Original Article

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# The Efficacy and Safety of Sesame Oil in Prevention of Chemotherapy-Induced Phlebitis in Children with Acute Lymphoblastic Leukemia

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**Abstract**

**Background:** Phlebitisis is the inflammation of the veins that negatively affect the patient's health status. This study was conducted to determine the effect of external use of sesame oil in prevention of chemotherapy-induced phlebitis in children with ALL.

**Materials and Methods:** This double-blind clinical trial was conducted on 60 patients aged 2 to 14 years old who were admitted for chemotherapeutic management to the 17th Shahrivar Hospital, Rasht, Iran, between January 2016 and January 2017.The patients were randomly divided into two groups: intervention and control. Ten drops of sesame oil in the sesame oil group and10 drops of oral liquid paraffin in the control group were given daily for 30 days. Data collection tools were run in both groups: a demographic questionnaire and the Visual Infusion Phlebitis Scale for the measurement of phlebitis. Data were analyzed using SPSS (version 23).

**Results:** The survival time for vein received chemotherapy in the sesame oil group was 44%.The results of the present study showed that there is statistically significant difference between the mean grade of phlebitis in both groups ($p = 0.0001$).The relative risk of phlebitis incidence was two times more than the sesame oil group.

**Conclusion:** External use of sesame oil can be effective in the prevention of chemotherapy-induced phlebitis.

**Keywords:** Chemotherapy, Children, Leukemia, Phlebitis, Sesame Oil

## Introduction

Chemotherapy is a medical method that uses one or more cytotoxic drugs employed in systemic anti-cancer treatment to cure localized or generalized diseases with the aim of the recovery or palliation (1, 2). Since most pediatric solid tumors have a high risk for micro metastatic disease at the time of diagnosis, chemotherapy is used in almost all cases (3). Chemotherapeutic agent is one that is capable of destroying malignant cells. Nowadays, several chemotherapeutic agents are used (4, 5). Multiple doses of chemotherapy are required in the long term to suppress tumor relapse (2, 6). Intravenous therapy is the most common method for using these types of drugs. The method in pediatric treatment is common and in some cases is the only possible method (2, 7, 8).Chemotherapy drugs have multiple adverse effects (3). One of its adverse effects is phlebitis (9). It has been reported that the peripheral intravenous infusion of chemotherapy drugs such as Epirubicin, Vinorelbine and 5-Fluorouracil cause phlebitis (10, 11, 12). Phlebitis defined as inflammation of the venous tunica intima and endothelial cells. Its symptoms, including painful swollen vein, warmth, erythema, tenderness, palpable venous cord, and pyrexia (10, 12, 13) are diagnosed with continuous observing in primary stages (14, 8).

Risk factors for phlebitis are solutions concentration and medicine irritating, size and situation of catheter, venipuncture damage, and microbial contamination (13,

14). The incidence of chemotherapy-induced phlebitis was reported as 33% - 80% (11, 12, 15, 16).

Venous irritation deteriorates the patient's quality of life and sometimes limits the continuation of chemotherapy (10). In cancer pediatric, preserving peripheral venous access is a priority because it leads to pain and discomfort. Therefore, this should be managed effectively to decrease patient discomfort (8, 15). Thus, phlebitis prevention, control of its evolution after its occurrence and reversal of its characteristic inflammatory signs are needed, mainly in the patients underwent antineoplastic chemotherapy (9). In order to prevent and treat chemotherapy-induced phlebitis, some preventative measures are proposed such as external application of Aloe vera (17), the increase of volume of normal saline as solvent of drug (11), the switche of drug formulation to lyophilized powder (10), the application of Chamomilla Recutita (9), and the use of topical trinitroglycerin (18). One of the suggestions in this regard is using Sesamum indicum, the product of the medicinal and edible plant of sesame (12).

