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Chronic Diseases Journal

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3. Kuczmarski RJ, Ogden CL, Grammer-Strawn LM, Flegal KM, Guo SS, Wei R, et al. CDC growth charts: United States. Advance data from vital and health statistics. No. 314. Hyattsville, Md: National Center for Health Statistics, 2000. (DHHS publication no. (PHS) 2000-1250 0-0431)

4. World Health organization. Strategic directions for strengthening nursing and midwifery services [online]. Available from: URL:http://www.wpro.who.int/themesfocuses/theme3/focus2/nursingmidwifery.pdf2002

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Effect of designed self-care educational program on anxiety, stress, and depression in patients with benign prostatic hyperplasia undergoing prostate surgery

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Original Article

Abstract

BACKGROUND: Stress, anxiety, and depression are common psychological problems in prostatic conditions. The aim of this study was to investigate the effects of designed self-care educational program on anxiety, stress, and depression in patients with benign prostatic hyperplasia undergoing prostate surgery.

METHODS: This was a quasi-experimental study including 33 participants in the intervention group and 34 participants in the control group. During the study demographic data and the rate of stress, anxiety, and depression were measured. In the intervention group, self-care educational program was presented in two sessions and was followed up one month after surgery. Stress, anxiety, and depression were measured before surgery, and during and one month after discharge using depression anxiety stress scales (DASS-21), which is a standard questionnaire. Later data were analyzed using SPSS software.

RESULTS: Participants in the study were between 45-80 years of age. Student's independent t-test before the intervention revealed no significant difference in mean score of stress (P = 0.684), anxiety (P = 0.937), and depression (P = 0.727) between the two groups. Mean score of stress and anxiety significantly reduced in the intervention group on discharge (stress: P = 0.031, anxiety: P = 0.043), and a month after the operation (stress: P ≤ 0.001, anxiety: P = 0.016). However, mean score of depression revealed no significant difference on discharge (P = 0.514), and a month after operation (P = 0.221).

CONCLUSION: The results showed that designed self-care educational program was effective in stress and anxiety reduction in patients under prostate surgery.

KEYWORDS: Self-Care, Stress, Anxiety, Depression, Benign Prostatic Hyperplasia

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Introduction

Benign prostatic hyperplasia (BPH) is a common medical condition among middle-aged and older males, affecting 40%–50% of men by age 50 and nearly 80% of men by age 70.[1] The increase in life-expectancy that has been observed over the last 50 years has resulted in the ageing of the global population. It is expected that the world population aged over 65 years will double between 1980 and 2050, and this will increase the prevalence of the disease.[2] The prevalence increased from 1.2% in adults aged 40–49 years to 36% in those aged 70 years.[3]

BPH is not a life-threatening condition.[4] However, male patients suffer from stress, anxiety, and depression due to social disruption, and

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inability to perform essential tasks due to psychological impact, sexual dysfunction, fear of cancer, and fear of surgery.[5-8] On the other hand, transurethral resection of the prostate (TURP) like any other surgery is a stressful condition, and studies show that most of the patients have anxiety before the operation.[9] Thus, BPH can cause depression, anxiety, and psychological disease resulting in poor quality of life and unhealthy ageing.[6-8] Due to increasing age of BPH patients and their vulnerability to disease and its psychological problems, decreasing anxiety level is one of the main nursing cares to prevent further ailment. According to Dorothea Orem (1995) self-care agency suggests that individuals use their resources, including knowledge, attitude, skills and personal values. Therefore, self-care ability increases through research, education, and learning process.[10] Accordingly, self-care education by nursing staff increases self-care by the patients and helps them adapt to the physical and mental health issues caused by the disease.[11,12] In Iran many studies have been conducted on patients' mental issues and several other diseases, nevertheless there are a limited number of studies conducted on the effect of self-care education on psychological problems of BPH patients undergoing prostate surgery. Therefore, the researcher aims to study the effects of a designed self-care educational program on anxiety, stress, and depression in patients with benign prostatic hyperplasia undergoing prostate surgery.

Materials and Methods

This is a clinical trial, registered in the Iranian Registry of Clinical Trials (IRCT2012070610196N1) and conducted in Milad Hospital in Tehran, Iran, using control and intervention groups. The subjects were patients suffering form BPH and candidates for TURP surgery admitted to Milad Hospital in Tehran from April 4th 2011 to August 21st 2011. The inclusion criteria of this study were: age ranges between 48-80 years, ability to read and write, no prior training, no prior information about the disease or its treatment and methods of reducing stress, and no evidence of anxiety and depression in a period of 6 month prior to intervention. Other criteria were willingness to participate in the study and absence of neurological disorders.

The exclusion criteria included: various stressful life events, history of treatment during the period of intervention, unwillingness to participate in the study, and positive results showing prostate cancer after tissue sampling.

Sample size was obtained using Pocock's formula and statistical tables of Quekand based on similar studies with confidence level of 95% and margin of error of 5%.[13,14] The sample size of 29 people per group was considered, but due to possible dropout rates the sample size of each group was raised to 35 people. After the study was approved, the researcher chose samples based on the study criteria. To reduce seasonal effects on dependant variables (stress, anxiety, and depression), the samples in both control and intervention groups were assigned to the groups 10 samples at a time. Initially, 10 patients in the control group were selected, and after completion the research and research tools by patients, and after their discharge from the hospital the next 10 people in the intervention group were chosen and the experiment was conducted on them. This process continued until all subjects in both groups were chosen and participated in the study (The whole process of the study is summarized in figure 1).

Research instruments for this study were demographic check lists, depression anxiety stress scales (DASS-21) questionnaire, and survey sheets to determine training requirements in terms of general anxiety, stress, and depression of the patients. With the exception of this questionnaire, other questionnaires were developed by the researcher, in which case content validity was determined subsequent to gaining expert opinion. Then, the tools were developed using different sources, including comments of 10 nursing professionals and 3 urologists. Later, after comments and suggestions, corrections were applied. DASS-21 is a shortened version of the questionnaire DASS 42 which was presented

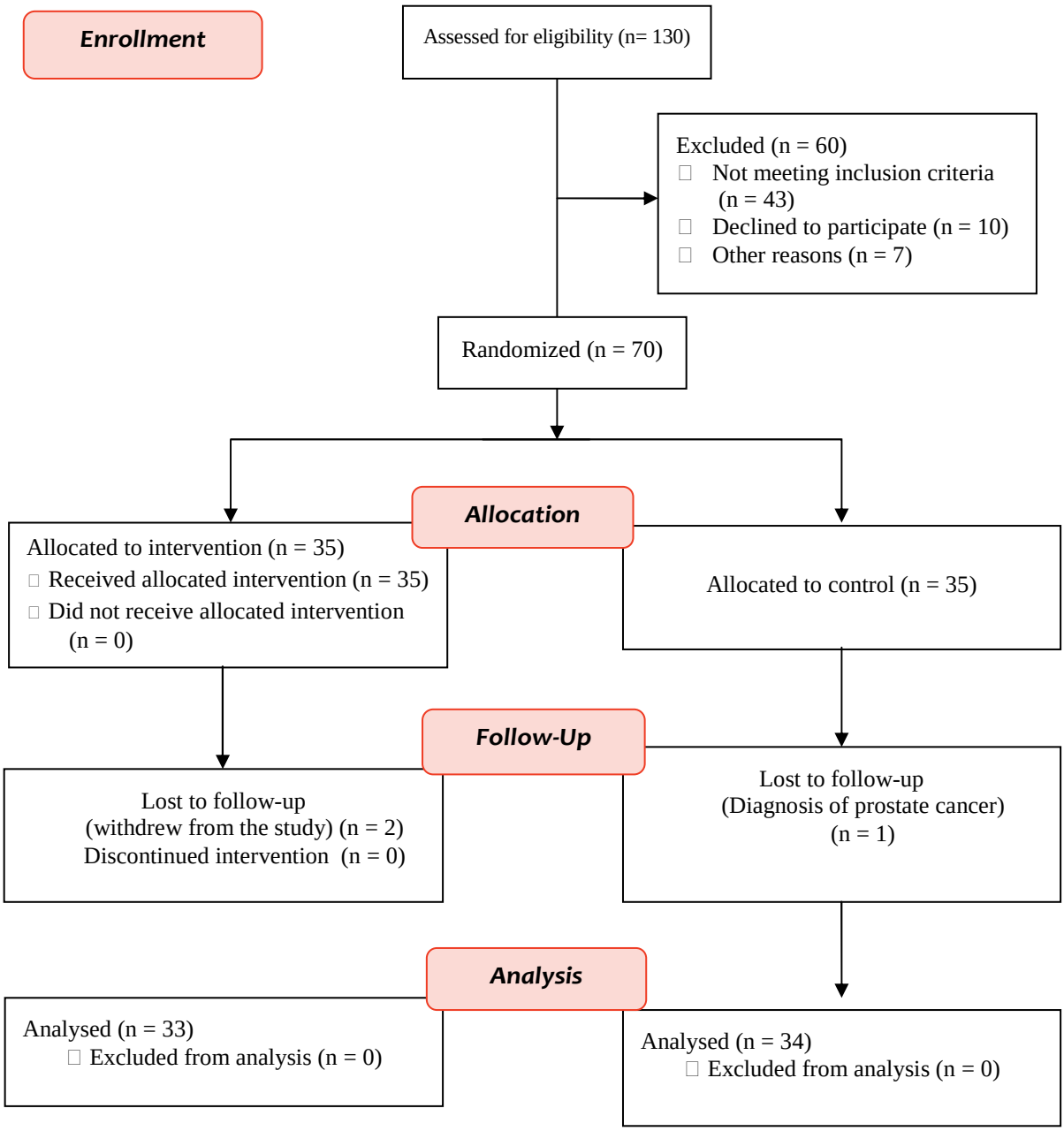

Figure 1. The consort flowchart of the study

for the first time by Lovibond in 1995.[15] Queries in the questionnaire are based on a grading scale scored 0 to 3. In this device 21 queries are used to assess stress, anxiety, and depression levels, each one constituting 7 queries, respectively. Likert scaling assumes the following options in the questionnaire: unlikely, low probability, average probability, and high probability. The lowest score is zero and the highest score is 3.[16]

The validity of the questionnaire has been confirmed by studies done in the home country or abroad.[16-19] The reliability of the instrument was determined by internal homogeneity and Cronbach's alpha coefficient. The questionnaires were completed by 10 patients suffering from BPH and under TURP surgery. The questionnaire was validated with Cronbach's alpha resulting in 0.78 in stress, 0.74 in anxiety,

and 0.83 in depression sections. Reliability was assessed using the test-retest method.[16,19]

This questionnaire was completed before the intervention, during discharge, and one month after it by the study samples in both groups, bearing in mind that patients in the control group received no intervention. Regarding research ethics, after completion of the study, educational pamphlets discussed in the intervention group were sent to the samples. The researcher designed the self-care educational program by using books, articles, urology specialists, and nursing professionals (including educational pamphlets and animation files about the disease). After determining the educational needs of patients and at the time of admission, the researcher delivered the package to the patients in the intervention group.

Content of the training program consisted of two educational sessions before and after the operation (average one hour). First session included learning about the nature of the disease, preoperative education, nature of operation, postoperative results, pre-and postoperative routines, and training on diet, patient movement, oral health, and fluid intake after surgery. The second session included training on discharge in areas like nutrition and diet at home, genital hygiene and prevention of infection in the genitourinary system, mobility, sexual activity timing, fluid intake to prevent constipation, medication, and sitting on a tub of warm water on a daily basis and during acute urinary irritation and obstruction. In addition, they utilized appropriate teaching aids, like educational pamphlets and display of animation files using a laptop. After the second session, DASS 21 questionnaires were completed by the patients for a second time; the questionnaire was put into envelopes and delivered to the patients one month after it was completed for the first time and submitted to the researcher. They received training in self-care at home, within a month after the operation samples were called, and the importance of the training was emphasized and reminded to them. Then patients' questions were answered at the same time, bearing in mind that patients in the control group did not receive these trainings. Finally, the data were analyzed using SPSS for Windows (version 16, SPSS Inc., Chicago, IL., USA), independent t-test (for comparison of stress variables, anxiety, and depression between the two groups) chi-square, and Fisher's exact test. Differences were considered significance if $P \leq 0.05$.

Results

Due to the potential dropout rate of participants, number of subjects for both intervention and control groups was considered to be 35 patients. By the end of study, 3 people withdrew from the study, 2 people from the intervention group quit the study and 1 withdrew due to prostate cancer; the study was conducted on 67 people. Demographic data samples are given in table 1. Since variables under study can have an influence on anxiety, stress, and depression of the patients, they were distributed into two groups using chi-square for qualitative variables and Student's t-test for quantitative data. Results showed that both groups had no significant difference in terms of demographic variables such as age, marital status, education, occupation, income, duration of disease, and living with family members. Student's independent t-test showed no significant difference between mean standard deviation of stress ($P = 0.684$), anxiety ($P = 0.938$) and depression ($P = 0.727$) scores in the two groups before the intervention. The difference in anxiety and stress scores at the time of discharge (stress: $P = 0.031$, anxiety: $P = 0.043$) and one month after surgery (stress: $P \leq 0.001$, anxiety: $P = 0.016$), were significant between the two groups. There was a decrease in anxiety and stress levels in the intervention group compared to control group. However, the intervention group showed a decrease in depression, but caused no significant difference between groups during discharge and one month after surgery.

Repeated measures ANOVA showed that although depression score was not significant ($P = 0.082$), there was a significant difference in

the mean stress (P ≤ 0.001), and anxiety (P ≤ 0.001) scores before and after the intervention in the intervention group. However, those in the control group showed no significant change (stress: P = 0.454, anxiety: P = 0.179, and depression: P = 0.082) (Table 2).

This test also showed a significant difference in mean stress and anxiety levels at three different times between experimental and control groups (stress: P = 0.012 and anxiety: P = 0.047).

The results indicate that the intervention group, who used the self-care education program, showed a statistically significant reduction in stress and anxiety scores.

