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Full Length Research Paper

Evaluation of the effect of preemptive administration of *Rosa damascena* extract on post-operative pain in elective cesarean sections

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Pain is the most common complaint in any kind of disorder. Despite its different nature, place and cause in various cases, pain is the main complaint of about half of the patients that are referred to physicians. Opiates and non-steroidal anti-inflammatory drugs, NSAIDS have been used for pain control many years ago, but these drugs also have some side effects. Regarding the complications and continuous pain in preoperative patients, some safe analgesics with better effects and little adverse effects are needed. Since many years ago in Iran, rose extract products are used in food production as jam and soft drink, and also in traditional medicine. The aim of the current research is to evaluate the effectiveness of preemptive prescription of rose extract in patients with elective cesarean sections (because of its little side effects) and compare its effects with placebo prescription. In a double blind placebo-controlled clinical trial, 92 patients had been studied in 2 equal groups. Group A were given rosehip extracts capsule and Group B were given placebo capsules. After preemptive prescription of Capsules A and B (15 min before anesthesia), the pain score was evaluated with visual analog scale (VAS) in varied hours after surgery in the ward, and then, the findings were analyzed. Analgesic drugs are needed for the palliation of post-operation pain. Total dosage of analgesics and the severity of pain in Group A at any time were lower than in Group B. There are no significant side effects in both groups. The initiation of breast feeding and its effects on newborns were same in both groups. According to our study, rosehip extract can be used in elective surgical patients without any significant side effects in order to improve pain and it is a more effective product when compared with NSAIDS and opiates.

Key words: Pain, rosehip extract, elective cesareans.

INTRODUCTION

Pain is the most common complication in different kinds of diseases. Nature, location and cause of the pain are different in each case. Pain is the primary complaint of almost half of the patients referred to physicians (Scott et al., 2003). 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).

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Abundant efforts have been done to control, reduce or relieve pain long time ago. The present treatment solutions for controlling perioperative pain are mainly based on treatments with pain killers, opioid and non-steroidal anti-inflammatory drugs (NSAIDS). Medications with less harmful effects from natural sources needed to be replaced with these conventional painkillers, because of their complications (Etches, 1999; De Andrade et al., 1994; Ethches et al., 1995).

"*Rosa damascena*" is one of the local plants in our area 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 proved in animal models and studies carried out on human models. Anti-inflammatory and analgesic activity of this herbal product is 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 to reduce 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 are 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 mostly is achieved administering N-methyl-D-aspartate including NSAIDS (Trenam et al., 1992; Winther et al., 2005). The objective of this study is to evaluate the effect of *R. damascena* extract administration on the postoperative pain in elective cesarean section.

MATERIALS AND METHODS

In a double-blind controlled clinical trial, 92 patients who underwent elective cesarean section were studied in two groups of 46 people, group receiving *R. damascena* extract (intervention group) and group receiving placebo. In these patients, the effect of administering *R. damascena* extract before operation (15 min before cesarean section) on postoperative pain was studied. Individuals were placed in groups randomly. This study was carried out in Alzahra Tabriz Educational Therapeutic Center Affiliated to Tabriz medical Science University. The duration of this study was 10 months and data collection and analysis were performed from July 2009 to May 2010.

R. damascena extract was provided by Medicinal Research Center of Tabriz Medical SCIENCE University one month before the commencement of this study. It should be mentioned that the studied patients were hospitalized in the study location during the study period.

Sampling was performed randomly from the patients who were qualified to enter this study. The inclusion criteria were pregnant females within the age range of 18 to 40 years having term pregnancy, without the history of hypersensitivity to local anesthetics (Lidocaine, Marcaine) and with the body mass index of 9.24 to 5.18 who were supposed to undergo cesarean section for different reasons. 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 one hour, emergence of intraoperative complications, having underlying diseases, such as diabetes and hypertension and existence of adhesions due to previous surgeries. 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 400 mg of *R. damascena* extract and "B" containing placebo (starch).

Method of providing the medication

Dried fruits of *R. damascena* were firstly ground by a mechanical mill and turned into fine powder. Later the solution was extracted by 70% ethanol using maceration technique. The extraction was performed for three times and each time for five minutes. The collected extract was completely dried under low pressure by rotary evaporator. The dried extract was kept in the refrigerator in the temperature of below 0°C until being used for making capsules. The scientific name of the plant used is *R. damascena* and the fruit of the plant was used. The effective dose of *R. damascena* when used as dried powder is 5 g per day (Winther et al., 2005), which calculating 15% of the extract, in case of being provided as extract form, is almost 750 mg per day and in the present study, it was used as 400 mg capsules, two capsules before the performance of local anesthesia in the operation room.

