

## The view of cesarean pain after preemptive use of *Rosa damascena* extract in women with elective cesarean section

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**Abstract:** Post cesarean section pain as an individual acute sensation requires special care. Studies have always shown that 30 to 40 percent of patients experience moderate to severe pain after operation. Opiates and non-steroidal anti-inflammatory drugs (NSAIDs) are effective for the control of pain, but they have some side effects. Hence, some safe analgesics with better effects and little adverse effects are needed. Rose hip products are used in Iran for many years as traditional medicine in the form of jam and syrup. The aim of this study is to evaluate the effectiveness of preemptive prescription of rose hip extract for postoperative pain in elective cesarean sections. In a double blind placebo-controlled clinical trial, 87 patients were studied in 2 groups. Patients in Group A were given rose hip extracts capsule and patients in Group B were given placebo capsules. After preemptive prescription of capsule A and B (15 min before anesthesia), we evaluated the pain score with visual analog scale (VAS) in various hours after surgery in the ward and then analyzed the findings. We found that there is need for patients with the palliation of pain to take analgesic drugs after surgery, though the total dose of analgesics and the severity of pain in various times in group A was better than that in group B. There was no significant side effect in both groups. The initiating of breast feeding was same in both groups. According to our study, we can use rose hip extract in elective surgeries without any significant side effects in order to control pain, and it is an effective product as compared with NSAIDs and opiates with less complication.

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**Key words:** Pain, rose hip extract, elective cesareans.

### 1. Introduction

Studies have always shown that 30 to 40% of the patients experience moderate to severe pain after operation. Agitation and discomfort caused by sensitization of the neural endings are individual or objective multifactorial phenomena which can be influenced by physiology, cultural, psychological and social factors (Edwards, 1990). Post cesarean section pain as an individual acute sensation requires special care. It always involves suffering of the patient and result in systemic complications, prolonged treatment and increased hospitalization cost and it can be the main cause of delayed breast feeding (Fijalkowska et al., 2006). Abundant efforts have been made to control, reduce or relieve pain a long time ago. The present treatment solutions for controlling postoperative pain are mainly based on treatments with pain killers, opioid and non-steroidal anti-inflammatory drugs (NSAIDs). Because of the complications of these conventional painkillers, medications with less harmful effects with natural sources are needed to be replaced (Etches, 1999; Andrade et al., 1994; Warriner et al., 1995). *Rosa*

*damascena* is one of the local plants in our area (Tabriz-Iran), which is broadly used in food industry (jam, rosewater and different beverages). The extract of *R. damascena* has numerous beneficial effects including analgesic and anti-inflammatory effects, which have been proven in animal models and studies carried out on human models (Gharabaghi et al., 2011). Anti-inflammatory and analgesic activity of this herbal product was due to its antioxidant activity. These herbal antioxidants inhibit the metabolism of arachidonic acid in the peroxidation enzymatic reactions. These products affect both cyclooxygenase and lipooxygenase cycles and induce their anti-inflammatory effects through this cycle (Greer, 1990). Therefore, a natural herbal compound can be used for reducing pain without side effects. In spite of the fact that a satisfactory analgesia can be achieved using conventional painkillers, in some cases the pain of the patients lingers on after operation. Therefore, *R. damascena* can be utilized to reduce pain in the patients without any complications which were usually seen in the administrations of opioids or NSAIDs. Different researchers have proved that treating

postoperative pain by administering analgesic before surgical incision can prevent neuronal hyperalgesia in the spinal cord. This approach is called preoperative analgesia and is mostly achieved by administering N-methyl-D-aspartate, including NSAIDS (Trenam et al., 1992). The objective of this study is to evaluate the effect of high dose R. damascena extract administration on the postoperative pain in elective cesarean sections.