Table 1. Demographic characteristics of the two groups

Variables		Intervention		Control		P
		No.	Percentage	No.	Percentage	
Age	51-60	10	30.30	9	26.47	0.777
	61-70	14	42.42	13	38.23	
	71-80	9	27.30	12	35.30	
Marital status	Married	33	100	31	91.18	0.239
	Single	0	0	3	8.82	
Living with family members	With spouse and children	33	100	33	97.05	1.000
	Alone	0	0	1	2.94	
Education	Under High School Diploma	25	75.75	26	76.47	0.318
	High School Diploma and above	8	24.24	8	23.53	
Occupation	Retired	23	69.69	25	73.52	0.783
	Employed	10	30.30	9	26.47	
Income	Sufficient	23	69.69	19	55.88	0.791
	Not sufficient	10	30.30	15	44.11	
Duration of disease (months)	Three months or less	6	18.18	3	8.23	0.305
	Four months or more	27	81.81	31	91.17	

Table 2. Mean differences in stress, anxiety, and depression in intervention and control groups at three different times

Variables	Time	Group	Mean ± SD	P	P (Repeated measurement test)		
					Intervention	Control	Within group
Stress	Before intervention	Intervention	8.21 ± 4.87	0.684	≤ 0.001	0.454	0.012
		Control	7.71 ± 5.23				
	On discharge	Intervention	4.42 ± 3.28	0.031			
		Control	6.97 ± 5.80				
	A month after operation	Intervention	3.17 ± 3.64	≤ 0.001			
		Control	7.74 ± 5.62				
Anxiety	Before intervention	Intervention	5.18 ± 4.43	0.937	≤ 0.001	0.179	0.047
		Control	5.26 ± 4.23				
	On discharge	Intervention	3.55 ± 3.97	0.043			
		Control	5.65 ± 4.23				
	A month after operation	Intervention	2.52 ± 3.88	0.016			
		Control	3.99 ± 4.76				
Depression	Before intervention	Intervention	5.88 ± 4.36	0.727	0.082	0.552	0.442
		Control	5.50 ± 4.48				
	On discharge	Intervention	4.24 ± 4.008	0.514			
		Control	4.94 ± 4.67				
	A month after operation	Intervention	3.15 ± 3.70	0.221			
		Control	4.59 ± 5.62				

Discussion

In this study, the designed self-care educational program caused a significant reduction in stress and anxiety levels during discharge and one month after surgery in the intervention group compared to the control group. This suggests the impact of self-care education program in the mentioned group. The reason for the significant decrease in anxiety and stress in the intervention group could be due providing patients with information about the nature of the disease and surgery, and regarding self-care in the hospital and at home in the form of a designed self-care program. Generally, surgical procedures have a negative impact on the patient's ability to follow self-care programs.[20] Moreover, BPH patients have concerns about success rate of the treatment, and other concerns, especially fear of surgery and fear of prostate cancer.[9,21] Regarding anxiety as a variable, the results of the present study is similar to the results of studies done by Callaghan et al., and Zhang and Xiaoyu.[22,23]

The results of studies done by Callaghan et al. showed that preoperative data, presented in the form of educational pamphlets, decreased anxiety in patients undergoing TURP surgery.[22] The study done by Zhang and Xiaoyu showed that teaching patients with BPH reduces patients' preoperational anxiety.[23] However, the studies done by Larsson et al. and Asilioglu and Celik showed that patient education has not been effective in reducing anxiety.[24,25] In the current study, designed self-care education program decreased anxiety levels in theintervention group. However, this reduction was not enough to cause significant differences between the two groups on discharge and one month after the operation. Contrary to what was found in the present study, the study by Sun et al., titled "Influence of cognitive psychology nursing on preoperative anxiety and depression of patients with benign prostatic hyperplasia", showed that mean difference of depression between the intervention and control groups were significant.[21] In this study, in addition to patient education about TURP surgery and self-care education, psychological interventions, such as emotion regulation, were conducted through social support, such as friends and family members, which had a positive impact on reducing depression.

One reason for the insignificant decrease in the intervention group compared to the control group was the lack of supplementary intervention in the designed self-care program. It can also be due to several factors such as annoying disease symptoms, surgical complications resulting in sexual dysfunction, such as erectile problems, after TURP surgery, and after patient discharge from the hospital, which may be weeks or months after the operation.[6,19,26-30] Another issue was sleep disruption, which had a direct effect on depression.[31] Our patients in the present study would agree that the above mentioned statements reflect their own ideas. Given the fact that depression was declining in the intervention group during the one month follow-up after surgery, it seems that by increasing the duration of follow-up better outcomes, with the aim of lowering the level of depression, can be achieved. Limitations of this study included items that were out of the control of the researcher, such as patients' mood during training sessions, individual differences in their learning, training presentations, patients' personality types and characteristics, their sense of responsibility towards their health, and urologists' differences based on their skills in TURP surgery (which could influence the treatment outcomes).

The results of this study showed that a designed educational program on self-care significantly reduces stress and anxiety levels of BPH patients under TURP surgery. Thus, in order to improve the health and quality of life of patients suffering from BPH and those under TURP surgery, patients' education on self-care, and nurses and health workers' participation in routine follow-ups are essential. Therefore, implementation of the program to observe its

impact on the quality of life of BPH and prostate surgical patients, and its effects on psychological symptoms in patients with prostate cancer is recommended.

Conflict of Interests

Authors have no conflict of interests.

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Chronic Diseases Journal

Quality of life among Iranian postmenopausal women participating in a health educational program

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Original Article

Abstract

BACKGROUND: Quality of life (QOL) in postmenopausal period has taken much attention especially in recent years, since almost one third of woman are living in postmenopausal age. The aim of this study was to determine the effect of health educational program among Iranian postmenopausal women.

METHODS: This quasi-experimental study was conducted in Sanandaj (Kurdistan, Iran). Forty menopausal women were recruited for the study. Data were collected using the Persian version of menopause-specific quality of life questionnaire (MENQOL) at the University of Toronto, Canada. After an initial evaluation and estimation of educational needs, educational intervention was performed weekly, for three consecutive weeks; each section lasted 45-60 minutes. The inclusive criteria were age of 45 years or older, married, residing in Sanandaj, having normal pressure and not using any types of alternative hormone therapy 6 months prior to the study.

RESULTS: Mean age was 45.5 ± 2.5 years. Results showed that the mean score of QOL scale positively was affected by the health educational program.

CONCLUSION: This study showed that an appropriate training to menopausal women can improve their QOL and promote their health.

KEYWORDS: Education, Menopause Women, Quality of life

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Introduction

Thousands of years ago, Roman philosopher, Lucius Annaeus Seneca (C.4 B.C-A.D.65) demonstrated importance of quality of life (QOL) by saying that "It is quality rather than quantity that matters".[1] The QOL in postmenopausal period has taken much attention especially in recent years, since almost one third of woman are living in postmenopausal age. QOL has been defined by the World Health Organization (WHO) as the "individual's perceptions of their position in life in the context of the cultural and value systems in which they live and in relation to their goals, expectations, standards and concerns".[2]

Factors that may affect menopause onset have been described as genetic, race, habits, geographical region of habitual, socio economic and educational level.[3] Headache, trouble sleeping, mood swings, vasomotor, somatic and psychological symptoms of menopause affect all dimensions of QOL.[4] The duration, severity and impact of these symptoms vary from individual

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to individual, and population to population. Some women have severe symptoms that profoundly affect their personal and social functioning and QOL.[5] Many studies showed that some of demographic characteristics in post-menopausal women such as age, marital status, educational level, social and economical level, marriage satisfaction and the number of children who lived with the family were among other factors affecting the post-menopausal life.[6-8]

The timing of menopause as well as women's experience of menopausal symptoms varies between populations and within populations.[9] The mean age of menopause have been reported at 51 in the world, and regarding the increase in life expectancy in many countries, more than a third of women's time is in menopausal period. The importance of menopause is due to its association with various diseases and QOL.[3] According to Rajaeefard et al., the mean age of menopause in Iran was calculated as 48.2 years.[10] Furthermore, Shahgheybi and Arya Nejad in Sanandaj showed that the mean age of menopause was 46.1 years.[11]

Evidence has shown that a woman's ability to cope with the stress of menopause can be enhanced through education and social support.[7] Therefore, the QOL is a multidimensional health concept, which mainly represents subjective symptoms that may influence the sense of well-being and day-to-day function.[2] The present study aimed to determine the effect of health educational program on QOL among Iranian postmenopausal women.

Materials and Methods

A quasi-experimental was used for the guiding methodology. The research took place within a seven-month period in 2011. Study subjects were recruited from the Qods Health Care Center in Sanandaj, (Kurdistan, Iran). A convenience sampling method was used and forty menopause women were recruited for the study. The criteria for subjects selection were 45 years or older, married, residing in Sanandaj, having normal pressure and not using any types of alternative hormone therapy 6 months prior to study. Ethical considerations were taken into account which included confirming the women's willingness to participate in the study, providing verbal consent and assuring that the data would be kept confidential and used only for the research.

For this study, QOL was assessed using the Menopause-Specific Quality of Life Questionnaire (MENQOL) proposed by Hilditch et al. at the University of Toronto, Canada.[12] Its Persian version validated among Iranian women population by Abedzadeh et al.[5] The questionnaire is composed of 29 items grouped in four domains: vasomotor, psycho-social, physical and sexual. Each item can be checked as non-present or present. In the later case, the item is graded according to its severity from 0 to 6. A mean score within each domain is generated according to each subject's response.[5]

After an initial evaluation and estimation of educational needs, educational intervention was performed weekly, for three consecutive weeks; each section lasted for 45-60 minutes. The content of the educational sessions were as the following: to give information about female genitalia and definition of menopause (the first session); to describe the symptoms and complications of menopause (the second session); and to offer some approaches in order to diminish menopausal complications (the third session). At the end of each session, the summary of the instructed program was delivered to the participants. Scores for QOL was evaluated and compared in two stages before the educational intervention and one month after the educational intervention.

One month after the intervention, the study subjects completed the questioners. Data were entered into SPSS for Windows (version 11.0, SPSS Inc., Chicago, IL, USA). Data was presented as means, standard deviation (SD) and percentages. Paired t-test was used in order to compare the mean scores for diverse criteria (total score of QOL before and after the educational program). P-value less than 0.05 was set as a significant level.

Results

A total of 40 women participated in this study. Mean age of the participants was 45.50 ± 2.15 years. Most participants described themselves as housewives (72%). The women differed in educational level and most were illiterate (47.5%). After educational intervention, t-test showed a considerable improvement in the mean score of participant's knowledge. Mean score of participant's knowledge before the education was 13.70 ± 2.92 and it was 17.0 ± 2.4 after the education (Table 1).

The score for vasomotor symptoms compared to the score prior to the intervention was improved (P = 0.05). The score for psychosocial function was improved after the intervention. In addition, after the intervention, mean score of physical well-being compared to the base scores showed a statistically significant improvement. In term of sexual health, the study showed a statistically significant improvement (Table 2).

Discussion

The aim of this study was to evaluate the effect of education on improving QOL. The result of the study showed that most subjects had a moderate level of knowledge before the intervention (educational program), therefore the need for planning and implementation an educational program becomes more obvious. The findings of this study supported previous researches.[13,14] Since most of subjects in this study were illiterate, there is need to improve source of information such as media or healthcare centers' educational program.

The study showed that the vasomotor problem scores after the intervention were improved than those before, it can be concluded that intervention led to an improvement in vasomotor symptoms of the subjects. This finding was in accordance with previous studies.[13-15] Booth-Laforce et al.[15] reported a decrease in hot flashes following the practice of yoga. The result of study showed a statistically significant improvement in psychosocial well-being in the participants after the intervention. Therefore, the applied intervention led to improvement of psychosocial status in participants. This finding also was reported by Elavsky and McAuley.[16]

The study also showed that participants' physical health status improved after the intervention. This result was similar to the other studies.[13,14,17] Rotem et al. reported improvement in physical health status following implementing education in menopause women.[17]

Table 1. Comparing the mean score for knowledge before and after the education

Knowledge	Pre-intervention		Post-intervention	
	Number	Percentage	Number	Percentage
Low (Scores 0-8)	10	25	2	5.0
Moderate (Scores 9-15)	24	60	7	17.5
Good (Scores 16-21)	6	15	31	77.5
Total	40	100	40	100.0
Mean ± SD	13.7 ± 2.92		17.0 ± 2.4	

SD: standard deviation

Table 2. Comparing the mean and standard deviation scores for four dimensions of quality of life (QOL) before and after the education

QOL	Pre-intervention		Post-intervention		Statistical tests
Dimensions	Mean	SD	Mean	SD	Results
Vasomotor	2.05	0.66	2.67	1.18	t = 0.77; P < 0.050
Psychosocial	5.32	2.25	7.05	2.91	t = 0.85; P = 0.340
Physical	10.28	3.07	13.39	5.20	t = 6.05; P = 0.001
Sexual	0.64	1.18	1.04	1.54	t = 0.44; P < 0.050
Overall QOL	19.30	6.22	24.1	8.60	t = 8.74; P = 0.001

QOL: quality of life; SD: standard deviation

According to Osinowo in Nigeria, an improvement of self-perception marital satisfaction and sexual activity was observed after informing women on menopause.[18]

Conclusion

QOL was improved significantly in the participants following the intervention. The finding of this study asserted that the four aspects of QOL well improved after the educational intervention, and the education can cause an improvement in the QOL by decreasing the problems of menopause stage and lowering their intensity. Therefore, the urgency of need to plan and implement an appropriate educational program is emphasized in order to promote the QOL among menopausal women.

Finally, the limited number of participants, and unfeasibility of categorizing them based on different age ranges were the limitations of the present study. Thus, broader studies with greater sample size, and different age ranges are recommended. In conclusion, this study was conducted to evaluate the effect of education on QOL and the improvement of health standards among menopausal women. The findings showed that an appropriate training to menopausal women can improve their QOL and promote their health.

Conflict of Interests

Authors have no conflict of interests.

