Department for safeguarding inValiasrhospital in Birjand,maternity and gynecological surgery ward as well as permanent presence of researcher in these wards and according to previous research (the study byMahdavian et al.,2002) and the sampling frame in women referred to Valiasr hospital in accordance with the inclusion criteria, the researcher firstly identified themand then explained the objectives and methodology of the study for mothers who were included in the study byobtaining a written consent.Before starting the study, four groups under study were recorded on 120 cards (30 cards for first Group, 30 cards for second group, 30 cards for third group, 30 cards in the control group).In total, 120 cards were stored in a box and after obtaining informed consent from the patients, they were asked to pick out a card from a box. Theywere assigned in one of three groups receiving grape seed powder (50,100 mg, 150 mg) and control group (receiving placebo capsule filled with starch powder) based on thepicked card.At the beginning and according to the purpose of the study, blood samples from mothers (3 ml) were collected for testing HB, HCT and were taken to the laboratory of Imam Reza (AS) within half an hour by the researcher, and then laboratory results obtained wererecorded in form view and patient's record.Mothers were assigned in one of the studied groupsby their cards. They were prepared for vaginal delivery and took their determined capsule dose after birth and placenta delivery with half a glass of water from the researcher.It is noteworthy that patients do not need to get oxytocin in physiologic delivery; however, oxytocin was intravenously administered under the requirements of delivery sectionand in accordance with the delivery section regulations (20 IU oxytocin was poured into 1 liter of Ringer at 5 ml per minute, then the infusion rate was reduced to 1-2 ml for transferring mothers to gynecological surgeryward and oxytocin infusion was discontinued, and the mother was handed over to the women's department of surgery; this procedure usually took about 2 to 3 hours).All data such as oxytocin administration or lack of oxytocin were recorded by the researcher in the questionnaire.Immediately after the transfer of the mother from delivery room to the recovery room, a drape withspecial weight and plastic cover was placed under mother and mother's perineal pad;then any changedpad was weighed with digital scale every 2 hours to 24 hours after delivery by the researcher.Each gram of pad weight gain was considered equal to a blood sample and finally, the weight and number of the pads (amount of bleeding) were recorded in form view.Other necessary cares of the mother during the fourth stage of labor were also recorded in the form view(it should be noted that the number of patient's pads and drapes, bleeding or bleeding complications and the breastfeeding by mother in hospital and gynecological surgery were monitored for 24 hours and recorded by researchers in the checklist form).Medications for the treatment of third stage of labor including oxytocin produced by Iranian pharmaceutical industry, Rasht (ampoules 1 ml containing 10 IU oxytocin) and grape seed powder derived from the dried seeds of red grapes purchased from the market in Birjand were prepared and packed into capsules 50, 150 100 by the researcher and were kept in the refrigerator and given to the researcher immediately after the placenta.

Third stage: After 24 hours, blood sample (3 ml) was taken for testing HB, Hct by the researcher and was sent to laboratory of Imam Reza Hospital within half an hour and the results were recorded by the researcher in the form view and patient records.

Findings

Table 1. Comparison of age, height, age, pregnancy, in pregnant women in four groups

Groups / Variable	Dose 50 mg N=30 X±SD	Dose 100 mg N=30 X±SD	Dose 150 mg N=30 X±SD	Control group X±SD	ANOVA test result
Age (years)	27 ± 6.4	25.7±5.4	24.8 ± 4.5	26.2± 4.5	3.16 =dF F=1 P= 0.39
Gestational age (weeks)	39.3 ± 1.2	39.2 ± 2.1	38.7 ± 1.9	39.1 ± 1	3.116 =dF F= 0.66 P=0.58
Maternal height (cm)	159.5 ± 2.5	158 ±2.9	159.5±3.1	158.9±2.2	df=3.116 F= 0.79 P= 0.05

According to the table above, no significant differences were observed in mean age, gestational age and maternal height in 4 groups and all 4 study groups were similar in terms of these variables.

Table 2. Comparison of the mean during labor and delivery stages and oxytocin administered in four groups of pregnant women

Groups / Variable	Dose 50 mg N=30 X±SD	Dose 100 mg N=30 X±SD	Dose 150 mg N=30 X±SD	Control group X±SD	ANOVA test result
Duration of labor (hours)	11.2 ± 5.1	13 ± 5.1	8.8 ± 3.3	8.5 ± 2.9	7.5 =dF F3.116 P=0.001
First Stage of Labor (hours)	10.2 ±5.1	12.1 ± 5.1	8 ± 3.2	7.7 ± 2.8	7.3 =dF F= 3 P=0.001

Second stage of labor (minutes(	16.2 ± 7.1	17.3 ± 7.1	14.2 ± 2.9	15.8 ± 6.7	X^2= 2/04 dF=3 p=0/56
Third stage of labor (minutes(	8.8 ± 2.8	9.6 ± 3.6	9.8 ± 2.8	9.5 ± 4.1	X^2= 1/27 dF=3 p=0/74*
oxytocin	26 ± 10	21.8 ± 8.7	28.9± 11.3	20 ±10	X^2=12/5 dF= 3 p=0/006 *