## 2. Materials And Methods

The double-blind placebo controlled clinical trial study was carried out in Alzahra Tabriz Educational Therapeutic Center affiliated to Tabriz University of Medical Science, Tabriz, Iran, from December 2009 to January 2011. The study group included 78 pregnant women who underwent elective cesarean section. Sampling was performed randomly from the patients who were qualified for this study which was divided randomly into two groups: intervention group received R. damascena extract and control group received placebo. In these patients, the effect of administering R damascena extract before operation (15 min before cesarean section) and postoperative pain was studied. The patients were hospitalized in the study location during the study period. This study was approved by the ethics committee of Tabriz Medical Science University, and written consent was obtained from all patients (intervention and control group). The inclusion criteria were pregnant females with age range of 18 to 40 years, having term pregnancy, without the history of hypersensitivity to local anesthetics (lidocaine, marcaine) and with body mass index of 18.5 to 24.9 who were supposed to undergo cesarean section for different reasons such as previous cesarean section-CPP-abnormal presentation, etc. Exclusion criteria were emergency cesarean sections, need to general anesthesia, history of psychological disorder, history of hypersensitivity to local anesthetics and R. damascena extract, prolongation of surgery more than 1 h, emergence of intraoperative complications, having underlying diseases such as diabetes and hypertension and existence of adhesions due to previous surgeries.

### 2.1. The method of providing the medication

Dried fruits of R. damascena were first ground by a mechanical mill and turned into fine powder. Later the solution was extracted by ethanol (70%) using maceration technique. The extraction was performed three times (5 min for each time). The collected extract was completely dried under low pressure by rotary evaporator. The dried extract was kept in the refrigerator in temperature below 0°C until it was used for making capsules. Winther et al., 2005 found that the effective dose of R. damascena when used as dried powder is 5 g per day ) which is

calculated as 15% of the extract. In case of being provided as extract form, it is almost 750 mg per day, but we need to do further researches to find the optimal dose. In present study it was used as 800 mg capsules. The administered medicine was provided in the form of capsules by Medicinal Research Center of Tabriz Medical Science University. Each capsule was labeled with "A" containing 800 mg of R. Damascena extract and "B" containing placebo (starch).

Powder 100g	Extract 15g
5g	X=750mg

### 2.2. Design and treatment

The researcher was present in the delivery room of the pregnant women who had the inclusion criteria and the research was explained to them; the objective of this study was to observe the medications being used and their probable complications. Informed written consent was obtained if the patient was eager to participate in this study. Subsequently, the required data including degree of postoperative pain and pain score from complete analgesia to severe pain which is defined numerically from 0 to 10 using VAS were given to the patients. In the operation room, 15 min before spinal anesthesia, patients were given two capsules (A or B) randomly with simple randomizing with 30 ml of water. The capsules given to the study group contained 800 mg of R. damascena extract and in placebo group they contained starch. All capsules had similar color, taste, smell; the researcher and the patients were unaware of the type of administered medicine during this study. After local anesthesia, cesarean section were performed in two groups by Pfannenstiel incision, the patients were excluded from the study if the duration of cesarean was more than 1 h or complication occur during the surgery. After completion of surgery, pain degree was evaluated in recovery of 3, 6, 12 and 24 h after being transferred to the ward. If the patient suffered from pain before 3 h after operation was being completed, the score of the pain was registered and the required analgesic was administered according to the severity of pain. The method of administering medication was as follows: based on the patient's experience of the pain, if pain score was seven, tramadol injection (100 mg) IM was administered; for pain score of 3 to 6 diclofenac suppository (manufactured by Abureyhan pharmaceutical company) was administered and if the pain score was 1 to 2, acetaminophen (tablet 500 mg) or no analgesic was administered according to the patients' tolerance and eagerness. All the stages of evaluation were carried out and registered by expert individuals. The studied items were age, education status, occupation, number of the pregnancies, delivery time, mother's weight before pregnancy,

mother's height, mother's body mass index (BMI), neonate's weight and APGAR score, reason of cesarean section, the duration of the operation and also pain score after operation in recovery, 3, 6, 12 and 24 h after being transferred to the ward. The severity of pain was also recorded in case of the patients being transferred to the ward from recovery and before the completion of three hours. The type of the medication

used in each of the above mentioned times and the total used medication, times of the administration, the time of starting lactation after operation and maternal complications of the medication (nausea, vomiting, decrease in blood pressure, drowsiness, frequent urination, diarrhea, constipation and etc.) were also noted.