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Chronic Diseases Journal

Comparison the efficacy of *Hypericum perforatum* and *vitex agnus-castus* in hot flushes: A double-blinded randomized controlled trial

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Original Article

Abstract

BACKGROUND: Treating hot flushes in middle-aged women is an important health issue. Recently, *Hypericum perforatum* and *vitex agnus-castus* were investigated to decrease hot flushes. This study was conducted to compare the efficacy of *Hypericum perforatum* and *vitex agnus-castus* in hot flushes among menopausal women.

METHODS: This was a randomized, double-blinded, controlled trial. The Hypericum perforatum group received 330 µg Hypericum perforatum and second group received vitex agnus-castus in the same tablet forms. Data were analyzed using repeated measurement for comparing Greene Climacteric Scale.

RESULTS: Trend of Greene Climacteric Scale and hot flushness attack were decreased in both groups and it presented a decreasing trend within two months; however, no statistically significant difference was observed between the two groups.

CONCLUSION: It seems that Hypericum perforatum and vitex agnus-castus could be similarly effective in decreasing hot flushes. These two medicines did not have any special severe side effects.

KEYWORDS: Hypericum, Menopause, Plants, Randomized Controlled Trial, Vitex Agnus-Castus, Herbal Drug

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Introduction

Treating hot flushes in middle-aged women is an important health issue. Now, hormone therapy is used as the main method of treating menopause symptoms; however, these hormones may cause some side effects and complications such as temper changes, abnormal uterine bleeding, flatulence, breast tenderness, nausea, and headaches.[1,2]

Recently, a tendency toward alternative and complementary herbal treatment methods has emerged.[3,4] There are also some alternative treatment methods that use herbal medicines to decrease menopause complications including *Ginseng, Hypericum perforatum* (St John's wort), *vitex agnus-castus* (chaste tree/berry), black cohosh and *Dong quai (Angelica sinensis)*. Among these methods, Hypericum perforatum and vitex agnus-castus are the most favored.[5-7] These two herbs contain substances with selective serotonin reuptake inhibitors (SSRIs) or serotonin norepinephrine reuptake inhibitors (SNRIs). SNRIs are used as anti-depression drugs and they are used for treating menopause

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complications as well.[8,9] Therefore, Hypericum perforatum is used as an anti-depression drug in some countries and due to its two products i.e. Hypericin and Hyperforin which prevent and control mono-amino oxides enzyme, It exerts anti-depression effects.[10,11]

Vitex agnus-castus which is another herbal medicine could decrease hot flushes via its dopaminergic effects. Moreover, under-activity of dopaminergic system could cause psychological dysfunctions and it has been proved that dopaminergic effects of Vitex agnus-castus could be effective in decreasing emotional symptoms of menopause.[7] In previous studies, Vitex agnus-castus has decreased duration, severity and other complications of hot flushes.[12,13] In the United States and Europe, Vitex agnus-castus is used for treating premenstrual syndrome and hyperprolactinemia.[14] Hence, considering previous studies, this study was conducted to compare the efficacy of Hypericum perforatum and vitex agnus-castus in hot flushes among menopausal women.

Materials and Methods

This was a randomized, double-blinded, controlled trial. Protocol for the study was approved by the Ethical Review Board and the Dean of Faculty, the Deputy of Educational Affairs, and the Educational Affairs Administration of the University of Shiraz. Participants were selected in an outpatient academic medical center in Zeinabieh Hospital (Shiraz, Iran) from April 2009 to March 2010 by convenience sampling method. Sample size calculated 26 subjects in each group according to the assumption of type 1 error (alpha) 5%, power 90% and mean of difference between the two groups equal to 10 score [standard deviation (SD) ± 11]. In this study, 64 subjects were evaluated (Figure 1).

Informed consent was obtained and all the participants were ensured about the confidentiality of information during and after the study. Inclusive criteria were 1) age between 45-65, 2) last menstrual period 1 year ago, 3) serum follicle stimulating hormone level of more than 40 mIU/ml, and 4) informed consent. Exclusive criteria were 1) existing use of Hypericum or Vitex Agnus-castus, 2) severe diseases (e.g. heart, liver, kidney or metabolic diseases ,psychiatric disorders), 3) abnormal thyroid-stimulating hormone 4) smoking, and 5) using hormones ,vitamins or supplements drugs.

The participants were allocated by simple randomization by a nurse. Each patient received a package contain one group drug. These packages were prepared by the nurse. The Hypericum perforatum group received 160 mg Hypericum perforatum 3tab/day (Goldaru Co, Iran) and the second group received vitex agnus-castus 3tab/daily in the same tablet forms for 8 weeks.

Outcome of the study was Greene Climacteric Scale and its factors[15,16] and hot flushness attacks. Assessment of Greene Climacteric Scale and hot flushness attacks was done by one blinded investigator at the baseline, first and second months from the interview. Greene Climacteric Scale that developed by Green, measures psychological, somatic and vasomotor symptoms.[16]

Data were entered into SPSS for Windows (version 11.5, SPSS Inc., Chicago, IL, USA); independent t test was also used for comparing quantitative variables in the two groups and repeated measurement was used for comparing the trend of Greene Climacteric Scale and its factors during different visits in the two groups according to per-protocol analysis.

Results

In this study, 76 subjects participated with a mean age of 52.9 ± 4.7 years. The mean postmenopausal period was 4.2 ± 3.2 years. Body mass index (BMI) was 26.7 ± 4.6. The mean number of children was 4.3 ± 2 and the mean menarche age was 13.5 ± 1.6 years. There was no

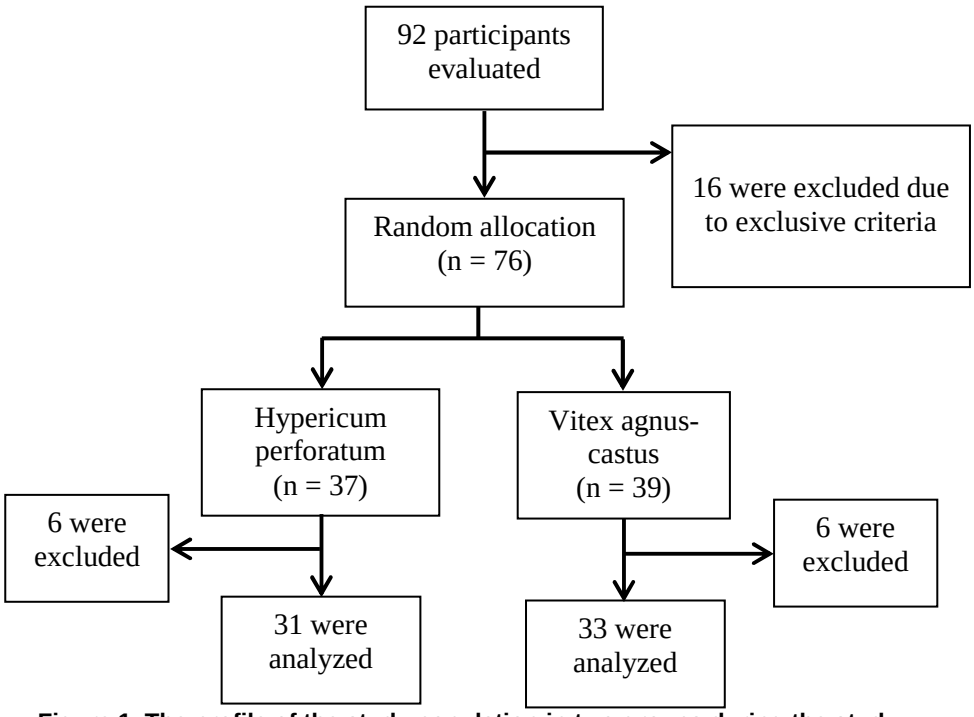

Figure 1. The profile of the study population in two groups during the study

statistically significant difference between the two groups regarding age, menopause age, menarche age and number of children.

The mean number of hot flushes was 3.6 ± 0.8 times. 62 subjects (81.6%) were married. No statistically significant difference was observed between the two groups of Hypericum perforatum and vitex agnus-castus regarding these variables (Table 1).

The general trend of Greene Climacteric Scale and its domains dropped in both groups and it presented a decreasing trend within two months; however, no statistically significant difference was observed between the two groups and the trend of reduction in both groups was similar. Both groups had a descending trend in hot flushes as well but there was no statistically significant difference between the two groups (Table 2) (Figure 2) and (Figure 3). Moreover, the percentage of successful treatment measured by Greene Climacteric Scale and its domains did not have any statistically significant difference between the two groups and at least 38% improvement was observed in each group. The maximum percentage of hot flush improvement was (58.7% and 55.5%) and the lowest percentage was in somatic domain (38.1% and 38.2%) (Table 3).

Some unexpected side effects were observed in the study illustrating in table 4. In the first month, some complications and side effects were observed in four subjects in the Hypericum perforatum group and four other subjects in the

Table 1. Comparison of demographic characteristics of the two groups

Variables	Hypericum perforatum	Vitex agnus-castus	P
Age	53.2 ± 4.7	52.7 ± 4.8	0.63
BMI	27.2 ± 4.8	26.2 ± 4.4	0.34
Age of menarche	13.4 ± 1.6	13.7 ± 1.6	0.39
Years after menopause (median)	4 (1-12)	3 (1-14)	0.65
Number of Children (median)	4 (0-8)	4 (1-10)	0.97
Married	29 (78.4%)	33 (84.6%)	0.48

Analysis was done by independent t test and mean ± SD; BMI: Body mass index; SD: Standard deviation

Table 2. Changes of value of Greene Climacteric Scale and its factors in the two groups during the study

Factors	Time	Hypericum perforatum	Vitex agnus-castus	P
Total	Baseline	29.54 ± 8.5	29.25 ± 8.7	0.88
	Month 1	22.13 ± 6.8	21.12 ± 7.0	0.53
	Month 2	15.86 ± 5.2	15.94 ± 5.6	0.95
Psychological	Baseline	15.08 ± 5.3	14.84 ± 5.9	0.85
	Month 1	11.1 ± 4.1	10.94 ± 4.8	0.87
	Month 2	7.83 ± 4.0	8.17 ± 3.8	0.7
Somatic	Baseline	6.81 ± 3.3	6.82 ± 3.3	0.99
	Month 1	5.27 ± 2.8	4.71 ± 2.5	0.37
	Month 2	4.05 ± 2.1	4.1 ± 2.4	0.92
Vasomotor	Baseline	6.64 ± 1.5	6.64 ± 1.7	0.98
	Month 1	4.86 ± 1.6	4.69 ± 2	0.48
	Month 2	3.56 ± 1.5	3.25 ± 2.2	0.34
Hot flushness	Baseline	3.67 ± 0.74	3.58 ± 0.84	0.64
	Month 1	1.59 ± 1.38	1.58 ± 1.63	0.98
	Month 2	1.4 ± 1.1	1.53 ± 1.71	0.68

Analysis was done by independent t test and mean ± SD; SD: standard deviation

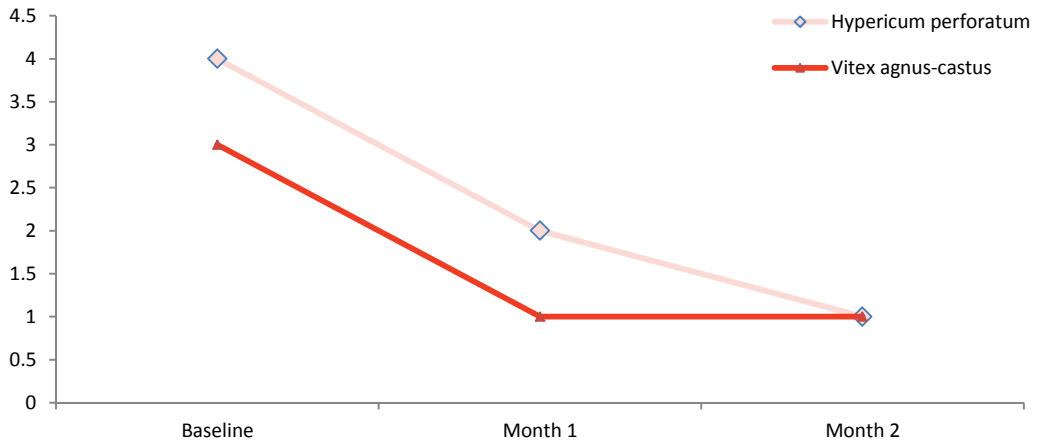

Figure 2. Comparing the frequency of hot flushness trend between the two groups

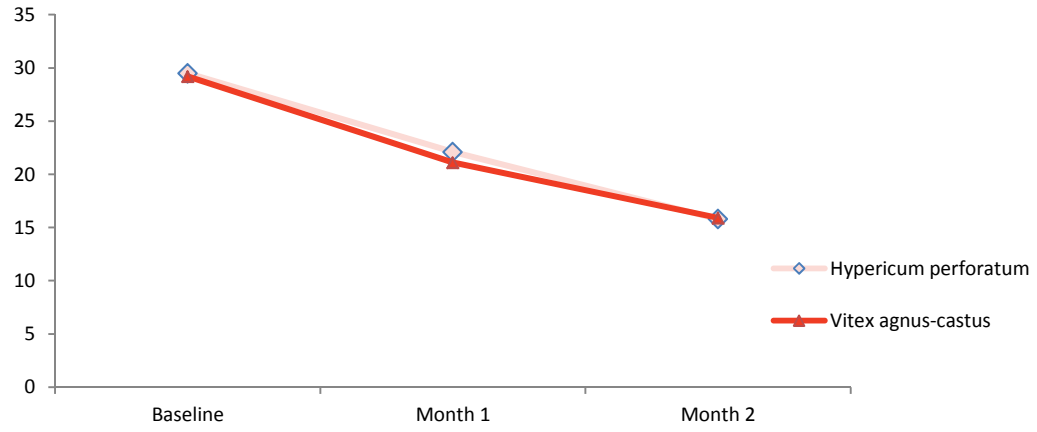

Figure 3. Comparison of Greene Climacteric Scale trend between the two groups

Table 3. Comparing the percentage of improvement in Greene Climacteric Scale and its factors and hot flushness between the two groups

Index	Hypericum perforatum	Vitex agnus-castus	P
Greene Climacteric Scale	45.5 ± 12.0	44.8 ± 14.5	0.82
Psychological	48.3 ± 16.9	44.1 ± 16.8	0.28
Somatic	38.1 ± 23.7	38.2 ± 23.6	0.98
Vasomotor	45.8 ± 21.0	49.4 ± 34.9	0.58
Hot flushness	58.7 ± 34.0	55.5 ± 49.9	0.73

Analysis was done by independent t test and mean ± SD; SD: standard deviation

Table 4. Occurrence of side effects in the two groups during the study

Side effect	Side effects leading to withdrawal				Side effects not leading to withdrawal			
	Hypericum perforatum		Vitex agnus-castus		Hypericum perforatum		Vitex agnus-castus	
	First month	Second month	First month	Second month	First month	Second month	First month	Second month
Pain over eyes	0	1	0	0	0	0	0	0
Rashes	1	0	0	0	0	2	0	0
Nausea	0	1	0	0	3	3	1	0
Dry month	0	0	0	0	0	0	0	0
Dizziness	0	0	2	1	2	3	4	1
Loss of appetite	0	0	0	0	0	0	0	0
Headache	1	0	1	1	4	3	4	1
Lethargy	1	0	0	0	0	0	0	0
Constipation	1	0	1	0	4	0	2	1
Diarrhea	0	0	0	0	2	1	2	2
Total	4	2	4	2	15	12	13	5

vitex agnus-castus group and consequently they discontinued medicines. Common mild side effects were headache and constipation in the Hypericum perforatum group and headache and dizziness in the vitex agnus-castus group.

