

Complementary and Alternative Medicine in Pediatric Oncology Patients in South of Iran

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Received: 23 August 2015

Accepted: 05 January 2016

Abstract

Background: Children suffering from cancer frequently use complementary and alternative medicine (CAM). Most of people do not disclose using CAM to their physicians as they fear to be blamed or prohibited using them. Some of these products may interfere with the conventional remedies. The aim of this study was to investigate the frequency and characteristics of CAM use in pediatric oncology patients in 2 referral centers in south of Iran.

Materials and Methods: In this cross-sectional study, all pediatric cancer patients (from 5 months to 18 years old) registered at two referral center (n=135) were investigated from January to July 2015 in Shiraz, southern Iran. Interview with their parents and completing the specific check list were done. Data were analyzed by SPSS v. 21 using Chi-square and Student t- test.

Results: From 150 families approached, 135 (90%) completed the questionnaires. Overall, 114 (84.4%) children ever used a kind of CAM product while 92.6% sought faith healing. Concurrently, 81.1% of the CAM admitted users applied them with their conventional treatments. The most common used CAM products were Zinc (43.7%) and multivitamins (31.9%). None of the evaluated variables significantly influenced CAM use in the patients. Most of the patients (77%) introduced their physicians as the source of knowledge about CAM which was the most trusted source as well. About half of the patients (50.9%) did not inform their physicians to use these products.

Conclusion: Oncologists should be aware of highly prevalent use of CAM among their patients. They should discuss with the families about the possible interactions of these products may have with chemotherapy drugs. A filled diary at regular intervals may help the physicians to monitor CAM use in their oncology patients.

Key words: Cancer, Complementary and Alternative Medicine, Oncology, Pediatric

Introduction

Complementary and alternative medicine (CAM) is a diverse group of products and practices which complement or substitute conventional medicine. It may include traditional Chinese medicine, nutritional supplements, vitamins, herbal products, acupuncture, homeopathy, yoga, massage, chiropractic among many others. Some even consider spirituality and faith healing (i.e. praying for self or others cure) as a kind of CAM(1). Some investigators prefer to use the term “integrative therapies” instead, as they believe this terminology more accurately describes

therapies that complement the mainstream conventional medicine(2). It is usually used in chronic debilitating conditions where conventional medicine may fail or bring little improvement to the patients(3-6).The use of CAM in pediatric cancer patients differs in different nations based on how it is defined and may reach up to 90% (7). A systematic review conducted by Bishop et al., which included 28 published studies from 3526 children suffering from cancer revealed that the frequency of CAM use ranged from 6 to 91% in different studied, with herbal

remedies, diets/nutrition and faith healing were the most popular CAM used (8). The cancer patients may use CAM for a variety of reasons including relieving adverse effects of chemotherapy, boosting the immune system, improving mood and quality of life, pain management, prevention of cancer recurrence or as the last resort in end-stage hopeless individuals (9-12). Despite the possible beneficial effects, most physicians are concerned about the safety of these products and the potential interactions they may have with the chemotherapy drugs.

CAM has been reported to be used in Iranian patients for a variety of illnesses including diabetes mellitus and other metabolic disorders, hyperlipidemia and obesity, obstetric indications, neuropsychology disorders, rheumatologic diseases, cutaneous lesions, gastrointestinal symptoms among others (13-23). Furthermore, there are some in vitro and in vivo studies about the possible beneficial role of CAM and Iranian Traditional Medicine including different herbal products and spirituality in treating adult cancer patients or relieving their symptoms or treatment-associated complications(24-30). However, there is lack of data regarding the frequency and type of CAM in pediatric cancer patients in Iran and the reasons behind using them.

The aim of this study was to investigate the frequency and type of CAM use in 2 referral centers for treating pediatric cancer patients in south of Iran. We also determined to know other issues regarding the self-reported efficacy, side effects, and the main reasons of use in children using these products or practices.

