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Complementary and alternative medicine use in thalassemia patients in Shiraz, southern Iran: A cross-sectional study



Mohammadreza Bordbar ^a, Mehdi Pasalar ^b, Sanaz Safaei ^c, Roza kamfiroozi ^d,
Sohelia Zareifar ^a, Omidreza zekavat ^a, Sezaneh Haghpanah ^{a,*}

^a Hematology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

^b Research Center for Traditional Medicine and History of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran

^c Islamic Azad University, Isfahan (Khorasgan) Branch, Iran

^d Amir Oncology Hospital, Shiraz University of Medical Sciences, Shiraz, Iran

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ABSTRACT

This study aimed to determine the frequency and pattern of complementary and alternative medicine (CAM) use in thalassemia patients in south of Iran. The survey was done using a validated questionnaire which was distributed among 122 thalassemia patients. Only 108 questionnaires were completed and turned back (response rate 88.5%). Patients referred to an outpatient thalassemia clinic in Shiraz, southern Iran for blood transfusion. The mean age of the patients was 22.9 ± 7.9 years (range 4–45 years) with female/male ratio 1.84. Seventy four (68.5%) of the responders used CAM at least once during their life, and about half of them used it concurrently with their conventional treatments. The most reported CAM product was mint juice (50%). The most common reason of CAM use was increased general health. The most common information source about CAM was physicians who were the most trusted source as well. CAM is frequently being used in thalassemia patients to ensure their sense of well-being and help them overcome the complications of their illnesses.

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1. Introduction

Complementary and alternative medicine (CAM; 補充與替代醫學 *bǔ chōng yǔ tì dài yī xué*) is recently being used frequently for chronic medical illnesses. The rate, kind, and cause of its use differs in our region^{1–3} and fluctuates in various nations and ethnic groups and has been reported up to 90% in some medical conditions.⁴ The rise in quality of life of CAM users may clarify the tendency toward these methods universally.⁵ Patients with chronic hemolytic anemia and hemoglobinopathies are among chronic diseases which are subjected to CAM use. In the field of hemoglobinopathy, there are a lot of reports on the use of CAM in sickle cell disease for their pain control.^{4,6,7} In this regard, some herbal products have been shown to have antioxidant and anti-sickle cell anemia effects.^{8,9}

Thalassemia (地中海貧血 *Dizhōnghǎi pínxiè*) is a chronic hemolytic anemia caused by beta-globin chain mutations leading to ineffective erythropoiesis. Patients with thalassemia are usually dependent on regular blood transfusion to maintain their normal life. Chronic blood transfusion put them at risk of iron overload which is the leading cause of their mortality. Iron chelation with different medicaments such as deferoxamine, deferiprone and deferasirox has long been the mainstay of therapy to reduce their iron burden. However, the biggest problem is the matter of compliance and adherence to treatment. Therefore, a large proportion of patients with thalassemia suffer from iron overload and its complications due to non-compliance with their medical treatments particularly iron chelators.¹⁰

On the other hand, researchers have been trying for a long time to introduce suitable alternatives to blood transfusion which may subsequently result in less iron overload in the long-term. Fetal hemoglobin induction by drugs such as hydroxyurea, butyrate, mithramycin, andrapamycin was found to have some effects in decreasing the transfusion requirements of some thalassemia patients especially those with thalassemia intermedia.^{11–13} Despite

* Corresponding author. Hematology Research Center, Nemazee Hospital, Shiraz University of Medical Sciences, P.O. Box: 7193711351, Shiraz, Iran. Fax: +98 713 6473239.

E-mail address: haghpanah@sums.ac.ir (S. Haghpanah).

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acceptable efficacy and safety especially with hydroxyurea, some scientists are still concerned with the long-standing carcinogenicity of these drugs. Introduction of novel hemoglobin F inducers like simvastatin and some herbal products such as Wheatgrass, Piceatannol, and Resveratrol has brought some hope to patients to get rid of transfusion with the aid of natural products.^{14–19} Furthermore, there are promising results that some botanical products as well as CAM practices such as cupping therapy (*Hijamat*) may help to decrease serum ferritin and reduce iron burden in thalassemia patients.^{19–22}

Regarding the paucity of surveys on the frequency of CAM use in thalassemia patients²³ and the importance of CAM therapies in iron level and hemoglobin production of this category of patients, the aim of this study was set to determine the frequency, types and pattern of CAM use in a group of transfusion-dependent thalassemia patients in south of Iran.