Discussion

Our results showed that Hypericum perforatum and vitex agnus-castus could reduce Greene Climacteric Scale in menopausal women. This improvement was observed in all items of Greens questionnaire but there was no statistically significant difference between the two groups. Previous studies have supported that Hypericum perforatum is useful in relieving the symptoms of menopausal syndrome.[7,9]

In our study, the percentage of improvement in Greene Climacteric Scale was 45.5% and 44.8% in Hypericum perforatum and vitex agnus-castus groups, respectively. There was no statistically significant difference between the two herbal drugs. The reasons for using vitex agnus-castus in our study were the efficiency, safety, and inexpensiveness of this combination since Hypericum perforatum is extensively found in the mountains of Iran. Furthermore, previous studies suggested further investigation about these herbal drugs.[7]

Previous studies compared Hypericum perforatum and placebo[7,9] but there are few studies comparing Hypericum perforatum and vitex agnus-castus.[7] Abdali et al.[9] showed that Hypericum perforatum was an effective treatment for vasomotor symptoms and hot flushes in premenopausal or postmenopausal women; this result was similar to our study results. In Abdali et al.[9] women who had used Hypericum perforatum showed more improvement in their frequency of hot flushes than the placebo-receiving group.

Al-Akoum et al.[10] indicated that Hypericum perforatum ethanolic extract can improve 30% of hot flushes. In addition, they found improvements in quality of life and its domains (vasomotor, physical, and psychosocial aspects) using the menopause-specific quality of life

(MENQOL) questionnaire. However, they suggested that further studies with larger clinical trials are needed.

Besides, our findings are in accordance with Grube et al.[17] They reported improvement in psychological and psychosomatic symptoms in menopausal women. Van Die et al.[7] measured Hypericum perforatum with vitex agnus-castus within menopausal symptoms. They showed that Hypericum perforatum and vitex agnus-castus were not superior to placebo in alleviating menopausal symptoms.

In a study[18] concerning the effects of vitex agnus-castus on hot flushes and nightly sweating among 50 pre and postmenopausal women, it was found that vitex agnus-castus was more efficient than the placebo. In Chopin [19], 33% showed major improvements and 36% mild to moderate improvements in symptoms. The most important improvement after hot flushes was regarding emotional symptoms. In our study, the most significant improvement was observed in hot flushes and then in psychological symptoms.

Based on the results of our study and other studies, it seems that Hypericum perforatum and vitex agnus-castus could be similarly effective in decreasing hot flushes. Therefore, taking these two substances could be helpful. These two medicines do not have any special severe side effects and their observed complications such as headache might be removed by simple medicinal treatments. Similar side effects have been observed in other studies as well.[10]

Conclusion

It seems that Hypericum perforatum and vitex agnus-castus could be similarly effective in decreasing hot flushes. These two medicines do not have any special severe side effects.

Conflict of Interests

Authors have no conflict of interests.

Acknowledgments

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Chronic Diseases Journal

Comparing the therapeutic effects of three herbal medicine (cinnamon, fenugreek, and coriander) on hemoglobin A1C and blood lipids in type II diabetic patients

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Original Article

Abstract

BACKGROUND: Cinnamon, fenugreek and coriander are among those herbs that are probably effective in lowering glucose; however, different results have been found in observed studies, and the effectiveness of these herbs is still controversial. This study was designed to compare the effects of three herbs of cinnamon, fenugreek and coriander on hemoglobin A1C (HbA_1C) and blood lipids in type II diabetic patients.

METHODS: This was a double-blind randomized controlled trial study and 150 non-insulin dependent diabetic patients were recruited in the study. Five similar concolor 500mg capsules containing cinnamon, fenugreek, coriander, -a mixture of three herbs-, and placebo were prescribed two capsules every 12 hours. Variables of HbA_1C, fasting blood glucose, cholesterol and triglyceride were tested after 6 weeks. Data were analyzed by chi-square, Fisher's exact test, Mann-Whitney test and one way analysis of variance (one-way ANOVA).

RESULTS: There was no statistical significant difference between the intervention and placebo groups regarding basic characteristics. Man age of patients was 53.76 ± 8.74 years and the disease duration was 8.00 ± 5.66 years. Mean fasting blood sugar (FBS) and HbA_1C was 189.4 ± 51.05 mg/dl and 9.2 ± 1.42 percent, respectively.

CONCLUSION: In type II diabetic patients, herbal medicines of cinnamon, fenugreek, and coriander and their mixture with a daily dosage of 2 g did not have any stronger effect than the placebo on lowering blood glucose, HbA_1C, and blood lipids; it might be the result of several factors including prescribing little amounts of medicine, short period of intervention, and ineffectiveness of the mentioned herbs.

KEYWORDS: Diabetes, Cinnamon, Fenugreek, Coriander, Hemoglobin A_1C, Blood Lipids

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Introduction

Type II diabetes is the most common metabolic disease all over the world[1] and right now 1.2 million diabetic patients live in Iran.[2] Medicine-therapy of diabetes is conducted through using anti-glucose drugs including biguanides, thiazolidinediones, sulfonylureas, D-phenylalanine derivatives, etc.[3] Due to several different side effects of these medications, there is a growing tendency toward finding medications with less subsidiary effects and as a result therapeutic herbs are taking lots of attention. The World Health Organization (WHO) has listed 21000 herbs which are used as medicines all over the world[4] and this magnifies the importance of herbs in curing diseases. According to previous studies, some herbs are effective in lowering blood glucose.[4-9] Their mechanism includes lowering glucose absorption in intestine, increasing glucose consumption in body, creating glycogen in liver,

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enhancing phosphorylation of glucose receptors, and increasing insulin sensitivity.[6,10-15]. However, in different studies performed using these herbs, different results have been observed and some quantitative researches were applied on human samples.[9,16-19]

Because of the cost-effectiveness of them and trivial risks, finding effective therapeutic herbs can be more favored by diabetic patients; therefore, introducing effective drugs for diabetes can make a significant revolution in curing diabetes. This study, hence, was performed to compare the effects of three herbs of cinnamon, fenugreek, and coriander to the effects of placebo on lowering HbA_1C and blood lipids in type II diabetic patients.

Materials and Methods

This was a double-blind randomized controlled trial study and included insulin-independent diabetic patients who referred to diabetes center of Yazd, Iran. Based on confidence interval 95%, power 90%, standard deviation (SD) 1.3% for HbA_1C, and taking the least significant difference for 1% in lowering the HbA_1C mean, the sample size required for the study was estimated 27 people for each group and as a result we had 150 people in five groups as the total sample size; and simple randomization was used for distributing participants in five groups.

Randomization was done by a well-trained nurse, and 31 subjects were allocated to coriander group, 31 to cinnamon group, 29 to fenugreek group, 29 to three-herbs mixture group, and finally 30 to the placebo group. In total, 193 individuals were analyzed from which 43 subjects did not match the inclusive criteria, and 3 subjects in placebo group, 5 in coriander group, 3 in cinnamon group, 4 in fenugreek group, and 1 in three-herbs mixture group were excluded from the study because they did not come back on time for follow-up activities (Figure 1).

Inclusive criteria included type II diabetic patients with fasting glucose 140 to 350 mg/dl who were taking food diets or edible anti-diabetes drugs. Exclusive criteria were any history of allergy to fenugreek or pea (because of intersecting reaction with fenugreek), taking

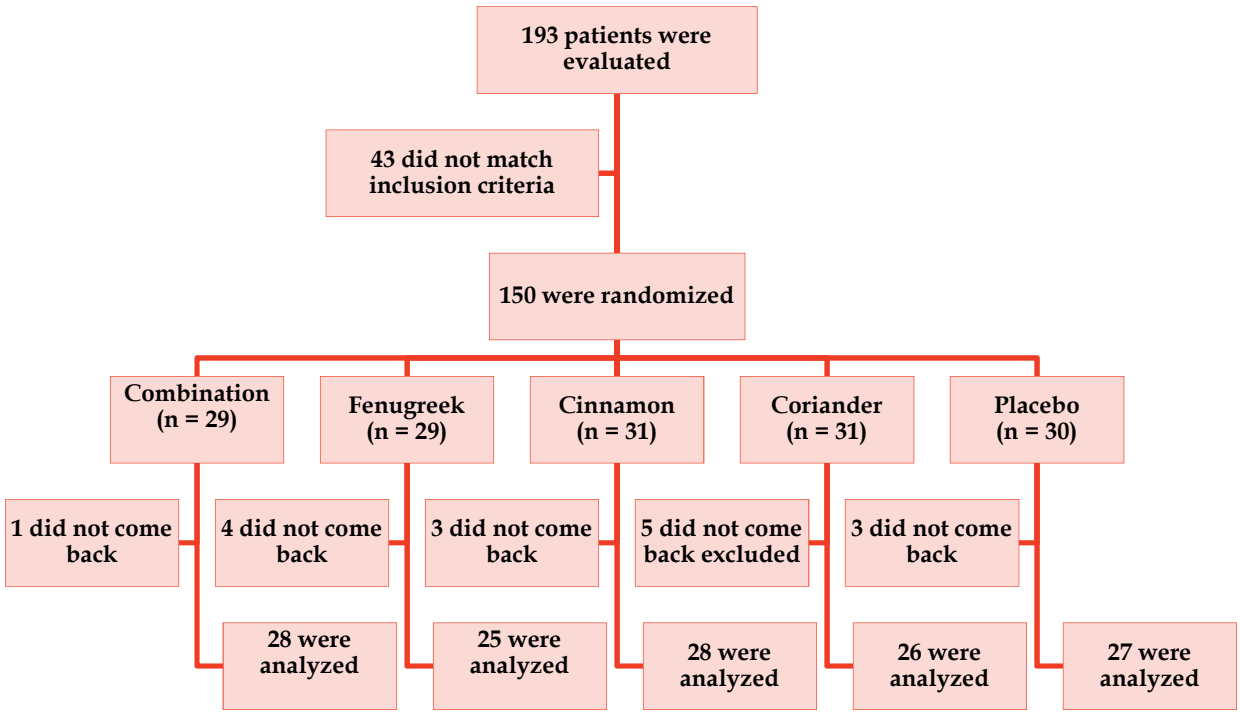

Figure 1. Patients' follow-up diagram

anti-clotting drugs or any history of coagulation disorders, alteration of anti-diabetes drugs or treating hyperlipidemia during the study, treatment with insulin, renal disorders or diabetic nephropathy, congestive heart failure, history of cerebral apoplexy during last previous month, chronic liver disease, chronic digestive diseases and ulcer peptic, asthma, bronchospasm and wheezing, and history of taking herbal medicines and vitamins in the last two weeks, pregnancy and breastfeeding. At the beginning of the study, HbA_1C variable as the major indicator and fasting blood glucose (FBS), cholesterol, triglyceride (TG), low density lipoprotein (LDL), high density lipoprotein (HDL) as minor indicators were tested by an authoritative laboratory.

For six weeks, every 12 hours, patients took two similar 500mg capsules of herbal drugs and placebo (pea flour) and after 6 weeks, indicators were re-measured. Patients were trained to discontinue and withdraw the drug or counsel diabetes center whenever they experienced respiratory distress, pain in chest, hives, rash, itching, skin inflammation, or hypoglycemia. Patients were visited weekly by physicians and their hypoglycemia and hyperglycemia were monitored and controlled and if their blood glucose was under 60 or above 350 mg/dl, proper cares were applied.

After entering data into SPSS for Windows (version 11.5, SPSS Inc., Chicago, IL, USA), the pre and post status of each variable was calculated. Then, chi-square and Fisher's exact tests were used to compare quantitative variables, and Mann-Whitney U test was used to compare the quantitative variables of intervention with the placebo group. And finally, the differences in outcomes between the subjects were assessed using one way analysis of variance (one-way ANOVA).

Results

This study included 27 males (18%), 123 females (82%), and among them 22 subjects were affected by neuropathy (14.7%), 2 by retinopathy (1.3%), 27 by blood pressure (18%), 69 by hyperlipidemia (46%), and 3 were cigarette smokers; there was no statistical significant difference between the intervention and placebo groups. None of the patients were suffering from nephropathy or diabetic foot sores. The mean age of patients was 53.67 ± 8.7 years, duration of diabetes 8 ± 5.6 years, and they took 2.23 ± 1.1 Glibenclamide pills and 2.4 ± 0.82 metformin, and there was no statistical significant difference between the intervention and placebo groups. The mean of body mass index (BMI), FBS and HbA_1C in all the participants were 29.5 ± 4.2, 191.3 ± 51.9 mg/dl and 9.23 ± 1.4%, respectively. There was no statistical significant difference between the intervention groups and placebo group in primary assessment (pre-intervention phase) regarding all the variables (Table 1).