Sesame seed is a reservoir of nutritional ingredients with numerous beneficial effects for health promotion in humans. The bioactive components present in the seed include vital minerals, vitamins, phytosterols, polyunsaturated fatty acids, tocopherols, and unique class of lignans such as sesamin and sesamolin. The phenylpropanoid compounds, including lignans along with tocopherols and phytosterols createa defense mechanism against increasing the maintenance the quality of oil by preventing oxidative rancidity. In consequence, value addition efforts in sesame can enable development of genotypes with high antioxidant activity and subsequently prevention of free radical related diseases (19). Furthermore, the antimicrobial activity of sesame oil against gram positive and gram negative organism is reported (20). Seed and sesame oil have extensive medicinal applications (21). Regarding the therapeutic effects of sesame indicum, researchers have conducted many studies and reported the following effects: enhancinganti-hyperglycemic efficacy in the patients with type 2diabetes (22), alleviation of the severity of primary dysmenorrhea (23), and reduction of amiodarone-induced phlebitis rate (24).

In the light of the results attained through the relevant researche performed, it can be concluded that sesamum oil may result in a better tolerance of patients during the treatment process, leading to a reinforcement of the chemotherapy effect.

Seemingly, there has been no study conducted in Iran over preventative measure against phlebitis in children with Acute Lymphoblastic Leukemia (ALL).The chemotherapy is scheduled for children at set times and days and by various predetermined routes while considering the fact chemotherapeutic agents have both side effects and toxic effects. Therefore, to monitore and prevent IV infusions of phlebitis, the present study was planned and performed.

## Materials and Methods

The present double-blind randomized controlled clinical trial was conducted following approval of the Ethics Committee of Guilan University of Medical Sciences in Rasht, Iran. This study was also recorded in IRCT database (IRCT2015101924594N1). Sixty patients who underwent chemotherapy and admitted to the oncology section of the 17th Shahrivar Hospital in Rasht, Iran, were recruited for the current investigation. According to 5% probability of type 1 error and 0.2 the difference of prevalence, the number of samples in each groups was considered 30.

The children received chemotherapy with BFM (Berlin-Frankfurt-Munster Study Group) 2002 protocol of developing ALL. Doxorubicin and vincristine were also used in some parts of this protocol (25).

The inclusion criteria of this study were as follows: (a) suffering from acute lymphoblastic leukemia; (b) undergoimg the same treatment regimen; (c) aging 2-14 years; (d) not having other disease (diabetic, hypertension autoimmunity); (e) not having fever and neutropenia; (f) not using antibiotic; (g) not using analgesics and using no drugs orherbal oil to prevent phlebitis during the study; (h) not using portacath for administration of chemotherapy;(i) having no allergy to sesame; (j) using upper limbs for intravenous catheterization, and (K) applying No 20-24 Angiocath of Mabna Teb Pars Company for catheterization and following the required aseptic conditions in catheterization. For data collection a bipartite questionnaire was used, containing demographic information (pediatric age and sex, mothers' age, job and educational background) and a question about the absolute number of neutrophil and some questions about the duration of disease, the duration of chemotherapy, and the chemotherapy diet (type, amount, time and the prescription type). In this study, Visual Infusion Phlebitis Scale (VIPS) was used to assess phlebitis and its severity, which was first introduced by Jackson in 1998 (Table I).

Nekuzad et al., (2012) have confirmed the questionnaire face and content validities (12).

Sesame oil was analyzed in Pharmaceutical Chemistry Research Center and then sampling was accomplished from January 2016 to January 2017. Parents of the patients were asked to participate in the current study with respect to our inclusion criteria. In the first stage, consent form and demographic questionnaire were completed through the interview and file completion.

Through simple randomization, the samples were divided into two groups: control and intervention (n=30).

Aseptic venipuncture technique was performed by a qualified nurse and according to similar studies, the intervention group received 10 drops of sesame oil (100% pure sesame oil manufactured by the Barij Essence Pharmaceutical (Company, Iran)) and the control group received 10 drops of placebo (edible liquid paraffin manufactured by the Farabi (Company, Iran)) on the anterior forearm and then slowly spread around 10 cm toward the arm. Then, it was continued every 12 h (morning and night before sleeping), from the 1st day of chemotherapy to the 30th day. In addition, each time before using the oil, the place was rinsed with water. This procedure was performed by the researcher in hospital and by the time of discharge the patient was trained and familiar with home hygiene to continue applying oil at home and training brochure was given to the patient's parents. Then, the VIPS was used daily to check the incidence and degree of phlebitis before and after the intervention. All the understudied cases were carefully considered and followed up in these 30 days (During hospital admission, after being discharged and at their next hospital readmission).The patients indicated with at least 2 signs of phlebitis (pain, erythema and swelling on the site), were referred to the phlebitis section for treatment.