2. Methods

2.1. Study design and sample

A retrospective cross-sectional study performed with structured interviews from December 2015 until March 2016. This survey was done in an outpatient clinic in Shiraz, southern Iran where patients with transfusion-dependent beta-thalassemia were being visited and regularly transfused. The target population was 468 patients who were registered in our clinic for at least 12 months and were transfused every 2–4 weeks. A random pilot study was firstly performed showing the prevalence of CAM use as 65%. Subsequently, considering $\alpha = 0.05$ and $d = 8.5\%$, sample size calculated as 122 thalassemia patients and they were selected using simple random sampling. All families accepted to take part in the interview but only 108 questionnaires were completed and turned back (response rate 88.5%).

2.2. Study instrument

The questionnaire was taken from a similar survey on children with chronic illnesses done in Canada by Adams et al.²⁴ Firstly, the original questionnaire was translated into Persian language by a professional translator. Due to the cultural differences, some questions about the specific CAM products or practices which were unavailable or odd to our patients were changed and replaced with suitable alternatives. Lastly, it was pilot-tested in a convenience sample of thalassemia patients and parents who brought their children to a general pediatric clinic to ensure its face and concept validity. The backbone of the questionnaire was kept unchanged compared to the original English version and included 19 questions about the patients and their family demographics, general health status, the specific CAM products and practices used, reasons of use and non-use, perceived effectiveness, self-reported adverse effects, concurrent use with conventional medicine, and the source of information about the CAM used.

2.3. Data collection process

A trained nurse distributed the questionnaires between the patients or their care givers while they were waiting to be transfused or visited by their physicians. Then the completed forms were collected and checked to be filled appropriately.

2.4. Statistical analysis

Data were analyzed by SPSS software version 21. Descriptive data were summarized as mean, standard deviation, frequency and

chart. Comparison of categorical and quantitative data was performed by Chi-square test and Student t test between two groups of patients, respectively. P values less than 0.05 were considered statistically significant.

3. Results

One hundred twenty-two individuals accepted to participate, but only 108 questionnaires were completed and turned back (response rate 88.5%). The study population consisted mostly of female patients (64.8%) with a mean age of about 23 years. The age range of the patients was 4–45 years old (Table 1). A minority of parents (13.9% of fathers vs. 4.7% of mothers) had achieved a university degree while almost 20% of them were illiterate. Most of the families (86.6%) reported that they had annual household income of less than 300\$ per month. Patients and their parents were asked about their general health status that 80.6% of the patients, 83.3% of mothers, and 65.7% of fathers responded that they were in good or excellent general health (Table 1).

The frequency of consumption of different CAM products and practices by patients with thalassemia as well as the most common reasons of use and their effectiveness has been demonstrated in Figs. 1 and 2, and Table 2. Overall, 74 out of 108 patients (68.5%) used at least one of CAM products or practices in last 6 months before the study. About half of the patients (53 patients, 49.1%) used CAM concurrently with their conventional treatments. The most common CAM product and practice which was used were mint juice (50%) [薄荷汁 Bòhé zhī] and faith healing (50%) [信仰癒合 Xìnyǎng yùhé], respectively. The other popular CAM products in decreasing order of frequency were vitamin C (39.8%), garlic (29.6%) [大蒜 Dàsuan], and chamomile (28.7%) [洋甘菊 Yánggānjú]. The most common reasons of CAM use were increased general health, appetite, and well-being (mentioned by 57 patients) in the product subgroup and improvement of osteoporosis (mentioned by 19 patients) in the practice subgroup. Most of the patients were satisfied with the CAM products or practices that they used (Table 2). Massage and acupuncture, which were used by 5 and 2 patients respectively, were reported to be 100% effective. On the other hand, jinseng was perceived to be the least helpful CAM product by the patients (Table 2).

Sixty three percent of parents reported that they have used some kind of CAM, and it was significantly associated with the use of CAM by their children. Children whose parents used CAM were 5.54 times more likely to use CAM ($P < 0.001$, 95% CI: 2.22–13.78).

Forty patients experienced some kind of adverse effects while using CAM that all of them were mild or moderate. There were no significant differences regarding age (patient or his/her parents), gender, fathers' or mothers' level of education, annual household income, and general health status (patient or his/her parents) between those used CAM and the opposite group ($P > 0.05$). The most common reason ignoring CAM use which reported by patients or their parents was “lack of knowledge about CAM” (56.8%).