**Table 1:** Demographic characteristic of patients

Variable	Case group (n = 46)	Control group (n = 46)	P
Age (years)	27.78 ± 4.04	22.28 ± 5.04	0.64
Gravidity	1	1.98 ± 0.93	0.65
	2	16 (34.8)	
	3	18 (39.1)	
	≥ 3	20 (43.5)	
Body weight (kg)	78.67 ± 13.63	81.11 ± 11.54	0.35
Height (cm)	161.96 ± 6.92	161.43 ± 5.64	0.69
Education status	Non educated	0 (0)	0.61
	Primary school	23 (50)	
	Under graduation	19 (41.3)	
	Post graduate	4 (8.7)	
Occupation (housewife)	41 (89.1)	44 (95.7)	0.43
Neonate birth weight (gr)	3420.87 ± 540.24	3416.52 ± 481.54	0.96
	1500 to 2500	2 (4.3)	
	250 to 3500	29 (63)	
	> 3500	15 (32.6)	
Cause of cesarean	Breech presentation	5 (10.4)	0.54
	Previous cesarean section	21 (43.8)	
	History of infertility	0 (0)	
	Elective	22 (45.8)	
	Meconium passing	0 (0)	
	Placental abruption	0 (0)	
	CPD	0 (0)	
	Elective	1 (2.2)	
Operation duration	50.87 ± 5.99	50.65 ± 6.01	0.86

Quantitative data are presented as mean ± SD; Qualitative data are presented as percent.

### 2.3. Statistical analysis

The obtained information was statistically analyzed using descriptive statistical approaches (frequency, percentage and mean ± standard deviation), mean difference test for independent groups, chi-square test, Fisher exact test, Mann-W hitney U test and repeated measurements test by using SPSS-15 software. Normality of data distribution was evaluated using Kolmogorov Smirnov test.

### 3. Results

In Table 1, it was shown that there were no significant differences in demographic characteristics of patients between two groups. The need of analgesic significantly started later in the intervention group. Analgesic administration (tramadol, diclofenac and acetaminophen) was also significantly lower in the intervention group. The results obtained from the

repeated measurement project test revealed that pain severity decreased solely in both groups and two by two comparison of the studied times revealed that pain severity significantly decreased in the intervention group at different times. However, decrease in pain severity at different times and its comparison in both groups revealed that decrease in pain severity was more in the intervention group compared to the control group.

All parameters related with postoperative pain and also the administration time of analgesics is presented in the two groups in Table 2. It should be mentioned that other complications such as drowsiness, agitation, diarrhea, respiratory depression, constipation and urticarial, were not seen in any of the patients of both groups. The time for starting lactation and postoperative complications in both groups are presented in Table 3.

**Table 2:** Comparison of post-operative pain between two groups

Variable	Case group (n = 46)	Control group (n = 46)	P	
First request for analgesia	≤ 30 min	1 (2.2)	29 (6.3)	0.001*
	30 to 60 min	0 (0)	9 (19.6)	
	60 to 120 min	4 (8.7)	7 (15.2)	
	≥ 120 min	3 (6.5)	0 (0)	
Needing analgesia	Recovery	0 (0)	13 (28.3)	0.001*
	After 3 h	44 (71.7)	46 (100)	0.04*
	After 6 h	41 (67.4)	46 (100)	0.03*
	After 12 h	28 (60.9)	46 (100)	0.02*
	After 24 h	6 (13)	42 (91.3)	<0.001*
Frequency of drug use	Once	1 (2.2)	0 (0)	0.002*
	Twice	19 (41.3)	0 (0)	
	3 times	22 (47.8)	4 (8.7)	
	4 times	3 (6.5)	29 (63)	
	5 times	0 (0)	13 (28.3)	
Frequency of tramadol administration	Never	41 (89.1)	11 (23.9)	0.003*
	1 dose	5 (10.9)	29 (63)	
	2 doses	0 (0)	5 (10.9)	
	3 doses	0 (0)	1 (2.2)	
Frequency of diclophenac sodium administration	1 dose	4 (8.7)	1 (2.2)	0.001*
	2 doses	36 (78.3)	21 (45.7)	
	3 doses	4 (8.7)	19 (41.3)	
	4 doses	1 (2.2)	5 (10.9)	
Frequency of acetaminophen administration	Never	27 (58.7)	18 (39.1)	0.01*
	1 dose	18 (39.1)	26 (56.5)	
	2 doses	1 (2.2)	2 (4.3)	
Score of pain (VAS)	Recovery	1.33 ± 1.62	3.31 ± 2.36	<0.001*
	3 h	4.70 ± 1.17	6.71 ± 1.05	
	6 h	2.87 ± 1.06	4.87 ± 1.50	
	12 h	2.50 ± 0.98	3.82 ± 1.11	
	24 h	1.20 ± 0.85	2.38 ± 0.93	