The data attained from the two groups were statistically compared and analyzed using SPSS (version 23) and running independent t-test, X2, Mann Whitney, Kaplan-Meier estimation, and Log Ranktest.

## Results

In the current study, the component analysis showed that this oil consisted of oleic acid 22.3%, linoleic acid 41.2%, and gamma-sitosterol 6.1%. Regarding gender, thirty three of participants were males and twenty seven were female. In the intervention group, there were eighteen boys and twelve girls, and in the control group, there were fifteen boys and fifteen

girls. The participants' age ranged between 2 to 14 years old (Table II).

The survival time for vein received chemotherapy in the intervention group was 44% till the 30th days; in the control group, all patients showed sign of phlebitis. The relative risk of phlebitis was 2 times more frequent in the control group and the absolute risk reduction showed that the phlebitis incidence in the control group was 44% more than the intervention group. Based on the chi-square test, there was a meaningful difference between the two groups regarding the phlebitis incidence (p=0.0001).

The median survivals in the intervention and control groups were 22 days to 3 days, respectively. The log rank test showed a significant difference in the two groups (p=0.0001) (Table III).

The main severity of phlebitis was 1.5 (SD=0.26) in the intervention group and 3.5 (SD=0.13) in the control group. Moreover, Mann-Whitney test showed a meaningful statistical difference between the mean of phlebitis incidence in the mentioned groups (p=0/0001). Almost, the degree of severity of phlebitis in the control group was two times more than the intervention group (Table IV)

Survival time (non-phlebitis) in the control group was 15% till the 9th day and it was 80% in the intervention group. The non-parametric log rank test manifested that there is a meaningful difference between the two groups regarding the time of phlebitis incidence (p=0/0001). In other word, the time of phlebitis incidence in intervention group had been delayed (Figure 1).

*Table I : Visual infusion phlebitis scale (VIPS)*

| PHLEBITIS GRADING SCALE(VIPS) | |
|---|---|
| Clinical characteristics | Grade |
| IV site appears health | 0 |
| One of the following signs is evident<br>• Slight pain near the IV site<br>• Slight redness near the IV site | 1 |
| Two of the following are evident:<br>• Pain at IV site<br>• Redness | 2 |
| ALL of the following are evident:<br>• Pain along path of cannula<br>• Redness around the site<br>• Swelling | 3 |
| ALL of the following are evident and extensive:<br>• Pain along path of cannula<br>• Redness around the site<br>• Swelling<br>• Palpable venous cord | 4 |
| ALL of the following are evident and extensive:<br>• Pain along path of cannula<br>• Redness around the site<br>• Swelling<br>• Palpable venous cord<br>• Pyrexia | 5 |

*Table II: Baseline information before conducting the study*

| Variable | Intervention group | Control group |
|---|---|---|

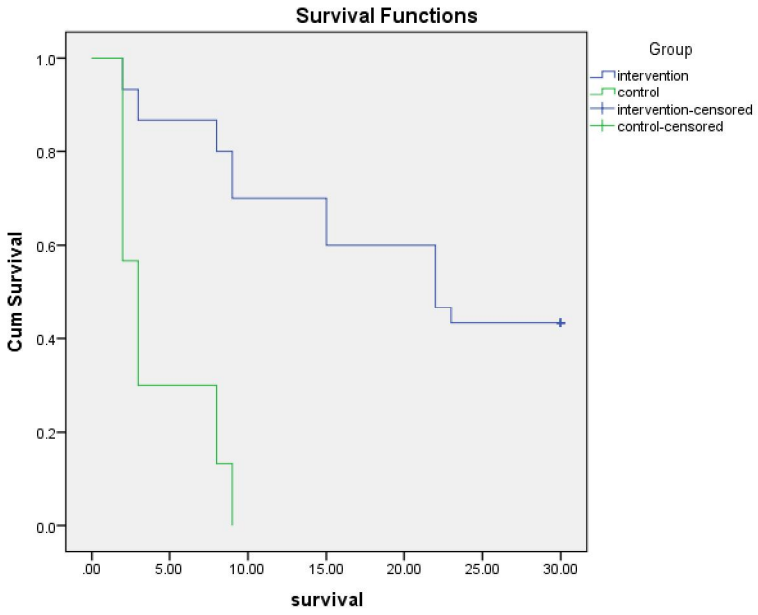
| | | N | % | N | % |
|---|---|---|---|---|---|
| Sex | Boy | 18 | 54/5 | 15 | 45/5 |
| | Girl | 12 | 44/4 | 15 | 55/6 |
| Age | Max | 14 | | 13 | |
| | Min | 2 | | 2 | |
| | Mean±SD | 7/5±3/88 | | 6/25±2/97 | |