The most common information source about CAM was physicians reported by 57 patients, followed by friends and families (41 patients) and grocery (41 patients) (some participants reported more than one source of information). The patients rated their level of trust to different sources of CAM information on a 10-point scale (1 = no trust, 10 = full trust). Among different sources, the most trusted source of information was reported to be physicians (mean: 8.86 ± 1.76 , 95%CI: 7.53–10.24) (Table 3).

When they were asked to whom they have talked about using CAM, 55 out of 73 responders (75.3%) answered that they have informed their responsible physician, while 10 patients (13.7%) had never talked about this issue to anyone.

Table 1
Demographic and characteristics of patients with thalassemia and their parents.

Variables	Values
Sex M/F (n)	38/70
Age (year)	Mean ± SD (Min–Max)
Patients	22.9 ± 7.9 (4–45)
Mothers	47.2 ± 8.8 (24–66)
Fathers	54.3 ± 10.4 (31–86)
General health status	Number (%)
(good and excellent vs. poor and moderate)	
Patients	87 (80.6)
Mothers	90 (83.3)
Fathers ^a	71/88 (65.7)
Annual household income	Number (%)^b
≤ 300 \$/month	84 (86.6)
> 300\$/month	13 (13.4)
Health insurance coverage	Number (%)
Yes	15 (13.9)
No	58 (53.7)
Not sure	35 (32.4)

a: 20 missing cases, b: 11 missing cases, SD: Standard Deviation, Min: Minimum, Max: Maximum.

4. Discussion

More than 90% of the participants reported the history of CAM usage at least once. The prevalence of CAM product or practice use in our investigation was high (68.5% and 70.8%, respectively). The most prevalent CAM product used in our patients was mint juice followed by vitamin C, garlic and chamomile. Mint juice was the most popular herbal remedy which was usually consumed to relieve gastrointestinal discomfort. Based on traditional Persian medicine (TPM) textbooks, mint has warm quality so; it is a good digestive agent for thalassemia patients suffering from gastrointestinal upset frequently. Mint is also used in folk medicine as a tranquilizer medication.

Herbal remedies (草藥 Cǎoyào), as an important part of CAM methods,²⁵ have been traditionally used by Persian people to treat their ailments. It may root back to the handwritings of Avicenna, the great ancient physician, and his eminent colleagues and pupils

in the field of TPM (傳統波斯醫學 Chuántǒng bōsī yīxué), although cultural and religious background of our region should be always kept in mind.^{3,26} High prevalence of herbal products usage for different chronic diseases and its recognition is a common finding in former documents and is in line with the previous studies.^{1,2,27–31} In other parts of the world, people use botanical and natural products mainly based on their cultural beliefs, too. For instance, it was reported by Efe et al.²³ that Turkish people frequently use carob and grape molasses to prevent or treat anemia. Wheatgrass is a popular vegetable in India and they call it 'green blood' due to its high chlorophyll content which has a great similarity to hemoglobin. It was shown to have hemoglobin F induction and anti-oxidant properties, and can reduce transfusion requirements in thalassemia patients. Furthermore, it was claimed to be an effective iron chelator, helping thalassemia patients to decrease their serum ferritin.^{18,19}

To our knowledge, this is the first survey about CAM use in thalassemia patients in Iran and the second reported one in the literature. Comparable to the survey done by Efe et al in Turkey, approximately 70% of our patients used CAM at least once in their life. It was similarly associated with the use of CAM in their parents but no other variables including age, sex, level of education, annual household income, health insurance coverage and general health status of the patients or their parents. In previous studies on other chronic diseases, researchers have introduced different factors that may predict use of CAM therapies in patients including female gender, middle-aged, high socioeconomic status, higher educational level, poor general health, and history of CAM use in the parents.^{4,7,24,32} Among the aforementioned factors, only CAM use in the parents influenced the use of CAM in our patients similar to the findings of some other investigators, considering the controversy about an association between CAM use and patients' socio-demographic characteristics.^{4,7,23,24,30,33}

Faith healing and spiritual practice like praying has variable prevalence in different nations and ethnic groups, although this rate is high in our region.^{3,34} It is generally believed that the type of the illness and its severity may affect how frequently it is used as a CAM.³² In a survey that we did recently in our pediatric cancer