Quantitative data are presented as mean ± SD; qualitative data are presented as percent; \*significant difference at  $P < 0.05$  level.

#### 4. Discussion

In this study, the effect of administering R. damascena extract on relieving postoperative pain in the elective cesarean sections was evaluated. The degree of pain relief was better in the group that received R. damascena extract compared to the group

that received placebo at different times ( $P < 0.001$ ). The duration of analgesia after operation and pain degree at different times, the total dose, and number of times analgesic was administered were better in the group that received R. damascena extract. No complication was observed as regards the reception of R.

**Table 3:** The time interval between operation and beginning of breast feeding and most surgical complications between two groups

Variable	Case group (n = 46)	Control group (n = 46)	P	
Time interval of breastfeeding	< 1 h	10 (21.7)	7 (15.2)	0.59
	≥ 1 h	36 (78.3)	39 (84.8)	
Complications	Vomiting	11 (23.9)	17 (37)	0.25
	Hypotension	0 (0)	1 (2.2)	0.99
	Tachycardia	0 (0)	2 (4.3)	0.49
	Frequent voiding	0 (0)	1 (2.2)	0.99

Data are presented as percent.

Damascene extract administration, and maternal complications were equal in both the case and control groups. There was no significant difference between the two groups regarding age, education status, gravidity, parity, and living area. Choi and Hwang (2003) in a study evaluated the analgesic, anti-inflammatory and anti-sensitivity effects of *R. hybrida* on animal models through claw edema, ear edema and induced arthritis. They proved the analgesic effects of this herbal product using hot plate test and also confirmed its potential anti-inflammatory effects. The study was however carried out on animal models. Other studies carried out on human models also confirmed these findings. In this study, to evaluate anti-inflammatory and analgesic effects, the *R. hybrida* (200 mg/kg) was utilized. The same dose was used for arthritis for one week; the dose utilized in the study which was carried out on animal models was different from ours (Choi and Hwang, 2003). Cosima et al. (2008) in a study evaluated all therapeutic effects of this herbal medicine, considering its frequent usage as traditional medicine for centuries. Studied items in the investigation included antioxidant, anti-inflammatory, anti-mutagen, anti-carcinogen and anti-microbial activities, effect on blood fats, biliary acids, blood sugar, urine secretion and contents, muscle tone, nerve conduction and healing gastric ulcers. The aforementioned characteristics of this herbal plant have been confirmed. The analgesic and anti-inflammatory effects of our study are similar to the results obtained from the above-mentioned study. In this study, to evaluate analgesic and anti-inflammatory effects, they utilized the extract being prepared by ethanol 80% in rats. In another part of their study which was carried out on human model, they utilized rosehip powder 45 g for 28 days. Analgesic effects significantly appeared in this dose (Cosima et al., 2008). Although, the administered dose in this study is different from our study, broad research is required to identify effective analgesic dose in different clinical conditions. On the other hand, one part of this study was carried out on animal models. In addition, Christensen et al., (2008) in an analysis studied the therapeutic effect of *R. canina*, a subtype of rosehip, on osteoarthritis. In their study, the prepared product was effective in reducing pain and pain score significantly decreased in the patients. Regarding complications in their study, some cases of acid regurgitation, gastrointestinal discomfort, diarrhea, constipation and short episode of urticarial were seen in some of the patients, which were not statistically significant (Astrup, 2008). In our study, however, there was no significant side effect after administration of *Rosa damascene*. This finding is similar to that