α= 05/0 is at significance level

According to the table above, no significant difference was observed in the mean duration of the second and third delivery in 4 study groups; but the average duration of delivery and the first stage of labor showed significant differences in 4 groups and Mann-Whitney test showed that the differences between the groups were not statistically significant as follows:

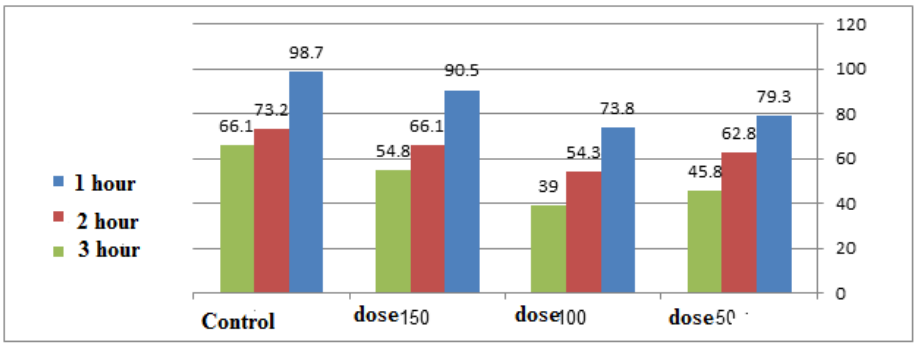
Control 100 mg P<0.001

100 mg and 150 mg P<0.001

Intervention / Groups	First hour N=30 X±SD(cc)	Second hour N=30 X±SD(cc)	Third hour N=30 X±SD(cc)	The result analysis of variance and LSD test
Group50 mg	27.6 ± 79.3	15.5± 62.8	45.8± 13.1	P<0.001 ، dF=2 ، F= 42/5 All hours are significant (P<0.001)
Group 100 mg	15.1± 73.8	17.± 8 54.3	14.5± 39	*0.001<p ،dF=2 ،F= 62/8 All hours are significant (P<0.001)
Group 150 mg	37.4 ±90.5	18.6± 69.5	19.8± 54.8	*0.001<p ،dF=2 ،F= 30/1 All hours are significant

				(P<0.001) * P<0.001 ،dF=2 ،F= 30/7
Treatment group	98.7± 16.8	21.6± 73.2	15.6± 66.1	All hours are significant P<0.001 P<0.045 Second and third hours
--	F= 5/59 dF= 3, 116 p= 0/001*	F= 5/99 dF= 3 , 116 P=0/001	F= 16/3 dF= 3 , 116 P<0/001*	ANOVA test result
Comparison between the groups	P= 0/02 Group50 mg P=0/002 Group 100 mg	P= 0/01 Group 150 mg P=0/001 Group 100 mg	P<0/001* Group50 mg P<0/001 Group 150 , 100 mg P<0/001 P= 0/03 Group 150 mg	

Table 3. Comparison the average amount of bleeding (cc) at 1, 2 and 3 hours after the intervention in four studied groups



According to the table above, blood volume showed a significant decrease in the first hour until the third hour in all 4 groups. The bleeding was highest in the control groupin the first to second hour and the least amount of bleeding was observed in the intervention group (100 mg). The table above also shows a significant difference between the study groups at different times.

Table 4. Comparison the average amount of bleeding (cc) within 24 hours after treatment in 4 groups

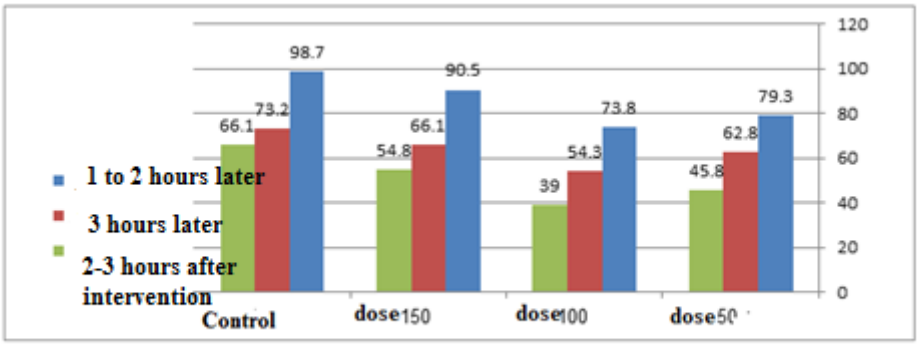
Statistical Indicators for Group	Frequency	X±SD	ANOVA test result
Group 50 mg	30	65.9±310.5	F= 35/3
Group 100 mg	30	94.8 ±297.1	Df= 3 , 116
Group 150 mg	30	9.51±242.3	P<0/001*

Treatment	30	68±427.8	

According to the table above, significant difference was observed in the average amount of bleeding in the first 24 hours in four studied groups.The highest volume of bleeding was recorded in the control group and the lowest rates of bleeding (150 mg). Average blood loss was also significant in all groups or the control group.