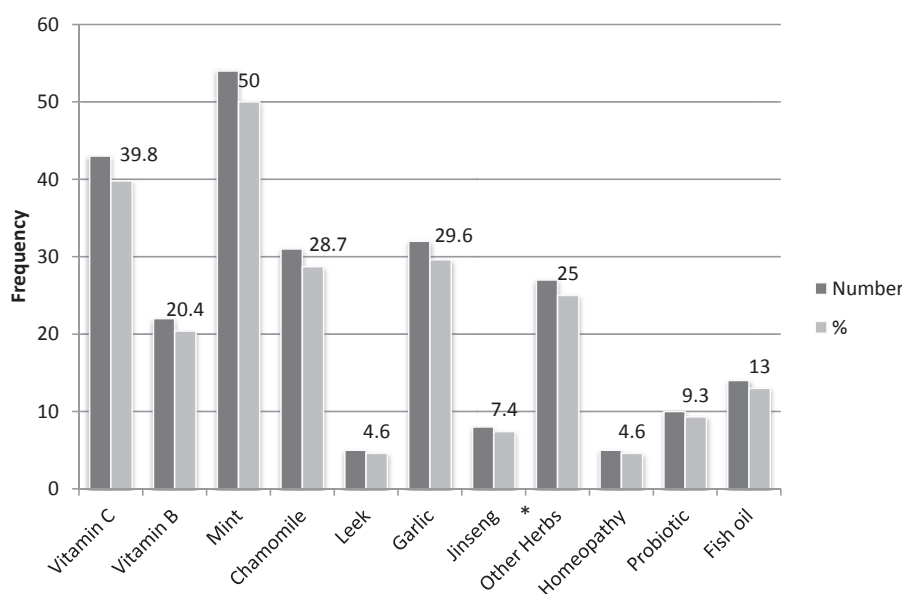


Fig. 1. CAM Products used by thalassemia patients (Some patients used more than one CAM product). *Other Herbs included green tea (*Camellia sinensis*), chicory (*Cichorium intybus*), Borage (*Borago officinalis*), Garden Thyme (*thymus vulgaris*), and Cinnamon (*Cinnamomum verum*).

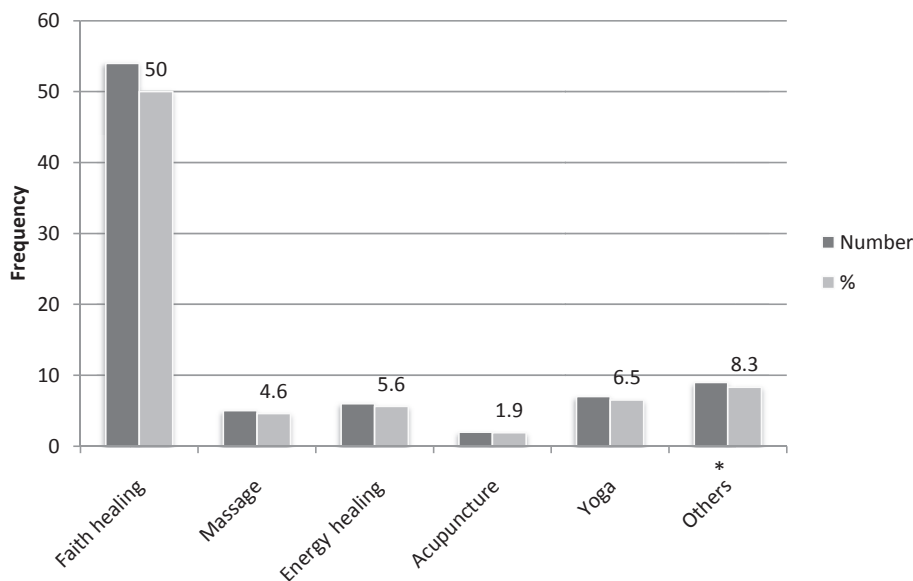


Fig. 2. CAM practices applied by thalassemia patients (Some patients applied more than one CAM practice). *Other practices include music therapy, meditation and Tai Chi training.

Table 2
Common reasons for use and perceived effectiveness of CAM modalities.