Materials and Methods

This cross-sectional study was done in two separate pediatric referral centers (both inpatient and outpatient) affiliated to Shiraz University of Medical Sciences, Shiraz, southern of Iran. The studied population was all children 18 years or less suffering from any kind of cancer who

have been registered in this centers for cancer treatment (n=150) from January to July 2015. Fifteen parents refused to participate in the study and finally 135 eligible patients were investigated and interview was done with their parents. The check list was taken from a similar survey done in Canada by Adams et al (31)[with permission]. After being translated into Persian language, some items regarding the products and practices used were changed and adapted based on the cultural differences and the specific products commonly used in the region. The final version was pilot tested to ensure its concept validity. Overall, the backbone of the data gathering form was the same as the original English version, and was composed of 19 questions about the patients and family demographics, general health, the specific CAM products and practices used, reasons for use, effectiveness and adverse effects, concurrent use with conventional medicine, and the source of knowledge about the CAM used. A trained person handed out the questionnaires between the patients or their care givers while they were waiting to be visited in the clinic or during their admission in the hospital. Then the completed forms were collected and checked to be filled appropriately.

Statistical analysis

Data were analyzed by SPSS (version.21). Descriptive data were presented as mean, standard deviation, frequency, percent, and appropriate charts. Categorical and quantitative data were compared by Chi-square test and Student t-test between two groups of patients, respectively. P value less than 0.05 was considered statistically significant.

Results

Characteristics of patients and their parents are summarized in Table I. The sample population had a mean age of 7.8 years± 4.7 (SD) with age range of 5 months to 18 years. Nearly half of the patients were

diagnosed with cancer more than a year prior to the survey. Approximately 80% of the patients and their parents stated that they were in good or excellent general health rather than moderate or poor. Majority of the parents (74.1% of fathers and 84.4% of mothers) had no university degree. In majority of the patients (79 %), annual household income of the family was less than 300\$ per month.

Table II shows the frequency of consumption of different products and practices related to the complementary and alternative medicine by children with cancer as well as the most common reasons of use and their effectiveness. Overall, the most common used CAM product and practice were zinc supplement (43.7%) and faith healing (92.6%), respectively. In subgroup of minerals and vitamins, the most common used product was zinc supplement (43.7%) followed by multivitamin (31.9%) and folic acid (20.7%). In herbal subgroup, the products were used by children from 24.4% to 37%, and leek extract was the most common herb used by the patients. Other popular herbal remedies were chamomile, mint, and garlic in decreasing order of frequency. Moreover, a variety of other products such as fox gallbladder, probiotics, fish oil, jinseng, etc. were used in a subgroup of patients (table II). Apart from prayer which was very popular among the parents or guardians of cancer children, other CAM practices such as yoga, massage, and hypnotism were used infrequently (table 2).

The most common reason of CAM use was increasing immunity in the product subgroup and improvement or cure of patients in the practice subgroup. Most of the participants in the survey reported that the products they used were quite effective (60.6%-88.9%). In practice component, perceived helpfulness of 69%- 100% was mentioned by patients or their parents.

Totally, out of 135 patients, 114 (84.4. %) used at least one of the products of

complementary medicine. The majority of the patients (81.1%) used CAM concurrently with their chemotherapy drugs. A small proportion of patients (12.6%) had used CAM before or instead of conventional treatment. The proportion of parents who consumed any kind of CAM was almost equal to those who never used them, and it had no significant effect on the use of CAM in their children. The most common reason for not using CAM reported by patients was “I do not believe these therapies” (74%) followed by “poor knowledge regarding CAM” (15%), and “I think these therapies are not necessary” (11%).

Fourteen patients (10.3%) experienced some kind of adverse effects while using CAM that most of them were mild or moderate. There were only four cases who reported severe side effects following consumption of probiotics and leek extract that had been relieved with CAM withdrawal.

The two groups of patients who ever used CAM or not, were compared regarding different variables which are presented in Table III. There was no significant association between the use of the products and any of the evaluated variables.

Figure 1 illustrates the different sources of knowledge about complementary medicine reported by the patients or their parents. Based on the results, the most common source of knowledge was reported to be physicians (77 patients), followed by friends and families (69 patients), and book and magazines (38 patients). Among different sources, the most trusted source of information which scored on a 10-point scale (1 = no trust, 10= full trust) was reported to be physicians (mean: 9.88, 95%CI: 9.42-9.91) (Fig 2).

When they were asked who they have talked with about using CAM, 55 out of 112 responders (49.1%) answered that they have informed their responsible physician. 36 patients (32.1%) had never talked about this issue to anyone.