*Table III: Kaplan-Meier estimated survival rates in interventions and control groups*

| Group | Total | Censored | | Median | | | |
|---|---|---|---|---|---|---|---|
| | N | N | % | Estimate | Std.Error | 95% Confidence Interval | |
| | | | | | | Lower Bound | Upper Bound |
| Intervention | 30 | 13 | 44 | 22 | 4/37 | 13/43 | 30/57 |
| Control | 30 | 0 | 0 | 3 | 0/31 | 2/39 | 3/62 |
| Overall | 60 | 13 | 21/7 | 8 | 1/66 | 4/75 | 1/25 |

*Table IV: The frequency distribution of the severity of phlebitis in the intervention and control groups*

| The Severity of Phlebitis | Intervention group | | Control group | | P- value |
|---|---|---|---|---|---|
| | N | % | N | % | |
| grade 0 | 13 | 43/3 | 0 | 0 | 0.0001 |
| grade 1 | 0 | 0 | 0 | 0 | |
| grade 2 | 8 | 26/7 | 3 | 10 | |
| grade 3 | 7 | 23/3 | 10 | 33/3 | |
| grade 4 | 2 | 6/7 | 16 | 53/4 | |
| grade 5 | 0 | 0 | 1 | 3/3 | |
| Mean±SD | 1/50±0/26 | | 3/50±0/13 | | 0.0001 |




**Day incidence of phlebitis-induced**

Figure1. Kaplan-Meier survival curve on the two hospitalized and censored groups (Censored groups are those who stayed until the end of the study and were not with phlebitis). The survival time for the censored group was equal to the total days of the study (from the beginning to the end).

## Discussion

This study showed that the external use of sesame oil in the children underwent chemotherapy can decrease the phlebitis incidence and increase vein survival time. Actually in the control group, the relative risk of phlebitis incidence was two times more than the intervention group. In addition, the mean degree of the severity of phlebitis in the control group was two times more than the intervention group. Although the patient characteristics such as old age, female gender, neutropenia, malnutrition, immunosuppression, and circulatory impairments also increase the risk of phlebitis (26), all these variables were statistically the same across the groups. The absolute risk reduction showed that the phlebitis incidence in the control group was 44% more than the intervention group. Despite the fact that the procedure of this study was trained to the patients' mothers, it was assumed that the patients and their mothers may not been careful in the implementation of the process, hygiene at home and protecting the skin.

According to the obtained results, the sesame oil contained high levels of unsaturated fatty acids (oleic acid and linoleic acid) and sitosterol. The medicinal plants appear to be rich in secondary metabolites, widely used in traditional medicine to combat and cure various ailments (27). Concerning the contents of sesame oil, various studies have been reported the antioxidant (28, 29), antimicrobial (20), and anti-inflammatory (27) properties. In this regard, Kalliopiet al., evaluated the beneficial effect of sesame oil on vascular endothelium in thirty hypertensive males (mean age 52.7 ± 10.4 years) using a two-phase study in an outpatient hypertension clinic at Alexandra University Hospital, Athens, Greece. It was revealed that sesame oil consumption exerts a beneficial effect on endothelial function and this effect is sustained with