Product	Ever used from total number of 108	Most common reason of use (number/responders)							Positive effect	
		Improvement of osteoporosis	Increasing hemoglobin	Increasing general health	Decreasing iron	Feel relaxed	Improvement of gastrointestinal discomfort	Other causes	Number (%)	
Vitamins										
Vitamin C	43			8/23	9/23					28 (65.1)
Vitamin B	22			11/15						15 (68.1)
Herbs										
Mint	54						14/24			35 (68.4)
Chamomile	31							10/17		24 (77.4)
Leek	5							3/3		4 (80)
Garlic	32							6/9		14 (43.7)
Jinseng	8							3/3		2 (25)
Other herbs ^a	27							5/14		17 (62.9)
Miscellaneous										
Homeopathy	5					1/1				2 (40)
Probiotic	10			2/5						4 (40)
Fish oil	14							3/6		5 (35.7)
Practice										
Faith healing	54	19/31								33 (61.1)
Massage	5		1/2					1/2		5 (100)
Energy healing	6		4/5							3 (50)
Acupuncture	2			1/1						2 (100)
Yoga	7							1		6 (85.7)
Other practices ^b	9		2							6 (66.6)

^a Other Herbs included green tea (Camellia sinensis), chicory (Cichorium intybus), Borage (Borago officinalis), Garden Thyme (thymus vulgaris), and Cinnamon (Cinnamomum verum).

^b Other practices include music therapy, meditation and Tai Chi training.

patients, over 90% of the study population had prayed for the cure of their patients (unpublished data). Spiritual therapy/mind-body systems constitute a remarkable portion of CAM therapies in a variety of chronic illnesses especially those with poor response to conventional medical treatments. It has been reported to be used from less than 30% to about 90% in different studies.^{24,32,34–38} People may try this kind of CAM for different reasons including having tried all possible therapeutic options, feeling of self-control over one's treatment, and bringing peace and tranquility to the family.³⁰ As thalassemia is not a life-threatening condition if managed appropriately, patients had prayed less for their health compared to our cancer patients (50% vs 91%, respectively). It is in

agreement with the notion that the type of disease and its severity or curability is a more important factor than ethnicity or religious beliefs in determining how frequently people seek God's help for the remedy of their patients.

Patients mostly got the information regarding different CAM products from their physicians. It was a surprising finding in our center in full contrast to some previous studies.^{32,34} It may arise from an excellent friendly relationship between our patients and their responsible physicians. Patients with chronic illnesses such as thalassemia hardly accept to try new drugs or other products or practices. Although, people usually do not consider herbal products as a medication, patients with thalassemia mostly consult with

Table 3

Distribution of mean, standard deviation and 95% confidence interval of the level of the trust of patients with thalassemia to different sources of information about CAM.

Source of information	Mean \pm SD	95% CI
Physician	8.89 \pm 1.76	7.53–10.24
Complementary medicine clinic	6.89 \pm 2.2	5.19–8.58
Drugstore	6.56 \pm 2.06	4.97–8.15
Grocery	8 \pm 1.73	6.67–9.33
Internet	4.78 \pm 2.58	2.79–6.77
Television	5.33 \pm 3.16	2.9–7.76
Book & magazine	6.44 \pm 3.04	4.1–8.79
Friends & families	6.44 \pm 2.78	4.3–8.59
Other sources	5.78 \pm 3.42	3.15–8.41

their treating physicians about what they have been told to consume or practice. That's why the physicians were also introduced as the most trusted source, as well. Patients and their families may get the required information from any possible source available, but it is encouraging that our patients mostly relied on their physicians and talked about this issue during their regular visits. This is of great significance reviewing notable no-disclosure rates of more than 50% in some studies.³² Although drug interactions is not that important in thalassemia patients as is true in cancer patients, it is useful to open the discussion about different self-prescribed medications or practices which are being used by patients, and ask them about their perceived helpfulness or possible adverse effects.

4.1. Limitations

Like other similar surveys, our study is subjected to recall bias. However, since most of the patients used CAM regularly, it may partly reduce the chance of their forgetfulness. Furthermore, the survey was done in a single center with a specific ethnicity and cultural beliefs. Conducting a multicenter study and including patients from different ethnic groups and cultural background may reveal the true incidence and pattern of CAM use in the region. It is known that a comparison of data of CAM use among thalassemia patients across different populations is restricted due to paucity of similar surveys in literature.

5. Conclusion

CAM is frequently used in thalassemia patients like any other chronic illness. The patients were often satisfied with its use and disclosed it to their physicians. Mint juice and prayer were the most frequent CAM product and practice, respectively. Physicians were the most frequent and the most trusted source of information about CAM. Considering the widespread use of CAM modalities in our region, research and education in this field has to be increased. Furthermore, patients and physicians need to be aware of their traditional and folklore medicine to improve CAM possible benefits and avoid its side effects.

Conflict of interest

The authors disclosed that they had no conflicts of interest.

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