Table 1. Comparing the intervention groups and placebo according to some variables

Variables	Placebo (n = 30)	Cinnamon (n = 31)	Fenugreek (n = 29)	Coriander (n = 31)	Combination (n = 29)
Sex					
Male	7 (23.3)	9 (29)	4 (13.8)	4 (12.9)	3 (10.3)
Female	23 (76.7)	22 (71)	25 (86.2)	27 (87.1)	26 (89.7)
Retinopathy	0 (0)	0 (0)	1 (3.4)	1 (3.2)	0 (0)
Neuropathy	4 (13.3)	3 (9.7)	3 (10.3)	7 (23.3)	5 (17.2)
Hypertension	7 (23.3)	3 (9.7)	6 (20.7)	6 (19.4)	5 (17.2)
Hyperlipidemia	14 (46.7)	12 (40)	16 (55.2)	12 (38.7)	15 (51.7)
Smoking	3 (10%)	0 (0)	0 (0)	0 (0)	0 (0)
Age (Mean ± SD)	53.1 ± 8.4	56.1 ± 9.8	52.3 ± 8	52 ± 7.9	54.3 ± 8.8
Duration of diabetes (Mean ± SD)	7.4 ± 4.8	7.5 ± 6.3	7.9 ± 5	7.4 ± 5.5	9.9 ± 6.1
BMI (Mean ± SD)	30.7 ± 3.3	29.6 ± 4	28.9 ± 5.1	29.7 ± 4.9	28.7 ± 3.5

There was no statistically significant difference between the placebo and intervention groups using chi-square, Fisher's exact test and Mann-Whitney U test to compare intervention with placebo groups.

There was no statistical significant difference between the study groups regarding lowering HbA_1C and other variables. Patients did not represent any allergic effect caused by drugs or placebo (Figures 2-7).

Discussion

In this study, no statistical significant difference was found in the two groups before applying interventions regarding the specified variables. Comparing with placebo, prescribed medicines

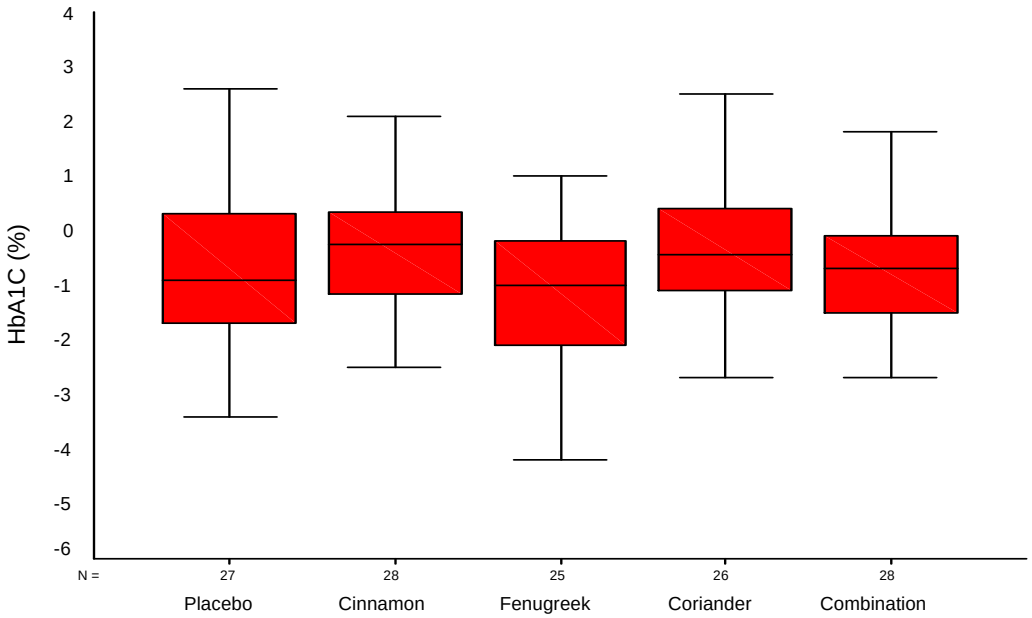

Figure 2. Alteration of hemoglobin A1C (HbA1C) (after minus before) value in the subjects
The median, minimum (Min), and maximum (Max) values and the values for quartile 1 (q1) and quartile 3 (q3) are shown. There was no statistical significant difference between the study groups using Kruskal-Wallis test (P = 0.382).

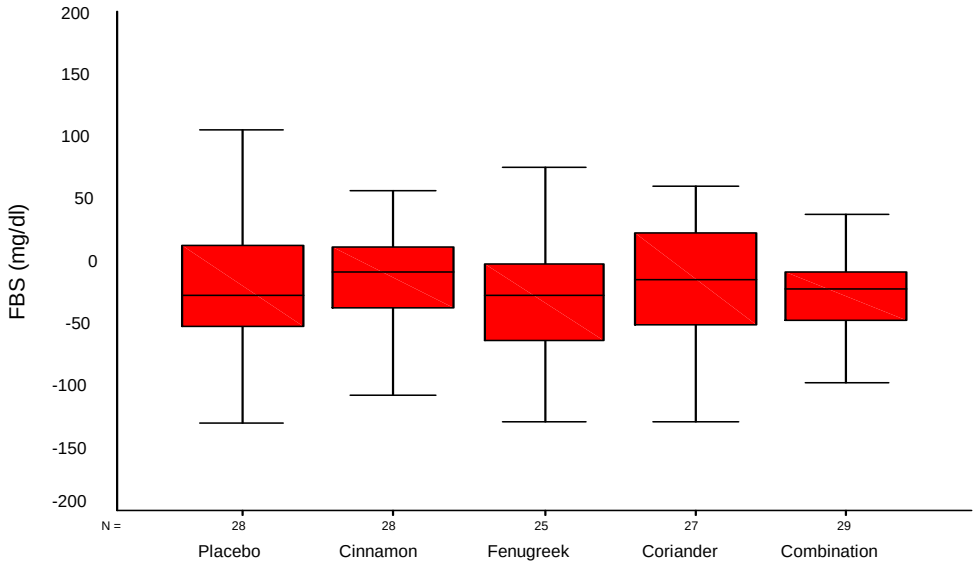

Figure 3. Alteration of fasting blood sugar (FBS) (after minus before) value in the subjects
No statistical significant difference was found between the study groups using one-way ANOVA (P = 0.569).

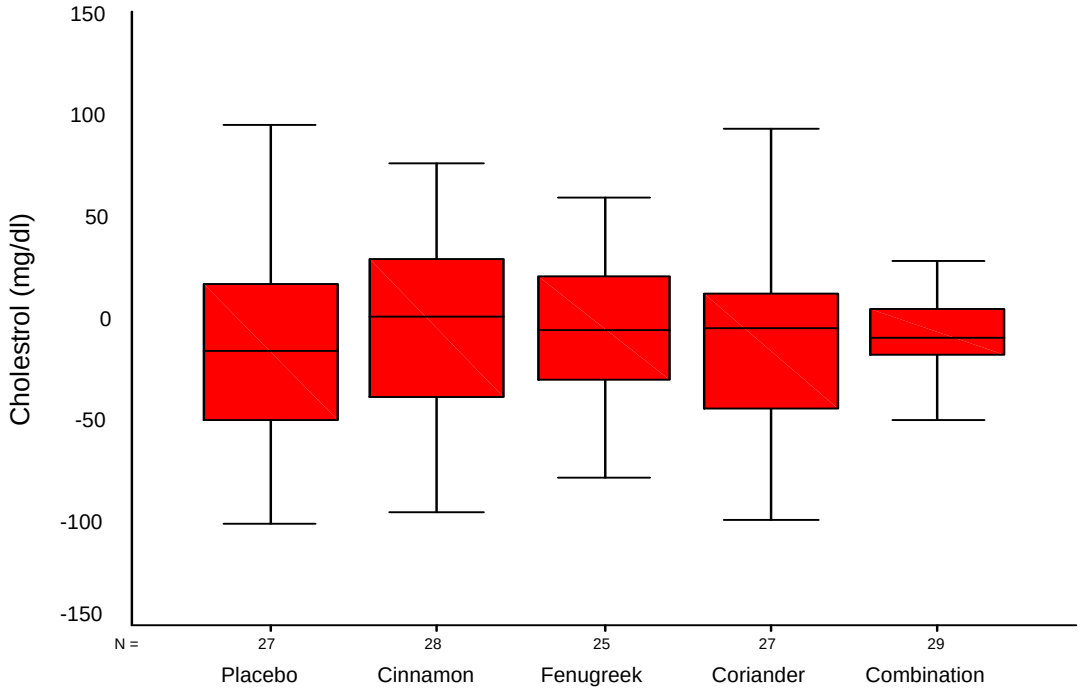

Figure 4. Alteration of cholesterol (after minus before) value in the subjects
No statistical significant difference was found between the study groups using one-way ANOVA (P = 0.944).

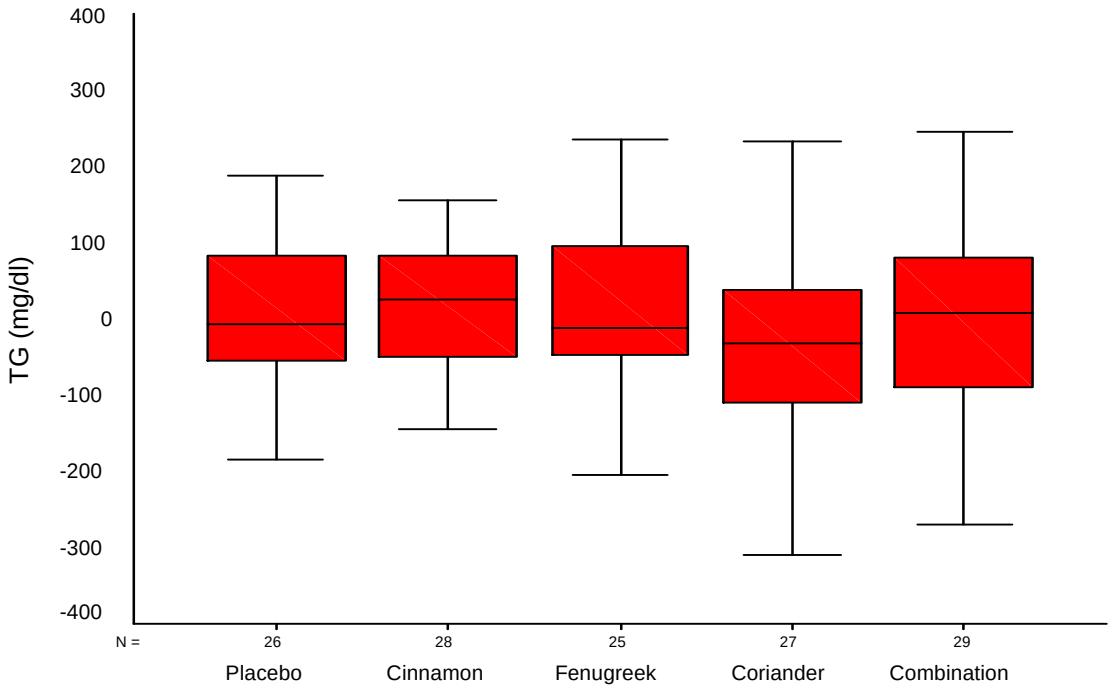

Figure 5. Alteration of triglyceride (TG) (after minus before) value in the subjects
No statistical significant difference was found between the study groups using one-way ANOVA (P = 0.398).

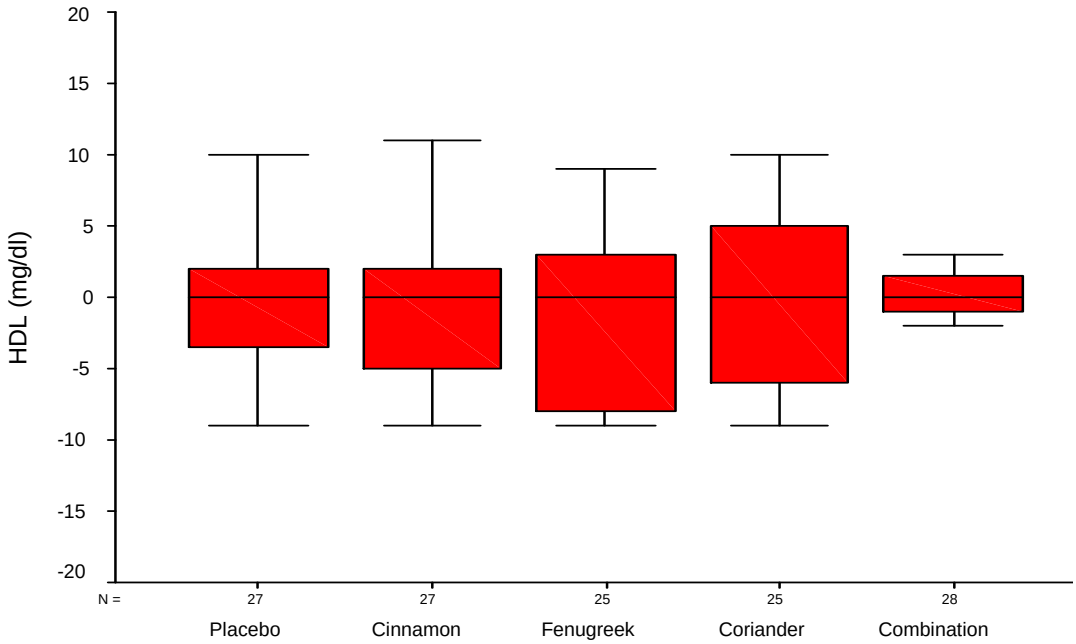

Figure 6. Alteration of high density lipoprotein (HDL) (after minus before) value in the subjects
No statistical significant difference was found between the study groups using one-way ANOVA (P = 0.998).