Table I. Demographic and characteristics of children affected by cancer and their parents

Variables	Values
Age (year)	7.8 ± 4.7
Mean ±SD (min-max)	(5m-18y)
Sex (m/f) number	86/49
Age of father (year)	39.4 ± 7.8
Mean ±SD (min-max)	(23-60)
Age of mother (year)	34.3 ± 7.7
Mean ±SD (min-max)	(19-60)
General health status of patient(excellent and good vs. moderate and poor)number (%)	110 (81.5)
General health status of mother(excellent and good vs. moderate and poor) number (%)	117 (86.7)
General health status of father(excellent and good vs. moderate and poor) number (%)	107 (79.3)
Time since diagnosis	
Number(%)	
<3months	18(13.3)
3-<6months	24(17.8)
6-12 months	27(20)
>12months	66(48.9)
Father education	
Number (%)	
Illiterate	14 (10.4)
Secondary school	86 (63.7)
University degree	35(25.9)
Mother education	
Number (%)	
Illiterate	11 (8.1)
Secondary school	103(76.3)
University degree	21 (15.6)
Annual income	
Number (%)	
≤ 300 \$/month	107 (79)
> 300\$/month	28 (21)
Insurance coverage	
Number (%)	
Yes	38 (28.1)
No	51 (37.8)
Not sure	46 (34.1)

Table II. Products and practices used by children with cancer, their common reasons of use and perceived effectiveness

Product	Ever used Number (%)	Most common reasons of use ^a Choice, number/responders, (%)	Effective (Yes) Number/responders, (%)
Minerals and Vitamins			
Multivitamin	43 (31.9)	(3) 18/35, (51.4)	24/38, (63.2)
Folic acid	28 (20.7)	(1) 18/23, (78.3)	18/24, (75)
Vitamin C	22 (16.3)	(1) 7/19, (36.8)	16/18, (88.9)
Vitamin B	14 (10.4)	(1) 6/11, (54.5)	7/10, (70)
Calcium	18 (13.3)	(4) 6/15, (40)	9/11, (81.8)
Zinc	59 (43.7)	(3) 38/49, (77.6)	36/50, (72)
Herbals			
Mint	36 (26.7)	(4) 17/30, (56.7)	20/33, (60.6)
Chamomile	48 (35.6)	(1) 28/43, (65.1)	27/41, (65.9)
Leek	50 (37)	(1) 41/46, (89.1)	28/44, (63.6)
Garlic	33 (24.4)	(1,2) 18/24, (75)	14/23, (60.9)
Miscellaneous			
Jinseng	2 (1.5)	-----	-----
Homeopathy	2 (1.5)	-----	-----
Probiotic	5 (3.7)	-----	-----
Fish oil	4 (3)	-----	-----
Fox gallbladder	10 (7.4)	(2) 6/9, (66.7)	2/8, (25)
Others 1^b	55 (40.7)	(1) 18/35, (51.4)	46/49, (93.8)
Practice			
Faith healing	125 (92.6)	(2) 114/135, (84.4)	93/103, (90.3)
Massage	7 (5.2)	(4) 3/6, (50)	4/4, (100)
Energy healing	2(1.5)	-----	-----
Hypnotism	1 (0.7)	-----	-----
Yoga	2(1.5)	-----	-----
Others2^c	18 (13.3)	(1) 3/5, (60)	9/13, (69)

a: Most common reasons of use, 1: increased immunity, platelets and hemoglobin; 2: improvement and cure of patient; 3: increased appetite and growth, sense of well-being; 4: others

b: Others1 included chicory (*chicoriumintybus*), honey, London rocket (*sisymbrium Sophia*), royal gel, and...

c: Others2 included meditation, physiotherapy, and...

Table III. Association of demographic and characteristics of patients with pediatric cancer or their parents with use of complementary medicine.

Variables	Value	P value
Age, mean \pm SD		
Yes n=114	7.8 \pm 4.5	0.978
No n=21	7.8 \pm 5.9	
Sex male %		
Yes n=114	61.4	0.226
No n=21	76.2	
Father age, mean \pm SD		
Yes n=114	39.3 \pm 7.8	0.731
No n=21	40 \pm 8.3	
Mother age, mean \pm SD		
Yes n=114	34.2 \pm 7.5	0.966
No n=21	34.3 \pm 8.7	
Father education (no university degree)%		
Yes n=114	74.8	0.400
No n=21	63.2	
Mother education (no university degree)%		
Yes n=114	83.2	0.527
No n=21	90.5	
Annual income (\leq 300 \$/month)%		
Yes n=114	81.3	0.373
No n=21	71.4	
Disease type (leukemia)%		
Yes n=114	70.9	0.271
No n=21	55.6	
Time since diagnosis >6months %		
Yes n=114	71.1	0.211
No n=21	57.1	
General health status of patient(excellent and good vs. moderate and poor)%		
Yes n=114	71.4	0.223
No n=21	83.3	
General health status of mother(excellent and good vs. moderate and poor)%		
Yes n=114	90.5	0.738
No n=21	86	
General health status of father(excellent and good vs. moderate and poor)%		
Yes n=114	76.2	0.770
No n=21	79.8	