Table 5. Mean changes in blood volume at various times in 4 groups

Variable / Groups	Changes in blood volume 2 hours to 1 hours after intervention	Changes in blood volume 3 hours to 1 hours after intervention	Changes in blood volume 3 hours to 2 hours after intervention
Group 50 mg	19.5±16.5	25 ±33.5	13.6±17
Group 100 mg	19.8 ±19.5	18±34.8	12.5 ±15.3
Group 150 mg	26.9±21	30.7±35.7	15.8±14.6
Control	27.9±25.5	4.5±24.6	18.3±7
Kruskal-Wallis test result	X^2= 0/39 dF=3 , p=0/94	X^2=0/53 dF= 3 , p=0/91	X^2=3/58 dF= 3 , p=0/31



According to the table above, the average decreased blood volume at different times in the four study groups was not significant.

Discussionand conclusion

Postpartum hemorrhage is fatal and can lead to serious complications and is considered one of the main causes of maternal mortality.Bleeding can occur suddenly or happen too slowly and is a continuous process.Postpartum hemorrhage is associated with two major risks of anemia and infection and the most vulnerable time for its occurrence is during the hours and days after birth.While bleeding, early diagnosis and taking the necessary measures to prevent complications are of great importance.Unfortunately, in many cases it is not easy to diagnose, because sometimes there is no obvious symptoms of decreased blood volume.Another problem is to replace the lost blood volume which accompanies some risks.In addition to the risks of blood transfusion therapy such as reaction caused by blood incompatibilities or transmission of viral infections,renal failure due to decreased blood pressure is also another danger that threatens women's lives.Thus, this study aimed to investigate the impact of grape seed powder on the hemorrhage after vaginal delivery.it is hoped that the results of the present study would be an important step in making decision regarding routine use of medication after delivery which in addition to maintaining the health of women after childbirth, can lead to cost savings and contribute to the economic growth of Iran.The results of our study show that grape seed powder is effective in reducing postpartum bleeding and can significantly reduce the amount of bleeding.Also in this study, grape seed powder was used to find the appropriate dose of three doses of 50, 100 and 150 mg of which have shown their own various effects.Based on our results, patientstreated with doses of 150 mg of grape seed powder had the lowest bleeding with 242 cc in 24 hours after delivery; the amount is much less than the control group with 427 cc of blood volume.Of course, in the early hours after delivery, the amount of bleeding in patients treated with 100 mg of grape seed powder with dose 100 mg (1/167 cc) was less than the other two groups and was much less than the control group with a blood

loss of 238 cc.Complications such as laceration, episiotomy and the need to oxytocin were identical in 4 groups and no differences were observed between groups.So far a wide variety of treatments have been proposed to control bleeding after childbirth, but no single study could be find that investigated the impact of grape seed on bleeding after childbirth.However, due to the presence of similar compounds such as tannins, fatty acids,catechin and epicatechin in grapes, we used the findings of studies conducted on dates, dill and cumin.In the studyby Mahdavian and colleagues in Mashhad, by using edible dill seed extract,it was shown that the mean blood loss between the two groups of dill seeds and oxytocin in the first and second hour after delivery was 52.6 to 87.6 and 42.5 to 104.4, respectively which was not statistically significantand it wasconcluded that consumption of edible seed extract can reduce postpartum bleeding within the first and second hour compared with oxytocin after delivery and had no side effects that are consistent with our study (22).Mujahidet al (2011) conducted a study in Yazd entitled as Impact of dates on bleeding after delivery.The results of this study showed that the mean bleeding at the end of the first 2 hours after delivery in oxytocin group was 127.11 ml and 68.5 in oxytocin group with dates which showed no significant differenceandcorrespond with the findings of this study (14).In the study by Hammoudet al in 2008, the effect of date fruit and oxytocin on bleeding after childbirth was investigated and bleeding during the first, second and third hours after delivery was significantly lower in the group receiving oxytocin (23).Additionally, Khadem et al., (2007) conducted a study with the aim of comparing the impacts of oxytocin on the dates and postpartum hemorrhage and came to the conclusion that the date affects bleeding at first, second and third hour after delivery and it was determined that the mean bleeding at the end of the first hour after delivery decreased significantly in the group using palm (104 cc vs. 141.6 cc); although at the end of the second and third hours after delivery, the bleeding rate was declined, the difference was not significant (13).Fazeli andIsmailiconducted a study in 2007 to determine the impact of cumin oil on postpartum hemorrhage which unlike other studies, the impact of cumin and placebo on postpartum hemorrhagewas identical and cumin oil did not lead to increased bleeding (21&24).As you can see, the results of this study and other studies show that herbal medicines especially grape seed powder can have a significant impact in reducing bleeding,however;it requires further studies.

Conclusion

Postpartum hemorrhage is a very important issue that could have a negative effect on the health of mothers and their control can greatly help to improve the health of mother.The present findings show that grape seed powder can effectively help to reduce postpartum hemorrhage and prevents the reduction of maternal hemoglobin.So by taking into considerations these issues, it is recommended to use it as a medication to reduce the amount of bleeding in the third stage of labor.

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