The researcher was present in the delivery room with the pregnant women who had the inclusion criteria and he explained the research, the objective of the study, the medications being used and their probable complications. Informed written consent was obtained if the patient was eager to participate in this study. Later 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 visual analogue scale (VAS) were given to the patients. Later in the operation room 15 min before spinal anesthesia, patients were given two capsules with 30 ml of water. The capsules given to the study group contained 400 mg of *R. damascena* extract and in placebo group they contained starch. All capsules had similar appearance and the researcher and the patients were unaware of the type of administered medicine during this study. Pain degree was evaluated in the recovery, 3, 6, 12 and 24 h after being transferred to the ward. The degree of the pain was also registered and the required analgesic was administered according to the severity of the pain after exiting the recovery and entering the ward, if the patient suffered from pain before three hours after operation being completed. The method of administering medication was as follows: based on the patient's experience of pain, if pain score was seven, tramadol injection (100 mg) IM was administered, if it was 3 to 6, diclofenac suppository (manufactured by Abureyhan pharmaceutical company) was administered and if it 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, three, six, 12 and 24 hours after being transferred to the ward. Pain severity was also recorded in case of the patients being transferred to the ward from recovery

Table 1. Demographic parameters of patients.

	Case group	Control group	P-value
Age (year)	28.78 ± 4.04	22.28 ± 5.04	0.64
Gravidity	1.98 ± 0.93	2.07 ± 0.90	0.65
Weight (kg)	78.67 ± 13.63	81.11 ± 11.54	0.35
Height(cm)	161.96 ± 6.92	161.43 ± 5.64	0.69
Infant weight (g)	3420.87 ± 540.24	3416.52 ± 481.54	0.69

and before the completion of three hours. The type of the medication used in each of the aforementioned times and the total used medication dose, 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, etc.) and neonatal complications (milk intolerance, restlessness, the time of passing meconium) were studied. This study has been approved by the Ethics Committee of Tabriz Medical Science University. Written consent was obtained from all patients. 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-Whitney U test and repeated measurements test by using SPSS-15 software. Normality of data distribution was evaluated using Kolmogorov Smirnov test.

RESULTS

The age range of the patients was 19 to 38 years, the number of the pregnancies (gravidity) was 1 to 6, the weight range of mothers was 58 to 115 kg, the height range of mothers was 148 to 176 cm, the normal weight range of the neonates at birth was 2700 to 5100 g, the range of operation duration was 25 to 75 min and the longest time for passing meconium was 12 h. Two groups were equal regarding all the evaluated parameters. Information obtained from the patients in both groups is presented in Table 1.

Needing analgesic significantly started later in the intervention group. Analgesic administration (tramadol, diclofenac and acetaminophen) also was significantly lower in the intervention group. The results obtained from the repeated measurement project test revealed that pain severity decreased in both groups solely and two by two comparison of the studied times revealed that pain severity significantly decreased in the intervention group in different times as decrease in pain severity in different times and its comparison in both groups revealed that decrease in pain severity was more in the intervention group as compared to the control group. All parameters related with postoperative pain and also the administration time of analgesics are presented in two groups in Table 2.

There was no statistically significant difference between the two groups in this regard. It should be mentioned that other complications, such as drowsiness, agitation, diarrhea, respiratory depression, constipation, urticaria, lactation intolerance, neonates' drowsiness, restlessness and icterus 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.

DISCUSSION

In this study we evaluated the effect of administering *R. damascena* extract on relieving postoperative pain in the elective cesarean sections. The degree of pain relief was better in the group having received *R. damascena* extract as compared to the group having received placebo in different times. The duration of analgesia after operation and pain degree in different times, the total dose and number of the times of administered analgesic were better in the group having received *R. damascena* extract. No complication was observed regarding receiving *R. damascena* extract administration and maternal and neonatal studies 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 *Rosa hybryda* 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 however was carried out on animal models. Other studies carried out on human models also confirm these findings. In this study, to evaluate anti-inflammatory and analgesic effects, they utilized *R. Hybryda* 200 mg/kg. 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). Chrubasik et al. (2006) in a study evaluated all therapeutic effect of this herbal medicine, considering its being frequently used in traditional medicine for centuries. Studied items in the mission study 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

Table 2. Analgesic requirement between two group and several analgesic drugs.

Requirement		Case group (%)	Control group (%)	P value
First request for pain relief after operation	<30 min	1 (2.2)	29 (63)	0.001
	30-60 min	0	9 (19.6)	
	60-120 min	4 (8.7)	7 (15.2)	
	>120 min	3 (6.5)	0	
Analgesic usage	In recovery room	0	13 (28.3)	0.001
	3 h later	44 (71.7)	46 (100)	0.04
	6 h later	41 (67.4)	46 (100)	0.03
	12 h later	28 (60.9)	46 (100)	0.02
	24 h later	6 (13)	42 (91.3)	<0.001
Analgesic prescribed count	Once	0	13 (28.3)	0.001
	Twice	44 (95.65)	46 (100)	0.04
	Three times	41 (89.13)	46 (100)	0.03
	Four times	28 (60.9)	46 (100)	0.02
	Five times	6 (13)	42 (91.3)	<0.001
Teramadol prescribed count	Never	41 (89.1)	11 (23.9)	0.03
	One dose	5 (10.9)	29 (63)	
	Two doses	0	5 (10.9)	
	Three doses	0	1 (2.2)	
	Four doses	41 (89.1)	11 (23.9)	
Diclophenace prescribed count	One dose	4 (8.7)	1 (2.2)	0.001
	Two doses	36 (78.3)	21 (45.8)	
	Three doses	4 (8.7)	19 (41.3)	
	Four doses	1 (2.2)	5 (10.9)	
Acetaminophen prescribed count	Never	27 (58.7)	18 (39.1)	0.01
	One dose	18 (39.1)	26 (56.5)	
	Two doses	1 (2.2)	2 (4.3)	