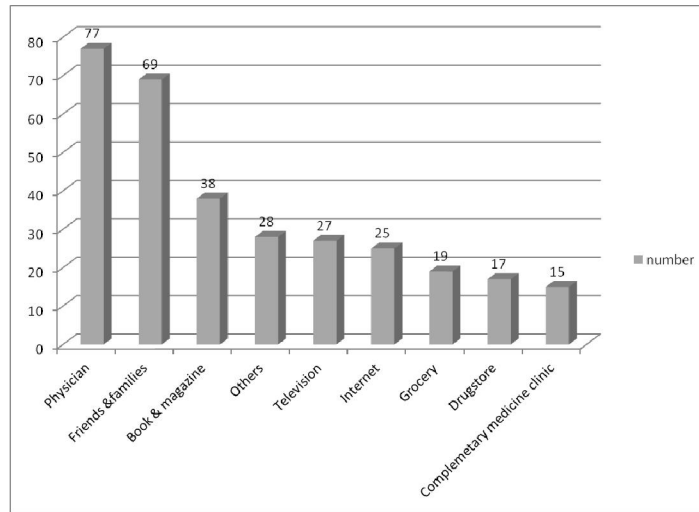


Figure1: Frequency of different sources of knowledge about complementary medicine reported by the parents of patients with pediatric cancers

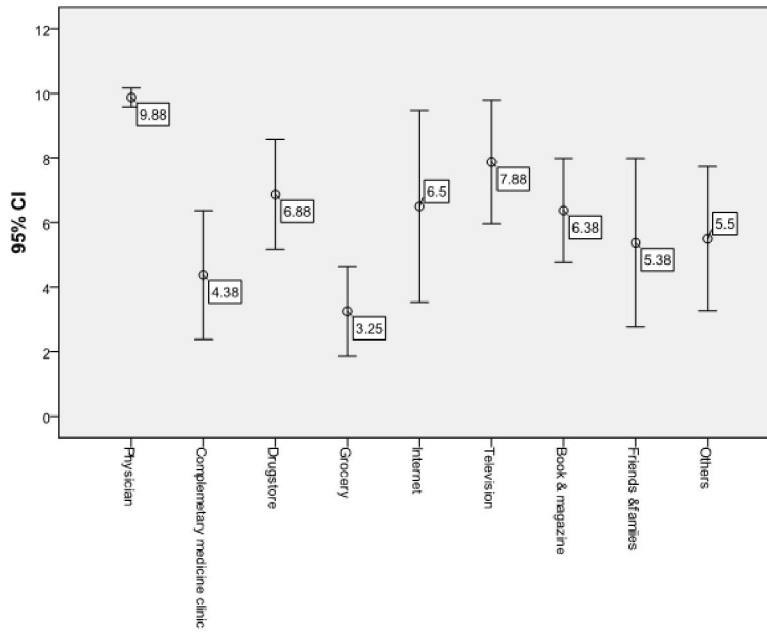


Figure 2: Ninety five percent confidence interval of trust in pediatric patients with cancers to obtained information about complementary medicine based on different sources.

Discussion

This is the largest survey in Iran investigating the use of CAM among pediatric cancer patients. Like similar studies (1, 7, 10, 11, 32), our patients frequently used some kind of CAM products during their illnesses. Zinc supplement was the most popular product exceeding the use of multivitamins, which is the most common CAM product in many countries (1, 7, 31-33). It was consumed mainly due to poor growth and loss of appetite which is a common and bothering symptom in pediatric cancer patients. Over 70% of the consumers reported that it was effective and they were satisfied with its use.