observed in the study of Christensen et al. (2008). Chrubasik et al. (2006) in a study evaluated the potential therapeutic effect of *R. canina* and concluded that the analgesic and anti-inflammatory effects of this product are in moderate level. This medication was used as an herbal powder 5 g daily (less than our study) for 3 to 4 months. After this time, pain relief improvement in physical function and decrease in need for analgesic were significant. Also in our study, improvement in physical function and decrease in need for analgesic were obviously observed. Winther et al., (2005) in a study also evaluated the effects of rosehip on reducing osteoarthritis signs and symptoms, and chemical medicine administration. They studied 94 patients with hip and knee osteoarthritis in a double-blind and placebo-control study. The administered dose in this study was herbal powder 5 g daily for three months and clinical signs were examined three weeks and three months later. The studied signs included pain relief and therefore analgesic administration, disability, general stiffness and general appearance of the patients. After three weeks of treatment, the need for analgesic drugs reduced significantly. Moreover, disability, general stiffness and general appearance of the patients significantly improved after three months. Observed complications in this study included nausea, vomiting, diarrhea and urticarial, which were not statistically significant (Winther et al., 2005). The aforementioned study, administered medication dose, analgesia results, functional improvements and even the number of the patients were similar to our study but the administered medication dose was different. The frequency of the complications was also similar. However, our study was different regarding the type and duration of medication administration due to lack of similar studies in operated patients. Furthermore, Chrubasik et al., (2008) studied 152 patients with acute flaring of chronic diseases. In total, 124 individuals of these patients had nonspecific lumber pain, 22 people had nonspecific lumber pain associated with osteoarthritis and eight people had special kind of backache. These patients used rosehip products for 54 weeks and later the signs and symptoms of the diseases were evaluated every six weeks (medicine dose was adjusted so that only maximally 3 mg of the effective galactolipid was administered daily). Signs and symptoms were effectively mended, at least two or three items from the following items were obviously better in the patients: pain, physical function and general evaluation of the patients. The palliative and analgesic effects and physical function of this study were similar to our study (Chrubasik et al., 2008). Willich et al. (2010) also carried out a study on 89 patients with rheumatoid arthritis and studied the effects of *R.*



canina powder (a subtype of rosehip). The administered dose of the medication in this study was 5 g of herbal powder which lower than administered dose in our study. Patients were given 10 capsules each containing 0.5 g of herbal powder in two divided doses. The duration of this study was six months. In this study, considerable pain reduction and also decrease in the mean duration of the signs in the group that received medication were seen, whereas in the group that received placebo, the disease deteriorated. Antioxidative effects have been confirmed in many studies. Therefore, these researchers have confirmed the benefits of using rosehip in patients with rheumatoid arthritis, including analgesic effect which is similar to the results obtained from our study.

Similar to our study, the aforementioned studies revealed no statistically significant difference regarding side effects and complications (Willich et al., 2010). The mentioned studies were carried out in patients with inflammatory arthritis who were given medication for a long time.

### 5. Conclusion And Recommendation

In patients receiving *R. damascena* extract before operation, reduction in pain was more significant as compared to the placebo group, as none of the patient's experienced severe early postoperative pain. In later hours, the severity of the pain was also less in the group receiving *R. damascena* extract at all times compared to the placebo group. The total administered medication dose and number of administration were also less in the group receiving *R. damascena* extract as compared to the placebo group. Due to low levels of pain score, analgesic injections were less frequently required in the group receiving *R. damascena* extract compared to the placebo group. The observed maternal complications included vomiting, nausea and one case of urinary frequency which were not statistically significant. Based on the results obtained from the present study, it can be concluded that *R. damascena* extract has considerable analgesic and anti-inflammatory effects which can play a useful role in reducing postoperative pain. As such, there is need for chemical medications which are often associated with numerous complications. Considering the low number of studies carried out in this regard, the following are however recommended:

1. Broad studies should be carried out on the operated patients to evaluate the palliative effects of this substance.
2. Other beneficial effects of this product should be studied in different investigations.
3. A suggestion was made to use this product in patients having gastrointestinal problems such as

ulcers and hemorrhage in which NSAID administration could cause complications.