long-term daily (30). Nekuzad et al., treated 60 patients with 5- Fluorouracil in oncology ward of Imam Hossein Hospital in Tehran, Iran. They showed that the external use of sesame oil is effective, safe. and well tolerated for phlebitis-induced prophylaxis . They found that 10% of the intervention group and 80% of the control group get affected with phlebitis. The mean degree severity of phlebitis was 0.1 in intervention group and 1.9 in the control group. There was a significant difference between the two groups concerning the incidence of chemotherapy-induced phlebitis ($p < 0.05$) (12). In addition, Carayanni et al., performed a study in the Burn Center of a state hospital in Athens, Greece, to compare the effectiveness of Moist Exposed Burn Ointment (MEBO) versus a combination of povidone iodine plus be panthenol cream on partial thickness burns. The results revealed that MEBO is the dominant therapy for superficial partial burn wound with significantly lower costs and significantly higher effectiveness due to a lesser time of recovery and consequently lower time of hospitalization and follow-up. The authors also suggested that topical application of MEBO may be considered for further investigation as a potential first-line treatment modality for superficial partial thickness burns (31). Therefore, as the preventative and treatment role of sesame oil has been proved in the previous studies in adult phlebitis, skin problems, and burns as an anti-infammatory agent, coupled with the present findings; it seems that the reduction of phlebitis in the intervention group could be due to the compounds in sesame oil.

## Conclusion

In this study, sesame oil was used as an agent for prevention of chemotherapy-induced phlebitis in children. The sesame oil contains high levels of compounds such as unsaturated and essential fatty acids (oleic and linoleic acids) and sytosterols (Gama sytosterol) excerting anti-inflammatory (27) and antioxidant properties (28, 29) and can protect the skin and blood vessels (21, 30). Sesame oil can be absorbed through the skin and it can play an important role in preventing phlebitis (12). Specifically, as it is found abundantly in Iran, sesame oil has no adverse effects and is quite cheap and compared to chemical drugs. The main reason for the conduct of this study was to highlight the priority of shielding and protecting the under chemotherapy veins in children and the results showed that sesame oil can improve the situation at clinical, educational and research levels. As a result of our research, sesame oil can be effective and safe as an agent for the prevention of chemotherapy-induced phlebitis in children, although further research are needed recruiting larger to affirm the accuracy of our findings.

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## Conflict of interest

The authors declare that they have no conflict of interest..

## References

1. Andreoli TH, Griggs R, Wing E. Cecil's Principles of Internal Medicine: diseases of the blood and cancer. 6th ed. Philadelphia: Lippincott, Williams& Wilkins; 2010.
2. Luckman J. Saunders manual of nursing care III. Translated: Barahimi N, Jafari S, Hosseinzah M. Tehran: Ayyz; 2003.
3. Marcdante K J, Kliegman R M. Nelson Textbook of pediatrics. 7th ed. Philadelphia: Saunders; 2015.