Herbal products were mainly used to boost the immune system and help them recover post chemotherapy myelo suppression. Among different products, allium porrum (leek), which is a part of the food basket of people living in Iran, had the highest popularity. Drunk as a freshly-juiced drink, the people believe that it may help to increase the white blood cells and platelet count following a course of chemotherapy. This effect of leek has not been reported previously in the literature, and merits further investigation in a randomized clinical trial. The other medicinal herb frequently used for the same purpose was chamomile which is usually infused and drunk as an herbal tea. Mint was also used commonly in our patients. It is usually consumed both as a vegetable at meal time, and an extract to relieve gastrointestinal discomforts such as dyspepsia, bloating, and abdominal distension. These herbal remedies were perceived to be beneficial in more than 60% of the users. Globally, herbal medicine is among the most common CAM products used for the treatment of cancer. The type of herbal products and their indications of using them differ in different parts of the world based on the cultural and ethnical variations.

There is a strong belief among some ethnical groups in the region that the gallbladder of some animals specially fox can kill cancer cells and cure the disease. Therefore, some people hunt these animals to remove their gallbladder and sell them to people seeking these organs. Let it dried, it is powdered and swallowed as a capsule. Our survey showed that about 10% of the studied population tried this product at least once. A quarter of the consumers reported it was effective and half of the responders believed it might have some beneficial effects. We couldn't find the same report in other parts of the world, and it seems that this belief is unique to this country and may have some cultural background.

Surprisingly, almost the entire interviewees (92.6%) claim that they have prayed for the health and cure of their patients and over 90% of them perceived it as helpful. This is exceedingly higher compared to similar surveys done in other parts of the world (1, 31, 34-37). A similar survey was conducted by Montazeri et al., in Tehran, the capital of Iran, on 625 adult cancer patients which showed that about 76% of the patients prayed for their cure and resuming their health. The most common reasons of using CAM in these patients were declared to be fear of cancer recurrence and dissatisfaction with their care physician (38). Adams et al., (31) in a large survey of children with chronic illnesses from 5 distinct subspecialties showed that just in oncology patients, faith healing was among the top 3 CAM products or practices used. However, less than 30% of their patients used faith healing which is far less than our results. It is speculated that those patients suffering from debilitating and end-stage diseases resort more to supernatural powers and seek God's help for the cure of their illnesses though highly variable in different religious and ethnic groups. It is a

novel topic in the field of psychoneuroendocrinology which demonstrated that anticancer immunity is modulated by the neuroendocrine system mainly excreted by the pineal gland and endocannabinergic system. It has been proposed that the efficacy of chemotherapy in cancer patients is partly influenced by the faith score and psychoimmunologic status of patients prior to chemotherapy (39-42).

As most of investigators declared, the big concern regarding CAM use is the safety issues and the interactions that they may have with the chemotherapy drugs. More than 80% of patients used some kind of CAM while they were given chemotherapy but only 50% informed their physicians to use them. Some dietary supplements or botanical products may alter absorption, distribution, and elimination of chemotherapy drugs thus affecting their efficacy or increasing their toxicities (12). Moreover, some patients may delay referring to oncologists or refrain from effective cancer treatments and try alternative medicine instead of mainstream oncology care (2). The oncologists should be prudent about how to counsel the patients about using CAM. It is highly advised that oncologists open the discussion about which products or practices are being used and if the patients are compliant using their conventional mainstream treatment.

the patients of the current study or their care givers admitted that their most common source of information about CAM were physicians followed closely by family and friends which is somehow inconsistent with other studies (1, 31, 32, 43-47). It may be partly explained by the fact that physicians have prescribed multivitamins and minerals like zinc as an appetizer to strengthen their patients, and as was mentioned before, these supplements comprised the most frequently used CAM product in these patients. The other sources might have been counseled for herbal products or

CAM practices. Since the patients trusted to their physicians much more than any other sources, it is a good opportunity for oncologists to talk with the patients about pros and cons of using CAM, and the possible interactions that they may have with their conventional treatments.

Although it was shown in previous studies(1, 2, 11, 12, 31, 33) that factors such as age, gender, health status, education, family income, and the use of CAM in parents may affect CAM use in children, this survey showed no significant association with the mentioned variables.

the present study is limited by the fact that it was totally dependent on the past memory of the patients or their care-givers and may be amenable to recall bias. Furthermore, the small sample size and limitation of the survey to a specific geographical area with specific ethnic groups hindered the generalization of these results. Doing a multicenter survey in different parts of the country, and filling diaries at specific time intervals during the course of treatments might be an acceptable solution. It will further help the oncologists to closely monitor which products their patients are using alongside their conventional treatment.