Table 3. VAS between two groups after operation.

VAS	Case group	Control group	P value
In recovery room	1.33 ± 1.62	3.31 ± 2.36	0.001
3 h later	4.70 ± 1.17	6.71 ± 1.05	
6 h later	2.87 ± 1.06	4.87 ± 1.50	
12 h later	2.50 ± 0.98	3.82 ± 1.11	
24 h later	1.20 ± 0.85	2.38 ± 0.93	

been confirmed. The analgesic and anti-inflammatory effects of our study are similar to the results obtained from the aforementioned study. In this study to evaluate analgesic and anti-inflammatory effects, they utilized the extract being prepared by 80% ethanol in rats. In another part of their study which was carried out on human model, they utilized rosehip powder of 45 g for 28 days. Analgesic effects significantly appeared in this dose (Chrubasik et al., 2008a). 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. Christensen et al. (2008) in an analysis studied the therapeutic effect of *Rosa canina*, a subtype of rosehip, on osteoarthritis. In this study the prepared product was also effective in reducing pain and pain score significantly decreased in the patients. Regarding complications in this study, some cases of acid regurgitation, gastro-intestinal discomfort, diarrhea, constipation and short spells

of urticaria were seen in some of the patients which were not statistically significant (Chrubasik et al., 2008b). Chrubasik et al. (2008b) 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 (similar to our study) for 3 to 4 months. After this time, pain relief, improvement in physical function and decrease in need for analgesic were significant (Christensen et al., 2008). In our study improvement in physical function and decrease in need for analgesic are also obviously observed. Winther et al. (2005) in a study 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, analgesic administration significantly reduced. Disability, general stiffness and general appearance of the patients significantly improved after three months. Observed complications in this study included nausea, vomiting, diarrhea and urticaria which were not statistically significant (Winther et al., 2005). The type of the aforementioned study, administered medication dose, analgesia results, functional improvements and even the number of the patients were similar to our study, the frequency of the complications also were similar. Our study however is different regarding the type and duration of medication administration due to lack of similar studies in operated patients. Churbaisk et al. (2008b) studied 152 patients with acute flaring of chronic diseases. 124 individuals of these patients had nonspecific lumber pain, 22 people had nonspecific lumber pain associated with osteoarthritis and 8 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 and, 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. Palliative and analgesic effects and physical function of this study were similar to our study (Chrubasik et al., 2008b). Willich et al. (2010) 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 equals the 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 the study was similar to ours, that is, six months. In this study considerable pain reduction and also decrease in the mean duration of the signs in the group receiving medication were seen, whereas in group receiving 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 effects and complications (Willich et al., 2010). The mentioned studies were carried out in patients with inflammatory arthritis who were given medication for longtime. Due to lack of similar studies in surgical patients, we used single dose in treating inflammatory arthritis.

CONCLUSION AND SUGGESTIONS

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 Rosa Damascena extract in all the times compared to the placebo group. The total administered medication dose and number of administration times were also less in the group receiving *R. damascena* extract as compared to placebo group. Due to low levels of pain score, analgesic injections were less frequently required in the group receiving *R. damascena* extract as compared to the placebo group. Observed maternal complications included vomiting, nausea and one case of urinary frequency which were not statistically significant. Neonate complications including lactation intolerance, ichterus, restlessness, drowsiness and delay in passing meconium were not observed in any of the children. Based on that results obtained from the present study, *R. damascena* extract has considerable analgesic and anti-inflammatory effects which can be useful in reducing postoperative pain and need chemical medications which are often associated with numerous complications. Considering the low number of studies carried out in this regard, it is however recommended:

1. Broad studies should be carried out in the operated patients to evaluate palliative effects of this substance.
2. Other beneficial effects of this product should be studied in different investigations.
3. The usage of this product in patients having gastrointestinal problems, such as ulcers and hemorrhage in which NSAID administration could cause complications is suggested.
3. Considering the fact that required dose of this product to have different therapeutic effects is reported differently, further studies to determine the effective dose for inducing different therapeutic effects are recommended.

4. Due to having enough palliative effect, early lactation is recommended.
5. In operated patients, this product can substitute conventional painkillers for postoperative pain.

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