4. Pillitteri A. Maternl & Child Health Nursing: Care of the Childbearing & Childrearing Family. 7th ed. Inc: Lippincott, Williams & Wilkins; 2014.
5. Peate I, Wild K, Nair M. Nursing Practice: Knowledge and Care. USA: John Wiley&Sons; 2014.
6. Hinkle J L, Cheever K H. Brunner & Suddarth's Textbook of Medical-Surgical Nursing. 13th ed. North American: LWW; 2014.
7. Black J M, Hawks J H. Medical Surdical Nursing clinical Management for Positive Outcomes. Translated:Asghari M. Mashhad:Parastaran Javan; 2013.
8. Pagnutti L, Bin A, Donato R, Lena G D, Fornasiero L, Gerratana A, et al. Difficult intravenous access tool in patients receiving peripheral chemotherapy: A pilot-validation study. Eur J Oncol Nurs 2015; xxx: 1-6.
9. Reis P E D D, Carvalhon E C D, Bueno P C P, Bastos J K. Clinical Application of Chamomilla Recutita in Phlebitis: Dose Response Curve Study. Rev Lat Am Enfermagem2011; 19(1): 3-10.
10. Nagata K, Egashira N, Yamada T, Watanabe H, Yamauchi Y, Oishi R. Change of formulation decreases venous irritation in breast cancer patients receiving epirubicin. Support Care Cancer 2012; 20: 951–955.
11. Yamada T, Egashira N. Decrease in the vinorelbine-induced venous irritation by pharmaceutical intervent. Support Care Cancer 2012; 20: 1549–1553.
12. Nekuzad N, Ashketorab T, Mojab F, Alavi-Majd H, Azadeh P, Ehtejab G . Effect of External Use of Sesame Oil in the Prevention of Chemotherapy-Induced Phlebitis. Iran J Pharm Res 2012; 11 (4): 1065-1071.
13. Pasalioglu K B, Kaya H. Catheter indwell time and phlebitis development during peripheral intravenous catheter administration. Pak J Med Sci 2014; 30(4): 725-730.
14. Sarani A A, Etemadi, Su, Abed Saeedi, Zh. Investigating Role of Mechanical and Chemical Factors in the Creation of Peripheral vein in Flammarion in hospitalization Patients in hospital in zahedan, Iran. Life Sci J 2013; 10(1): 379-383.
15. Yoh K, Niho S, Goto K, Ohmatsu H, Kubota K, Kakinuma R, et al. Randomized trial of drip infusion versus bolus injection of vinorelbine for the control of localvenous toxicity. Lung Cancer 2007; 55: 337-341.
16. Suga Y, Kumazaki M, Nishigami J, Takeda K, Kawagishi A, Ishizaki J, et al. Improvement of epirubicin-induced phlebitis to switch from liquid preparation to lyophilized formulation. Gan To Kagaku Ryoho2009; 36(1): 93-6.
17. Zheng GH, Yang L, Chen HY, Chu JF, Mei L. Aloe vera for prevention and treatment of infusion phlebitis. Cochrane Database Syst Rev 2014; 4(6): CD009162.
18. Rahmani R, Haghkhahe S. Effect of topical TNG to prevent from phlebitis through using venous catheter on patients who were under chemotherapy treatment [MSc. dissertation]. [Tehran]:Bagiyatallah University of Medical Scinces; 2008.
19.Pathak N, Rai A K, Kumari R, Bhat K V. Value addition in sesame: A perspective on bioactive components for enhancing utility and profitability. Phcog Rev 2014; 8(16): 147-55.
20. Saleem T S M. Anti-microbial activity of sesame oil. Int J Phytochem Pharmacol 2011; 1(1): 21-23.
21. Zargary A. pharmaceutical plants volume 3. Tehran: Tehran University; 2012.
22.Sankar D, Ali A, Sambandam G, Rao R.Sesame oil exhibits synergistic effect with anti-diabetic medication in patients with type 2 diabetes mellitus.Clinical Nutrition2011; 30:351-358.
23. Haidari F, Mohammad Shahi M,Shirbeigi E.The Effect of Sesame Butter – Supplemented Breakfast in Comparison

to Common Breakfast on the Severity of Primary Dysmenorrhea in the Students of Ahvaz Jundishapur University of Medical Sciences.Sci Med J Ahwaz Jundishapur Univ Med Sci 2012; 11(2): 193-200.
24. Nesami B M, Shorofi A S, Hashemi-Karoie S Z, Khalilian A. The effects of sesame oil on the prevention of Amiodarone-induced phlebitis. Iran J Nurs Midwifery Res2015; 20(3):365-370.
25. Adamson pc, Bagatell R, Balis F. General principles of chemotherapy.In:pizzo pa, poplack dg. Principles and practiceof pediatric oncology. 6th ed, Philadelphia: Lippincott Williams and Wilkins Inc; 2011.
26. Macklin,D. Phlebitis:Apainful complication of peripheral IV catheterization that may be prevented. Am J Nurs 2003; 103(2): 55-60.
27. Savithramma N, Linga Rao M, Suhrulatha D. Screening of Medicinal Plants for Secondary Metabolites. Middle East J Sci Res 2011; 8(3): 584-579.
28. Mohamed H M A, Awatifb I I. The use of sesame oil unsaponifiable matter as a natural antioxidant. Food Chem 1998; 62(3): 269-276.
29.Borchani C, Besbes S, Blecker Ch, Attia H.Chemical Characteristics and Oxidative Stability of SesameSeed, Sesame Paste, and Olive Oils. Asian Pac J Cancer Prev2010; 12: 585-569.
30. Kalliopi K, Kimon S, Maritta L,Pigi M, Sofia S, Nikolaos Z. Sesame oil consumption exerts a beneficial effect on endothelialfunction in hypertensive men.Eur J Prev Cardiol2013; 20(2): 202-208.
31. Carayanni V J,Tsati E G,Spyropoulou G C H,Antonopoulou F N, Ioannovich J D.Comparing oil based ointment versus standard practice for the treatment of moderate burns inGreece: a trial based cost effectiveness evaluation. BMC Complement Altern Med 2011; 11:122.