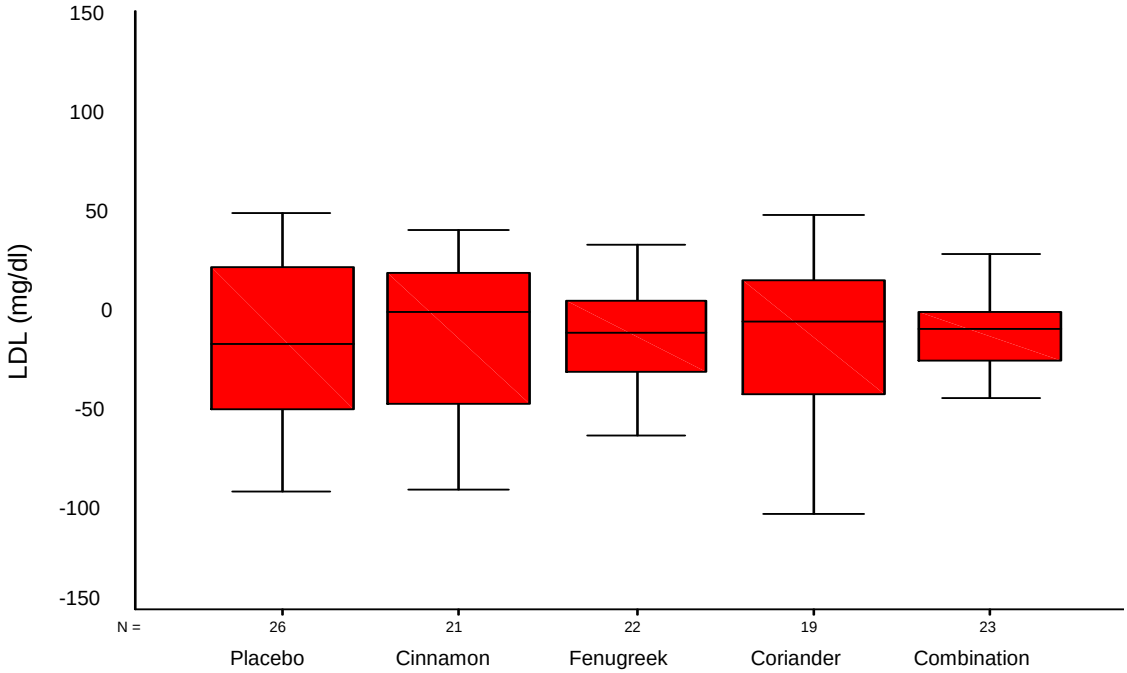

Figure 7. Alteration of low density lipoprotein (LDL) (after minus before) value in the subjects
No statistical significant difference was found between the study groups using one-way ANOVA (P = 0.956).

containing cinnamon, fenugreek, coriander and their mixture did not have any significant effect on lowering HbA_1C which is a good indicator for assessing blood glucose control.[20] Besides, their effects were not diverse in other groups, regarding other variables including cholesterol,

triglyceride, LDL, etc. multi-variable analysis for other probable confounder factors represented that treatment group did not have any effect on lowering HbA_1C.

In the study of Khan et al. in Pakistan,[21] the exact amounts of 1, 3 and 6 g of cinnamon that was taken for 40 days significantly reduced levels of glucose, cholesterol, triglyceride, and LDL in type II diabetic patients, comparing to those levels in control group and similar results were found in Crawford study.[22] However, in Altschuler et al.,[20] cinnamon did not prove beneficial effects on HbA1C comparing to the control group and studies of Mang and Blevins[16,23] had the same results. In Baker et al. meta-analysis[24] which included several studies, it was demonstrated that cinnamon was not stronger than the placebo in reducing blood sugar, blood lipids and HbA_1C.

In Xue study, implemented on diabetic rats, fenugreek was efficient in lowering blood sugar, HbA1C, cholesterol, and triglyceride though the same effect was not achieved in lower dosages.[25] Nevertheless, in Jelodar et al. fenugreek did not reduce blood glucose in rats.[26] In Sharma study, a dosage of 50 g fenugreek powder, that was taken twice daily, was efficient in reducing 54% of 24-hour glucose-urine excretion in diabetic patients who were insulin-users. In addition, their study demonstrated a significant reduction in cholesterol, VLDL (very low density lipoprotein), and LDL.[27] Gutpa study, in which 25 diabetic patients took part, represented that taking a dosage of 1 g fenugreek seeds daily did not make any statistical significant change comparing to the control group (2 hours after taking drugs and also 2 months later); however insulin sensitivity was increased and TG was decreased.[28] His collogues showed that fenugreek essence reduced blood glucose by 58% in diabetic rats.[29] Moreover Kannappan and Anuradha showed that using fenugreek seeds can increase cells susceptibility to insulin and this effect was comparable to the metformin.[30] In Bordia et al. 2.5 g of fenugreek seeds powder was prescribed to be taken twice each day for 3 months, and obvious reduction of cholesterol and TG was observed.[8] Studies concerning coriander were performed on animals and there are a few cases of human objected study. It has been proved that coriander can reduce glucose and lipid in rats[18] and it has demonstrated other effects in other studies such as decreasing glucose, increasing insulin secretion, and pseudo-insulin effects.[19] The mechanisms achieved by these three herbs is being described as lowering glucose absorption in intestine, increasing glucose consumption in body, producing glycogen in liver, increasing the phosphorylation of insulin receptors, and increasing insulin sensitivity.[6,10,15] However the results of different studies are not completely similar, it might be the result of different disease phases, insulin resistance, different dosages of prescribed drugs, small number of samples, drug consumption interval, and the diversity of food habits in different parts. In seems that for achieving accurate results, we need to do multi-centered controlled trials with sufficient sample size, while we consider insulin resistance status and other effective factors.

One of the limitations of this study was the short time period of the study which did not provide enough time for observing the effects of these medicines in lowering HbA_1C, since red cells life time is 120 days. Therefore studies designed for assessing HbA_1C should last at least 4 months to observe all the curing effects.[7] Another limitation was the small dosages of herbal medicines that were prescribed and in later studies this should be taken into consideration. No especial side effect of drugs was found in this study.

Conclusion

According to this study, cinnamon, fenugreek, coriander and their mixture with a daily dosage of 1 g cannot make any stronger effect than the placebo on lowering blood sugar, HbA_1C, and blood lipids in type II diabetic patients. It might be the result of small dosages of the prescribed drugs, short intervention interval, diversity of disease features in patients, and food habits or diest.

Conflict of Interests

Authors have no conflict of interests.

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Chronic Diseases Journal

The barriers of failure to meet the codes of professional ethics from viewpoints of nursing staff in Tehran University of Medical Sciences, Iran in 2011

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Original Article

Abstract

BACKGROUND: Compliance with nursing ethics leads to improvement in nursing care. Therefore, this study carried out to determine the barriers of failure to meet the codes of nursing ethics from the viewpoint of nursing staff.
METHODS: This was a descriptive cross-sectional study conducted on 138 nursing staff in Tehran University of Medical Sciences (Tehran, Iran) by random sampling method using a demographic questionnaire.
RESULTS: 50% of the barriers of failure in meeting with codes of professional ethics were contributed to management, 25.4% to environmental aspect, and 24.6% to individual care. Results indicated that there was no statistically significant difference between the demographic variables and the barriers of failure to meet the codes of professional ethics.
CONCLUSION: Given the management, as the most important barrier, it is suggested to enhance the awareness and knowledge of nursing ethics in nurses.
KEYWORDS: Barriers, Nursing Staffs, Codes of Professional Ethics

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Introduction

Nursing is an independent branch in medical sciences and its mission is to provide required healthcare services, and rehabilitation to provide the highest code and maintain and improve the community health.[1] Therefore, considering nursing ethics in nursing works is more delicate and important.[2] Mariner believes that care is a collection of three fundamental principles of ethics, clinical judgment, and care.[3] Vinson also believes that among the five elements in the basic terminology in nursing, nursing ethics is defined as use of critical thinking, and logical reasoning.[4] Conducted studies indicate that nurses' level of observance in code of nursing ethics is low, which according to nurses is may be due to time shortage, large numbers of patients, increased workload, financial and institutional constraints and the limited number of nursing staff.[5,6]

Grundstein-Amado claimed that lack of education in the field of ethical issues is the principle obstacle in observing professional ethics.[7] A study by Ghavami et al. revealed that only 30.9% of the patient' rights have been observed.[8]

Despite the importance of research evidence and clinical practices in nursing, due to several

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reasons nurses still do not observe the codes of professional ethics in their clinical performances. This study conducted to determine the obstacles of non-compliance in nursing ethics from the viewpoint of nursing staff.

Materials and Methods

This was a descriptive cross-sectional study investigating the barriers of non-compliance with codes of professional ethics from the viewpoint of nursing staff in 2011. The study conducted in Imam Khomeini Hospital, Imam Khomeini Clinic and Children Medical Center chosen by quota nonrandom from all the hospitals in Tehran, Iran. Initially using a quota sampling, the number of samples allocated to each center was determined, and then by simple random sampling method in each center, the sample numbers were selected. A total sample size of 138 individual chosen based on the sample size formula (P = 0.9).

Two questionnaires (demographic information and obstacles assessment) were used in three fields of management, environment and personnel.

The questionnaire of barriers in failure of meeting with professional ethics had 32 questions of which 14 were managerial, 4 were environmental and 14 were related to the nursing care. The questionnaires included agree, disagree and no idea. Validity of the tool was confirmed after presenting it to 10 lecturers at the University of Tarbiat Modares. For reliability, Cronbach's alpha reliability coefficient was used with Likert scale (a = 0.89). Then the questionnaires were distributed.

Results

In this study, 58% of the nurses were married, and 82% had less than 5 years of working experience (Table 1). The results showed that 50% of barriers were related to management aspect, 25.4% to environment, and 24.6% to personal care (Table 2). The results indicated that there was no statistically significant difference between age, gender, educational level, job position, work experience, shifts and barriers of failure to meet the codes of professional ethics.

Discussion

Dealing with management, inadequate staff numbers and long working hours are major

Table 1. Absolute and Relative frequency distribution of demographic subjects

Demographic data		Frequency	Percent
Age	20-30	74	53.6
	30-40	52	37.7
	40-50	12	8.7
Sex	Female	126	91.0
	Male	12	9.0
Educational level	BSc	132	96.0
	MSc	6	4.0
Job position	Nurse	134	97.0
	Head nurse	4	3.0
Work experience	Less than 5 year	68	49.3
	5-10	39	28.3
	10-15	16	11.5
	Over 15	15	11.0
Shifts	Morning	12	9.0
	Morning and evening	10	7.0
	Evening	3	2.0
	Evening and night	25	18.0
	Rotatory Shift	88	64.0

BSc: Bachelor of Science; MSc: Master of Science

Table 2. Absolute and Relative frequency distribution of barriers from the viewpoint of nursing staff

Aspect	Item	Barriers to non-compliance with codes of professional ethics	Agree		No idea		Disagree	
			Number	Percentage	Number	Percentage	Number	Percentage
Management	1	Inappropriate sharing of responsibly	100	72.5	21	15.2	17	12.3
	2	Inappropriate nursing supervision	82	59.4	34	24.6	22	15.9
	3	Inappropriate training needs	109	79.0	11	8.0	18	13.0
	4	Inappropriate codes of nursing ethics	79	57.2	43	31.2	16	11.5
	5	Ineffective crisis management	93	67.4	29	21.0	16	11.6
	6	poor working hours	122	88.4	6	4.4	10	7.2
	7	Lack of personnel	134	97.1	2	1.4	2	1.4
	8	Long working hours	128	92.8	4	2.9	6	4.4
	9	Inappropriate relationship between head and staff nurses	83	60.1	29	21.0	26	18.8
	10	Inappropriate training programs	106	76.8	17	12.3	15	10.8
	11	Inappropriate written nursing care policies	108	78.3	21	15.2	9	6.5
	12	Inappropriate educators	99	71.7	21	15.2	18	13.0
	13	Inappropriate training on nursing ethics in nursing education	104	75.4	24	17.4	10	7.2
	14	Inappropriate managers support	121	87.7	15	10.9	2	1.4
Environment	15	Inappropriate wards facilities	112	81.2	20	14.5	6	4.3
	16	Night shifts and lack of sleep	125	90.6	10	7.2	3	2.2
	17	Crowded wards	106	76.8	18	13.0	14	10.2
	18	Shift work	115	83.3	15	10.8	8	5.9
Personal-care	19	Inappropriate awareness of professional ethics codes	76	55.1	43	31.2	19	13.8
	20	Lack of time	112	81.2	21	15.2	5	3.6
	21	Inexperience of the new nurses	97	70.3	29	21.0	12	8.6
	22	High workload and exhaustion	120	87.0	7	5.1	11	7.9
	23	Uncooperative patients	111	80.4	17	12.3	10	7.2
	24	Negative attitude towards nursing ethics	102	73.9	25	18.1	11	8.0
	25	Fear of diseases (AIDS and hepatitis)	87	63.0	25	18.1	26	18.8
	26	Lack of motivation	97	70.3	21	15.2	20	14.5
	27	Failure to satisfy basic needs such as adequate income	125	90.6	8	5.8	5	3.6
	28	Dissatisfaction	80	58.0	42	30.4	16	11.6
	29	Lack of nursing skills	72	52.2	43	31.2	23	16.6
	30	Lack of critical thinking and ethical decision-making	78	56.5	35	25.4	25	18.1
	31	Failure to communicate effectively and appropriately with patients	76	55.1	24	17.4	38	27.5
	32	Disbelief in nursing ethics	65	47.1	36	26.1	37	26.8

obstacles. Bennett et al. reported that lack of time and insufficient staff, are the top barriers for the application of evidence-based research and professional ethics.[9] In a study, Grundstein-Amado showed inability of physicians and nurses in appropriate ethical decision-making and failure to comply with coherent patterns due to the lack of necessary training on ethical issues.[7]

In the present study, 75.4% of the nurses reported that lack of necessary education in ethical issues during the undergraduate nursing education is one of barriers to compliance with codes of professional ethics.