Conclusion

Children suffering from cancer frequently use CAM concurrently with their chemotherapy. A considerable proportion of these patients never disclose it to their physicians. Besides the potential side effects, they may affect the efficacy or toxicity of chemotherapy drugs. Oncologists should dedicate enough time to discuss with their patients about the risks and benefits of these products. Having the families to fill diaries about anything used for medical purposes alongside the conventional treatment is an acceptable alternative to closely monitor the use of these products.

Acknowledgement:

We would like express our special thanks for MS. Sh. Parand for English editor of the manuscript. We should also express our deep and sincere gratitude to our patients and their families who took the time to take part in our survey. This research project was funded by Vice Chancellor of Research of Shiraz University of Medical Sciences with project number 92-01-32-6977.

Conflict of interest

None declared.

References

- 1.Valji R, Adams D, Dagenais S, Clifford T, Baydala L, King WJ, et al. Complementary and alternative medicine: a survey of its use in pediatric oncology. *Evid Based Complement Alternat Med*. 2013;2013:527163.
- 2.Deng G, Cassileth B. Integrative oncology: an overview. *Am Soc Clin Oncol Educ Book*. 2014:233-42.
- 3.Braganza S, Ozuah PO, Sharif I. The use of complementary therapies in inner-city asthmatic children. *J Asthma*. 2003;40(7):823-7.
- 4.Hagen LE, Schneider R, Stephens D, Modrusan D, Feldman BM. Use of complementary and alternative medicine by pediatric rheumatology patients. *Arthritis Rheum*. 2003;49(1):3-6.
- 5.Soo I, Mah JK, Barlow K, Hamiwka L, Wirrell E. Use of complementary and alternative medical therapies in a pediatric neurology clinic. *Can J Neurol Sci*. 2005;32(4):524-8.
- 6.Wong AP, Clark AL, Garnett EA, Acree M, Cohen SA, Ferry GD, et al. Use of complementary medicine in pediatric patients with inflammatory bowel disease: results from a multicenter survey. *J Pediatr Gastroenterol Nutr*. 2009;48(1):55-60.
- 7.Ladas EJ, Rivas S, Ndao D, Damoulakis D, Bao YY, Cheng B, et al. Use of traditional and complementary/alternative medicine (TCAM) in children with cancer in Guatemala. *Pediatr Blood Cancer*. 2014;61(4):687-92.
- 8.Bishop FL, Prescott P, Chan YK, Saville J, von Elm E, Lewith GT. Prevalence of complementary medicine use in pediatric cancer: a systematic review. *Pediatrics*. 2010;125(4):768-76.
- 9.Martel D, Bussieres JF, Theoret Y, Lebel D, Kish S, Moghrabi A, et al. Use of alternative and complementary therapies in children with cancer. *Pediatr Blood Cancer*. 2005;44(7):660-8.
- 10.Huebner J, Prott FJ, Micke O, Muecke R, Senf B, Dennert G, et al. Online survey of cancer patients on complementary and alternative medicine. *Oncol Res Treat*. 2014;37(6):304-8.
- 11.Edwards GV, Aherne NJ, Horsley PJ, Benjamin LC, McLachlan CS, McKay MJ, et al. Prevalence of complementary and alternative therapy use by cancer patients undergoing radiation therapy. *Asia Pac J Clin Oncol*. 2014;10(4):346-53.
- 12.Fouladbakhsh JM, Balneaves L, Jenuwine E. Understanding CAM Natural Health Products: Implications of Use Among Cancer Patients and Survivors. *J Adv Pract Oncol*. 2013;4(5):289-306.
- 13.Asadi-Pooya AA, Shokouhyar S, Emami M, Sharifzade M. Perception and use of complementary and alternative medicine among patients with epilepsy. *Archives of Neuroscience*. 2014;1(2):60-6.
- 14.Babaeian M, Naseri M, Kamalinejad M, Ghaffari F, Emadi F, Feizi A, et al. Herbal Remedies for Functional Dyspepsia and Traditional Iranian Medicine Perspective. *Iran Red Crescent Med J*. 2015;17(11):e20741.
- 15.Barikani A, Beheshti A, Javadi M, Farahani S, Barikani F. Viewpoints of Patients in Qazvin Towards Complementary and Alternative Medicine. *Biotechnology and Health Sciences*. 2016;3(1).
- 16.Firoozabadi MD, Navabzadeh M, Roudsari MK, Zahmatkash M. Comparative efficacy trial of cupping and serkangabin versus conventional therapy of migraine headaches: A randomized,