4. Considering the fact that the different therapeutic effects of the required dose of this product were reported differently, further studies to determine the effective dose for inducing different therapeutic effects are recommended.

5. Due to having enough palliative effect, early lactation is recommended.

6. In operated patients, this product can substitute conventional painkillers for postoperative pain.

### References

1. Choi EM, Hwang JK. Investigations of anti-inflammatory and antinociceptive activities of *Piper cubeba*, *Physalis angulata* and *Rosa hybrida*. *J Ethnopharmacol* 2003;89(1):171-175.
2. Christensen R, Bartels EM, Altman RD, Astrup A, Bliddal H. Does the hip powder of *Rosa canina* (rosehip) reduce pain in osteoarthritis patients?--A meta-analysis of randomized controlled trials. *Osteoarthritis Cartilage* 2008;16(9):965-972.
3. Chrubasik C, Duke RK, Chrubasik S. The evidence for clinical efficacy of rose hip and seed: a systematic review. *Phytother Res* 2006;20(1):1-3.
4. Chrubasik C, Roufogalis BD, Müller-Ladner U, Chrubasik S. A systematic review on the *Rosa canina* effect and efficacy profiles. *Phytother Res* 2008;22(6):725-733.
5. Chrubasik C, Wiesner L, Black A, Müller-Ladner U, Chrubasik S. A one-year survey on the use of a powder from *Rosa canina* Lito in acute exacerbations of chronic pain. *Phytother Res* 2008;22(9):1141-1148.
6. De Andrade JR, Maslanka M, Maneatis T, Bynum L, Burchmore M. The use of ketorolac in the management of postoperative pain. *Orthopedics* 1994;17(2):157-166.
7. Edwards WT. Optimizing opioid treatment of post-operative pain. *J Pain Symptom Manage* 1990;5(1): S24-36.
8. Etches RC. Patient- controlled analgesia. *Surg Clin North Am* 1999;79(2):297-312.
9. Gharabaghi PM, Tabatabaei F, Abdollahi Fard S, Sayyah-Melli M, Ouladesahebmadarek E, Del Azar A, Atash Khoei S, Gharabaghi MM, Ghojzadeh M, Mashrabi O. Evaluation of the effect of preemptive administration of *Rosa damascena* extract on post-operative pain in elective cesarean sections. *African Journal of Pharmacy and Pharmacology* 2011;5(16):1950-1955.

10. Greer IA. Effects of ketorolac tromethamin on hemostasis. *Pharmacotherapy* 1990;10(6):71S-76S.
11. Linton AD, Maebius NK. Health and Illness. In: *Introduction to Medical-Surgical Nursing*. Saunders, 3<sup>rd</sup> edition, USA 2003; 68-72.
12. Trenam CW, Blake DR, Morris CJ. Skin inflammation: reactive oxygen species and the role of iron. *J Invest Dermatol* 1992;99(6):675-682.
13. Warriner CB, Etches RC, Badner N, Buckley DN, Beattie WS, Chan VW, Parsons D, Girard M. Continuous intravenous Administration of ketorolac reduces pain and morphine consumption after total hip knee arthroplasty. *Anesth Analg* 1995;81(6):1175-1180.
14. Willich SN, Rossnagel K, Roll S, Wagner A, Mune O, Erlendson J, Kharazmi A, Sørensen H, Winker K. Rose hip herbal remedy in patients with rheumatoid arthritis-A randomised controlled trial. *Phytomedicine* 2010;17(2):87-93.
15. Winther K, Apel K, Thamsborg G. A powder made from seeds and shells of a rose-hip subspecies (*Rosa canina*) reduces symptoms of knee and hip osteoarthritis: A randomized, double-blind, placebo- controlled clinical trial. *Scand J Rheumatol* 2005;34(4):302-308.

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