Moreover, Mohammadi mentioned providing patients' rights requires standard facilities and working environment,[10] which was in consistent with the above findings. Merakou et al. believe that nurses are in close contact and in a better position to protect patients, but until now they have not undertaken such a role in Greece due to staff shortages, lack of time and lack of proper education about this subject.[11] The results also showed that circadian rhythm disturbance due to shift are the main barriers to non-compliance with professional ethics in nursing practice. Sometimes lack of facilities and equipments in the workplace affect ethical and professional functions. Although patient care is of high priority for the nurses, substandard environment have negative effect on the performance of the nurses.[12,13]

Poor economic conditions resulting in extra working hours , fatigue and professional disappointment and dissatisfaction, poor working environment, inadequate facilities and shortage of staff and large numbers of patients and high working pressure, all indicate that nurses' rights are not respected which is resulted in lack of professional ethics in nursing practice. In this study, 70.3% of nurses have mentioned unwillingness and decreased motivation to nursing staff as a barrier to individual care in compliance with ethical codes of professional nursing practice. A qualitative research on factors affecting the nursing ethics showed that personal factors such as motivation and job interest have an important role in observing professional ethics.[14]

Conclusion

Based on the study results, it is determined that the main barrier was related to managerial aspect. Therefore, it is recommended to establish ethics committees in the nursing councils and hospitals.

Conflict of Interests

Authors have no conflict of interests.

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Chronic Diseases Journal

Undetected leprosy in an endemic area: A case report

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Case Report

Abstract

Leprosy is an infectious disease causing irreversible disability if unnoticed. A 69-year-old man with undetected leprosy from 30 years ago referred to us with claw hand and Madrosis (Milphosis). The patient complained of non-healing and painless ulcers on the extremities as well as numbness in the right leg. He told the medical team that he could not feel his feet in his shoes. The patient had blurred vision and lacrimation two weeks before admission. He had a history of recurrent foot ulcers from 25 years ago although he referred to medical staff about 5 years ago with infected wound on the hands and multiple scars of pervious ulcers. The disabilities were mainly in consequence of late visit to healthcare centers, misdiagnosis, difficult access to medical centers and patient's unawareness. The case showed the significance of medical education and public awareness for signs and symptoms of leprosy to be recognized and treated on time. In conclusion detecting leprosy should not be delayed just because of a decrease in the number of cases especially in an endemic area like Kurdistan, Iran.

KEYWORDS: Leprosy, Chronic Disease, Disability, Mycobacterium Leprae

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Introduction

Leprosy is a chronic infectious disease principally affecting peripheral nerves and skin. This disease can initiate the development of severe disabilities and serious psychosocial impacts.[1] The World Health Organization (WHO) reported leprosy as an important health problem in 23 countries in 1998,[1] later due to duty free medication policy, number of cases with leprosy declined severely.[2]

Existence of leprosy in Iran is recorded in Avesta, the Zoroastrian religious book. The equivalent Persian word for leprosy is "Khoreh" meaning something which eats or destroys the tissues, indicating the destructive character of disease. However, in the Islamic era the Arabic word "Jozam" has been gradually substituted and is still in use in Iran.[3]

The mortality rate of leprosy is low, but development of deformities and disabilities make the disease a real burden.[4] Urgent diagnosis of the disease is important, otherwise there will be lifelong consequences, like claw hands with paresthesia, yet there are many missed cases that may take years before a diagnosis is made.[5] Diagnosis of leprosy prior to nerve damage could evade grade II disabilities.[6]

As a differential diagnosis, leprosy should be considered in patients with cutaneous and neurological signs and symptoms.[7] Since the clinical signs in leprosy are not difficult to diagnose, particularly in endemic areas, health and medical education should revise on its

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policies to bring the disease into light.[7] This will lead to the goal of eradication of leprosy and its due disabilities.

This study has two important aspects i.e. first, importance for medical team to see why in an endemic region there are still undetected leprosy cases and second, for the health system to revise in its future strategies because such cases could be an important public health threat.

Case

A 69-year-old man was presented with non-healing and painless ulcers on the extremities which lasted for a period of three months. The patient was residing in a surrounding village of northwestern city of Marivan, Iran.

He was admitted to the infectious disease department of Towhid Hospital in Sanandaj, Iran. Patient history revealed that there has been deformity in the upper and lower limbs, as well as paresthesia over extremities but there was no fever or joint pain. He suffered from numbness in the right leg and could not feel his feet in his shoes. The patient had blurred vision and lacrimation two weeks before the admission. Clinical examination showed seven plaque-like skin lesions in the arms and knee regions as well as Madrosis (Figure 1) which was seen on his eyebrows and eyelashes (in the 1/3 outer layer) without any sign of a thickening earlobe.

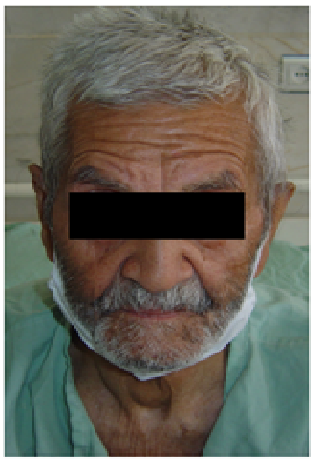

Figure 1. Madrosis

The patient had "claw hand" (Figure 2) deformity and stretching of the 3rd, 4th and 5th fingers; however no sign of peripheral nerve hypertrophy was noticed. The case presented here did not show involvement of common cutaneous nerves with thickening and/or tenderness, which is the second clinical sign to diagnose leprosy.

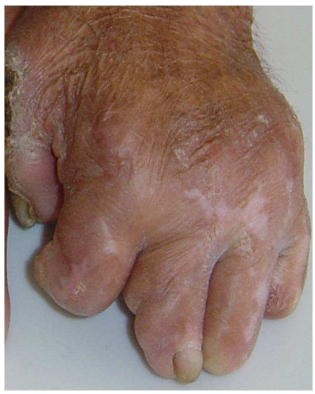

Figure 2. Claw hand

According to the patient, he had a history of recurrent foot ulcers from 25 years ago. Consequently he referred to medical staff about 5 years ago with infected wound on the hands and multiple scars of pervious ulcer. Consultations with ophthalmologist and neurologist resulted in the diagnosis of uveitis and mononeuritis multiplex, respectively. Laboratory results showed acid-fast positive bacilli (3 plus positive) after nasal smears were prepared and stained by Ziehl-Neelsen staining method. Our diagnosis (based on clinical suspicion) was confirmed through bacteriological and microbiological analysis. Other preclinical examinations included normal chest X-ray which excluded sarcoidosis and routine laboratory workup which revealed the following results: FBS = 93 mg/dl, BUN = 101 mg/dl, Cr = 17 mg/dl.

Other laboratory findings showed no signs of hemolytic anemia [normal glucose-6-phosphate dehydrogenase (G6PD) and complete blood cell (CBC)] although white blood cell count (WBC) and erythrocyte sedimentation rate (ESR)

(= 58 mm/h) were elevated. Therefore the patient started clofazimine, rifampicin, and dapsone treatments which resulted in the management of the infection. Later follow ups showed that the patient was symptom-free and the disease was well controlled. Other close contacts of the patient has been checked and found to be symptom-free.

Discussion

This case report indicated the importance of paying attention to leprosy in daily clinical encounters especially in endemic areas, bearing in mind that our case has not been detected for almost 25 years which could be due to the following reasons: 1. Living in a remote village with arduous access to medical facility; 2. Long incubation period and numbness made it difficult for the patient to notice the disease process, leading to failure in referring to medical centers; and 3. Absence of nerve hypertrophy as a distinctive criterion in diagnosing the disease leading to misdiagnosis.

The question is why typical signs of a case of leprosy, are often missed by medical physicians and other medical team working in an endemic area.

Prevalence of disability varies in different parts of the world which may be due to improper technique of physical examination. Delay in referral to health centers is more common in old age and male gender which makes the disabilities exacerbated. In another study done by Rad et al. most of the clients were residing in rural areas in which factors like low social level, cultural lag, and inaccessibility to health care centers were reasons behind increased rate of leprosy in those regions.[1] The disease should still be considered in the differential diagnosis of dermatological cases with neuropathy even in non-endemic regions.[8] Hansen's disease can mimic tinea corporis by presenting as one or more annular, sometimes scaly, plaques.[9]

In a study which is in accordance with our case report, a long history of repeated rash and leg numbness was revealed in a patient who had primarily been diagnosed as systemic lupus, later diagnosed as lepromatous leprosy.[10] In another study, epidermolysis bullosa dystrophica, granuloma multiforme, and mycosis fungoides were considered as leprosy first;[11] however, later skin biopsy revealed that the diagnosis was sarcoidosis.[12] Multibacillary (MB) leprosy which is close to lepromatous end of the spectrum may mimic other diseases, and the patient cannot be diagnosed without a biopsy or a slit skin smear examination, which indicates the importance of microbiological findings in reaching a clear diagnosis of the disease. Clinical diagnosis is an important tool for decision making about such cases as well.[13]

The above studies underline the fact that training in the diagnosis of leprosy and its management to young physicians, nurses and rural social workers, will prevent an increase in cases of leprosy with severe deformities. This rather enables earlier intervention, improved patient outcomes and prevention of further transmission. It is essential to check all contacts of any diagnosed leprosy patient, principally in highly endemic areas, to facilitate an early diagnosis.

Conclusion

We all know that in today's global village chronic infectious cases like leprosy could relocate easily. In other words, germs do not respect borders and we must keep it on our radar screens. Encouraging leprotic patients share their experiences will decrease the stigma which is a leading cause of delay in detection. In the final analysis, a paradigm shift in leprosy care services and control program is required to detect leprosy and its complications as a major challenge. Consequently leprosy should not be lost just because of a decrease in the number of cases especially in an endemic area.

Conflict of Interests

Authors have no conflict of interests.

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Chronic Diseases Journal

Hereditary spherocytosis in an 18-month-old boy with pancytopenia: A case report

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Case Report

Abstract

Hereditary spherocytosis (HS) is a familial hemolytic disorder with marked heterogeneity of clinical features, ranging from an asymptomatic condition to a fulminant hemolytic anemia. Although a positive family history of spherocytosis increases the risk for this disorder, it may be sporadic in some cases. In severe cases the disorder may be detected in early childhood, but in mild cases it may go unnoticed until later in adulthood. The case was an 18-month-old boy from Sanandaj, Iran with 3 days decreased activity movement, poor feeding, pallor and urine discoloration since 3 days ego following an episode of fever. He was a case of anemia who was managed conservatively on nutritional supplements. Blood film showed 80% spherocytes, reticulocyte was 0.5%, increased osmotic fragility test and a negative direct Coombs.

KEYWORDS: Hereditary Spherocytosis, Familial Hemolytic Disorder, Hemolytic Disorder, Anemia, Spherocytes, Reticulocyte, Osmotic Fragility Test

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Introduction

Hereditary spherocytosis (HS) is a hemolytic disorder with marked heterogeneity of clinical features. It is a dominant inherited disorders characterized by the presence of sphere-shaped red blood cells.[1] HS has been commonly presented in northern Europe, North America, and Japan. It seems to be less common among African-Americans.[1,2]

HS is a result of deficiency of membrane surface area and an in vitro abnormal osmotic fragility. The intrinsic genetic defect is on the red blood cell along with spectrin defects.[3] Overall α-spectrin mutation occurs in recessive HS, whereas β-spectrin mutation occurs in the dominant HS.[4] Mild to moderately severe cases with ß-spectrin deficiency do not need a transfusion.[3] HS is categorized as mild, moderate, moderately severe, and severe in line with basic clinical laboratory variables, including primarily on the concentration of hemoglobin, as well as the reticulocyte count.[5] Clinical symptoms are hemolysis with anemia, jaundice, reticulocytosis, gallstones, splenomegaly, spherocytes on the peripheral blood smear, increased erythrocyte osmotic fragility, and a positive family history for the disease.[6] Intact spleen and intrinsic membrane-protein defect leads to abnormal red blood-cell and hemolysis. Most of the patients have moderate disease presenting with fatigue, pallor, or both due to anemia, otherwise it is asymptomatic. In case of a viral infection, jaundice arises in about 50% of the cases. Laboratory findings include

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hemoglobin concentration between 6 to 11 g/dl, and increased proportion of reticulocytes.[7]

Case Report

An 18-month-old boy from Sanandaj was brought by to the Pediatric Emergency Ward of Be'sat Hospital by his parents on 30th December-2012, with decreased activity and movement, poor feeding, pallor and urine discoloration following an episode of fever which occurred three days ago.

Previous medical history included hospitalization with the diagnosis of pneumonia and incidental finding of relatively severe anemia when the patient was 6 months old; despite bone marrow aspiration (BMA) and other evaluation, no definite cause for anemia was established and the patients discharged with oral iron supplementation.

His father had been assessed for anemia and splenomegaly 20 years ago with no definite diagnosis. His sister was assessed for anemia resulting in decreased serum B12 levels which treated with parenteral supplementation of vitamin B12. The patient was breast fed for 12 months, six months of which was exclusive breast feeding.

In the physical exam, his weight was 12.5 kg (70th percentile for weight). Vital sign was stable with no signs of fever with only mild tachycardia. Skin and mucosal membrane were apparently pale, with no significant skin lesion. No significant lymphadenopathy was detected. Liver size was normal; however tip of spleen was palpable 3 cm below the costal margin.

Laboratory results were as follows in table 1.

Liver function tests [(LFT): aspartate aminotransferase (ALT), alanine aminotransferase (AST), alkaline phosphatase (ALKP), bilirubin total and direct)], erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) were normal, direct Coombs was negative and Glucose-6-phosphate dehydrogenase (G_6PD) was sufficient.

Peripheral blood smear (PBS) showed numerous spherocytes with marked anisocytosis and severe hypochromic and microscopic red blood cells. Bone marrow aspiration detected red-cell hyperplasia. Abdominal Ultrasound revealed mild splenomegaly and gallbladder sludge.