- open-label, comparative efficacy trial. *J Res Med Sci.* 2014;19(12):1134-9.
- 17.Hasani-Ranjbar S, Zahedi HS, Abdollahi M, Larijani B. Trends in publication of evidence-based Traditional Iranian medicine in endocrinology and metabolic disorders. *J Diabetes Metab Disord.* 2013;12(1):49.
- 18.Hashempur MH, Heydari M, Mosavat SH, Heydari ST, Shams M. Complementary and alternative medicine use in Iranian patients with diabetes mellitus. *J Integr Med.* 2015;13(5):319-25.
- 19.MEHRPOOR G, OWLIA M, MIRJALILI M, FARZAN A, AKRAMI A. Complementary alternative medicine in rheumatologic diseases; data from outpatient clinics in Yazd, Iran. *Journal of Case Reports in Practice (JCRP).* 2014;2(3):92-6.
- 20.Pasalar M, Choopani R, Mosaddegh M, Kamalinejad M, Mohagheghzadeh A, Fattahi MR, et al. Efficacy and safety of jollab to treat functional dyspepsia: a randomized placebo-controlled clinical trial. *Explore (NY).* 2015;11(3):199-207.
- 21.TONEKABONI SH, NAEINI SJ, KHAJEH A, YAGHINI O, GHAZAVI A, GORJI FA. Use of Complementary and Alternative Medicine for Epileptic Children in Tehran: A Cross-Sectional Study (2009-2011). *Iranian journal of child neurology.* 2014;8(1):26.
- 22.Zohalinezhad ME, Hosseini-Asl MK, Akrami R, Nimrouzi M, Salehi A, Zarshenas MM. Myrtus communis L. Freeze-Dried Aqueous Extract Versus Omeprazol in Gastrointestinal Reflux Disease: A Double-Blind Randomized Controlled Clinical Trial. *J Evid Based Complementary Altern Med.* 2016;21(1):23-9.
- 23.Fahimi F, Hrgovic I, El-Safadi S, Munstedt K. Complementary and alternative medicine in obstetrics: a survey from Iran. *Arch Gynecol Obstet.* 2011;284(2):361-4.
- 24.Aghabati N, Mohammadi E, Pour Esmaiel Z. The effect of therapeutic touch on pain and fatigue of cancer patients undergoing chemotherapy. *Evid Based Complement Alternat Med.* 2010;7(3):375-81.
- 25.Ameri A, Heydarirad G, Rezaeizadeh H, Choopani R, Ghobadi A, Gachkar L. Evaluation of Efficacy of an Herbal Compound on Dry Mouth in Patients With Head and Neck Cancers: A Randomized Clinical Trial. *J Evid Based Complementary Altern Med.* 2016;21(1):30-3.
- 26.Esmaeili-Mahani S, Falahi F, Yaghoobi MM. Proapoptotic and Antiproliferative Effects of Thymus caramanicus on Human Breast Cancer Cell Line (MCF-7) and Its Interaction with Anticancer Drug Vincristine. *Evid Based Complement Alternat Med.* 2014;2014:893247.
- 27.Jafari N, Farajzadegan Z, Zamani A, Bahrami F, Emami H, Loghmani A, et al. Spiritual therapy to improve the spiritual well-being of Iranian women with breast cancer: a randomized controlled trial. *Evid Based Complement Alternat Med.* 2013;2013:353262.
- 28.Khazaei Kooohpar Z, Entezari M, Movafagh A, Hashemi M. Anticancer Activity of Curcumin on Human Breast Adenocarcinoma: Role of Mcl-1 Gene. *Iran J Cancer Prev.* 2015;8(3):e2331.
- 29.Raeessi MA, Raeessi N, Panahi Y, Gharaie H, Davoudi SM, Saadat A, et al. "Coffee plus honey" versus "topical steroid" in the treatment of chemotherapy-induced oral mucositis: a randomised controlled trial. *BMC Complement Altern Med.* 2014;14:293.
- 30.Samarghandian S, Hadjzadeh MA, Afshari JT, Hosseini M. Antiproliferative activity and induction of apoptotic by ethanolic extract of *Alpinia galanga* rhizome in human breast carcinoma cell line. *BMC Complement Altern Med.* 2014;14:192.
- 31.Adams D, Dagenais S, Clifford T, Baydala L, King WJ, Hervas-Malo M, et al. Complementary and alternative medicine use by pediatric specialty outpatients. *Pediatrics.* 2013;131(2):225-32.

32. Huebner J, Micke O, Muecke R, Buentzel J, Prott FJ, Kleeberg U, et al. User rate of complementary and alternative medicine (CAM) of patients visiting a counseling facility for CAM of a German comprehensive cancer center. *Anticancer Res.* 2014;34(2):943-8.
33. Revuelta-Iniesta R, Wilson ML, White K, Stewart L, McKenzie JM, Wilson DC. Complementary and alternative medicine usage in Scottish children and adolescents during cancer treatment. *Complement Ther Clin Pract.* 2014;20(4):197-202.
34. Ezeome ER, Anarado AN. Use of complementary and alternative medicine by cancer patients at the University of Nigeria Teaching Hospital, Enugu, Nigeria. *BMC Complement Altern Med.* 2007;7:28.
35. Heath JA, Oh LJ, Clarke NE, Wolfe J. Complementary and alternative medicine use in children with cancer at the end of life. *J Palliat Med.* 2012;15(11):1218-21.
36. Lengacher CA, Bennett MP, Kip KE, Keller R, LaVance MS, Smith LS, et al. Frequency of use of complementary and alternative medicine in women with breast cancer. *Oncol Nurs Forum.* 2002;29(10):1445-52.
37. McCurdy EA, Spangler JG, Wofford MM, Chauvenet AR, McLean TW. Religiosity is associated with the use of complementary medical therapies by pediatric oncology patients. *J Pediatr Hematol Oncol.* 2003;25(2):125-9.
38. Montazeri A, Sajadian A, Ebrahimi M, Haghghat S, Harirchi I. Factors predicting the use of complementary and alternative therapies among cancer patients in Iran. *Eur J Cancer Care (Engl).* 2007;16(2):144-9.
39. Lissoni P, Messina G, Balestra A, Colciago M, Brivio F, Fumagalli L, et al. Efficacy of cancer chemotherapy in relation to synchronization of cortisol rhythm, immune status and psychospiritual profile in metastatic non-small cell lung cancer. *In Vivo.* 2008;22(2):257-62.
40. Lissoni P, Messina G, Parolini D, Balestra A, Brivio F, Fumagalli L, et al. A spiritual approach in the treatment of cancer: relation between faith score and response to chemotherapy in advanced non-small cell lung cancer patients. *In Vivo.* 2008;22(5):577-81.
41. Messina G, Lissoni P, Marchiori P, Bartolacelli E, Brivio F, Magotti L. Enhancement of the efficacy of cancer chemotherapy by the pineal hormone melatonin and its relation with the psychospiritual status of cancer patients. *J Res Med Sci.* 2010;15(4):225-8.
42. Messina G, Lissoni P, Rovelli F. Psychoimmunological analysis of cancer patients: correlation with the prognosis. *Curr Aging Sci.* 2012;5(3):263-72.
43. Broom A, Tovey P. The role of the Internet in cancer patients' engagement with complementary and alternative treatments. *Health (London).* 2008;12(2):139-55.
44. Mayadagli A, Aksu A, Goksel F, Gocen E, Karahacioglu E, Gumus M, et al. Determination of parameters affecting the use of complementary and alternative medicine in cancer patients and detection of prevalence of use. *Afr J Tradit Complement Altern Med.* 2011;8(4):477-82.
45. Shen J, Andersen R, Albert PS, Wenger N, Glaspy J, Cole M, et al. Use of complementary/alternative therapies by women with advanced-stage breast cancer. *BMC Complement Altern Med.* 2002;2:8.
46. Tuna S, Dizdar O, Calis M. The prevalence of usage of herbal medicines among cancer patients. *J BUON.* 2013;18(4):1048-51.
47. Walsh MC, Trentham-Dietz A, Schroepfer TA, Reding DJ, Campbell B, Foote ML, et al. Cancer information sources used by patients to inform and influence treatment decisions. *J Health Commun.* 2010;15(4):445-63.