Four days after hospitalization, his 10-year-old brother referred to the hospital with fatigue, fever, sore throat, lack of energy and significant pallor, without any history of anemia or hospitalization. His physical examination showed splenomegaly (4 cm below costal margin) and marked pallor. Laboratory results were shown in the table 1.

LFT (ALT, AST, ALKP, bilirubin total and direct), ESR, CRP were normal, D-Coombs was negative and G_6PD was sufficient.

The parents' complete blood count (CBC) were normal. Increasing initial lysis occurs in the osmotic fragility test with and without incubation. A serum folate level typically was normal and B_{12} serum level fall below the normal

Table 1. Laboratory results of the case and his brother

White blood cells (WBC)	Patient's laboratory results 5400 (Neutrophil: 26%; Lymphocyte: 74%)	Patient's brother laboratory results 7400 (Neutrophil: 35%; Lymphocyte: 65%)
Red blood cells (RBC)	1.3 × 106	1.7 × 106
Hemoglobin (Hb)	2.7 mg/dl	4.4 mg/dl
Hematocrit (Hct)	8.5	12.7
Mean corpuscular volume (MCV)	64.3	72
Mean corpuscular hemoglobin concentration (MCHC)	20	34.6
Platelets (PLT)	31	214000
Red cell distribution width (RDW)	108000	20
Reticulocyte	26.9	1.2

limits. Patient's condition at discharge was likely to improve after transfusions of three units of packed-cell.

Discussion

Osmotic fragility test is a useful diagnostic test for this disorder. It is widely proposed that the membrane defect, fluidity and cytoskeletal change, is the main etiology for increased fragility of red blood cell. Hereditary spherocytosis is globally rare inherited red cell membrane disorder.[8-10] This is caused by a molecular defect in one or more of the proteins of the red blood cell cytoskeleton.[8] Spectrin deficiency is the most common defect. The defects are associated with a variety of mutations that result in different protein abnormalities and varied clinical expression. Most cases of HS are heterozygous because homozygous states are deadly.[8-11] In pedigrees that have a dominant defect, affected family members tend to have similar degrees of hemolysis and clinical severity.[12-14] Regardless of the molecular basis for a case of HS, the resulting spherocytes become trapped in the spleen as they course through the sinuses, and the red cells were engulfed by macrophages.[12-14]

Several reports and text books have associated a triad of anemia, jaundice and splenomegaly to the morphological findings of spherocytes as the hallmark to the diagnosis of HS like the finding in our case.[8-9,11-13] Our diagnosis was supported by an increased osmotic fragility and a negative direct Coomb's test, although a negative result may be obtained especially for osmotic fragility where a high reticulocytes count of more than 10% interferes with the test.[4]

Bone marrow suppression due to infection with parvovirus B19 can be presented with low reticulocyte count that is matched with our case.[4,8]

In the first few postnatal months, anemia can be developed in children who do not mount an adequate reticulocyte response.[4]

Later in the childhood, HS can manifest with anemia, jaundice, and splenomegaly.[4-8]

Affected patients may have mild, moderate, or severe anemia. Children who have moderate to severe anemia may have poor exercise tolerance, growth failure, and academic difficulties.[2-5] Older individuals develop bilirubin stones and may present with cholecystitis.[2-5] It is often not uncommon for the diagnosis to be missed until adulthood.

The peripheral blood smear in HS shows numerous spherocytes. Larger bluish cells (polychromasia) also may be seen. The CBC and reticulocyte count reveals a low hemoglobin concentration and elevated reticulocyte count.[1-3] The mean corpuscular hemoglobin concentration is usually high at greater than 35 g/dl (350 g/l). The mean corpuscular volume may be low or high if there is substantial reticulocytosis.[1-3] The test of the osmotic fragility can be useful in establishing the diagnosis of HS. Spherocytes have reduced cell membranes and thus they swell at higher concentrations of saline than do normal red cells. The direct antiglobulin (Coombs) test is usually negative. Other test includes elevated unconjugated bilirubin, elevated lactic dehydrogenase, and low haptoglobin levels. However, these findings are associated with any case of haemolysis and are nonspecific for HS.[1-3,6] Thus this might be recessively inherited or sporadic as it occurs in 25% of the cases or a silent carrier state, as it has been suggested to exist in 1.4% of the population.[4] The patient was managed conservatively with nutritional supplementation consisting of folic acid, ascorbic acid.

Specific indications for transfusion included exacerbation of anemia due to blood loss such as related to trauma or surgery, hypersplenism, and infection with parvovirus B19.[4]

Cure is achieved with splenectomy[4] but there was no indication for this in our patient. Splenectomy is carried out in cases with severe anemia and extramedullary hematopoiesis.[4-11]

Complications of hereditary spherocytosis include pigment gallstones, aplastic, haemolytic and megaloblastic crises, growth failure, skeletal deformities, and less commonly skin ulceration, and chronic dermatitis.[1-8]

As we noticed earlier in our case, the patient's 36-year-old father and 6-year-old sister had a history of anemia after a diagnostic work-up. However, they were not diagnosed correctly which caused anemia for a period of time. On the other hand, the patient's brother did not have any history of anemia or hospitalization despite suffering from this sickness for a long period of time. He had pallor and some complaint including fatigue, lack of energy, anorexia, significant pallor, splenomegaly, and growth failure.

Although HS is rare, it does occur in our environment and when suspected hematological assessment is necessary to avoid diagnostic pitfalls and mismanagement.

Conflict of Interests

Authors have no conflict of interests.

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Chronic Diseases Journal

Iran's healthcare system challenges at a glance

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Letter to the Editor

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Healthcare systems on the whole are looking for better ways to meet present and future challenges, whereby Iran is not an exception.[1] Nowadays it seems that healthcare system in Iran is facing a new challenge of doubled burden of diseases. Prevalence of chronic diseases in Iran and collection of therapeutic centers in large cities have caused inaccessibility or expensive availability of these services in other deprived areas. Besides, Iran is one of the aging countries in which the elderly population in the country has increased significantly over the past forty years. Nowadays, almost 10% of the population is over 60 years, leading to an increase of chronic diseases.[2] According to the World Health Organization (WHO), pocket payment related to the healthcare costs in Iran was about 60.2% in 2007.[3] It should be noted that according to the statistics provided by Iranian databank in 2009, approximately 9 million people were not covered by any health insurance plan.[4] Critics argue that Iranian populations have become too dependent on expensive technology and people are not only over-diagnosed but are over-treated.[5] From the another point of view, statistics show that ratio of nurses per hospital bed is 0.5 to 0.8, compared to1.8 in the more developed countries. This shows the existence of a large gap between the standards of healthcare system in Iran compared to other global standards which have caused a dramatic decline in the quality of nursing services in Iran.[6]

Growing out of pocket payments could be related to the fact that almost 12% of the population is not covered by insurance plans. Currently, there are several different insurance plans under agencies and ministries which have led to a lack of an effective control and integration in the health insurance system. Physicians' "per case", which is an effective incentive for hospitals and physicians to provide additional medical services, is another reason for out of pocket payments.[7] In this case, diagnosis-related groups (DRG) reimbursement system in the U.S. might be a good option. DRG system can help medical institutions to complete their information about comparing the costs of treatment and treatment outcomes.[8] Another strategy could be utilizing programs such as public-private mix model due to high coverage of private physicians in Iran.[9] In sum, success of a healthcare system depends upon a paradigm change within its context which can distinguish its challenges and offers innovative

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and logical solutions based on local and cultural circumstances.

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Chronic Diseases Journal

Chronic disease program in Iran: Thalassemia control program

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Health Care System

Abstract

BACKGROUND: β-thalassemias (beta-thalassemia) is the most common genetic disorder; it is an inherited globinopathy which is transmitted to people due to a mutation in genes that create globin chain. In Iran, the disease gene is more common in the northern and southern regions. It is estimated that more than 60 mutations of the disease exist in different geographical areas of Iran. Iran has begun to adopt strategies to control the β-thalassemia for two decades; the most important of which is the screening of couples when they want to get marry. The present study aimed to review the thalassemia control program in Iran, the history of the disease, and the disease control strategies.

METHODS: This review was conducted according to hand and electronic resources. Books, guidelines and document that exist in thalassemia control program were reviewed in the Iranian Ministry of Health, World Health Organization resources, PubMed, Google Scholar, SID (scientific information database), Magiran and, Iranmedex.

RESULTS: Thalassemia program was appropriately structured and has been achieved successes. Reduction the numbers of new cases of β-thalassemia were notably. In some areas, thalassemia program has some defects and the program faced some cultural barriers.

CONCLUSION: Due to the improvements in the social and economic situation of the people, it seems necessary to focus on prenatal diagnosis (PND) and pre-implantation genetic diagnosis (PNG) technique strategies and provide their necessary facilities.

KEYWORDS: Thalassemia, Surveillance, Epidemiology, Program, Iran

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Introduction

Thalassemia is the most common genetic disorder in humans which is an inherited globinopathy. It is estimated that about 4% to 7% of the world population i.e. 300 million are carriers of the gene. It is transmitted to the people due to mutation of genes that create α or β globulin chains. It is an autosomal recessive disorder leading to reduced production or non-production of β globin chains. B-globin is identified by a structural gene that is located on the short arm of chromosome 11. More than 95% of all β-thalassemia mutations in the world are point mutation in β-type globin gene and only a small percentage are gene-deleted. Nowadays, more than 200 mutations that affect β-globin gene have been identified that cause β-thalassemia phenotype. A small number of mutations, i.e. four mutations are responsible for the illness of 90% of patients.[1-3]

If both β-gene chains are defective, the individual will be affected by major or severe thalassemia and anemia. β-thalassemia, which is the most common form of disease, has three types; mild (minor thalassemia or carrier); average (intermediate thalassemia); and severe (major Thalassemia).[4] Because of anemia and increased erythropoietin, hematogenesis happens outside the bone marrow and liver and spleen may become enlarged. Extensive expansion of

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bone marrow impairs growth, change the face, and long bones and spinal column may suffer from pathological fractures. The disease may also cause hemolytic anemia, splenomegaly, leg ulcers, liver dysfunction, diabetes, zinc deficiency, metabolic disorders and heart failure.[5,6]

In addition to the above mentioned physical problems, endocrine disorders are among the other complications of this disease. Hypogonadism is caused due to pituitary sensitivity to hypoxia; secondary amenorrhea, spermatogenous cell abnormalities, short stature, osteoporosis, osteopenia, hepatocellular carcinoma, and hepatitis C are the other complications [3,7,8]. The disease can be diagnosed in childhood based on the symptoms of severe anemia, hypochrome, and microcytic hemoglobin. Disease can be treated either via frequent blood transfusions or using iron-chelating drugs; both methods impose high costs on patients and society.[3]

Thalasemia is an important health issue in high burden area because it could be prevented and its treatment has expensive cost.[9,10] Based on thalassemia situation in Iran and without appropriate strategic for control of this diseases, it can have heavy burden in the country. Therefore, we have reviewed and discussed thalassemia program in Iran. The present study aimed to review the thalassemia program in Iran health system and existing studies about the thalassemia in Iran, the history of disease, and disease control strategies were reviewed.

Materials and Methods

This review was conducted according to hand and electronic resource. Hand research was done in books, guidelines and document that exist in thalassemia control program in Iranian Ministry of Health (MOH). We interviewed with experts in thalassemic office in several provinces for finding all documents about thalassemia program in Iran. These documents were reviewed for history, epidemiology and trend of the program by two researchers. Electronic search was done in the World Health Organization (WHO) internet site, MOH internet site, PubMed, Google Scholar, SID (scientific information database), Magiran and Iranmedex. We used thalassemia, epidemiology, program and Iran as keywords for searching. Abstract of papers were reviewed and full text of appropriate paper were studied accordingly.

Results

Distribution of thalassemia in the world

The disease occurs worldwide and in all races. It is estimated approximately 1.5% of the world population are carriers of β-thalassemia and at least 60000 new cases are born annually.[3] The disease has higher outbreak rate among the Mediterranean, i.e. Italy, Greece, Cyprus and Sicily Island, and also some parts of North and West Africa, the Middle East i.e. Iran, Turkey, Syria, and parts of east and south-east Asia, i.e. India and Pakistan; these countries and regions are commonly known as the thalassemia belt.[3,9] The disease is spread over south-west Europe to the Far East and it is seen in large areas of central Africa. Such a form of distribution is due to the spread of malaria which has been endemic to these regions for centuries; malaria parasite is unwilling to the red blood cells of thalassemia patients, therefore they are resistant against malaria.[11]

Distribution of thalassemia in Iran

In Iran, about 20,000 thalassemia patients have been registered until 2003. The disease has been spread all over the country, but it is more prevalent in the outlying parts of the Caspian Sea (Gillan, Mazandaran and Golestan), bordering parts of the Persian Gulf and Oman Sea (Bushehr, Hormozgan and Sistan-o-Baluchestan), and Khuzestan, Fars and South of Kerman provinces. In these areas, approximately 10% of the populations are β-thalassemia carriers while in other parts of the country, 3% to 8% are the carriers of the gene.[11,12]

In Iran, there are about 2 to 3 million carriers.[13] The national program for control of thalassemia was started in Iran in 1996 and since then the emergence of new cases has reduced and number of thalassemia major patients was 13,000 to 14,000

people.[14,15] It is estimated 1,000 thalassemia major patients are born in Iran annually. Recent studies have shown that β-thalassemia mutations in Iran are different and heterogenic and there are more than 60 different mutations in different geographical regions of the country.[16-19]

Due to the high proportion of consanguineous marriages and its impact on gene pool, the rate of severe forms of the disease has been increased. The proportion of consanguineous marriages in Iran is 38%, from which 27.9% are the consanguineous marriages between cousins. Consequently, it is very important to screen and identify rare mutations in our population.[12,20]

Because of the positive effects of thalassemia major prevention program, the number of newborns with β-thalassemia has been decreased. Since the initiation of the program, 2819 couples underwent prenatal diagnosis (PND) in genetic laboratory network of Iran. Age analysis of patients with severe symptoms of thalassemia has shown significant decrease of the number of thalassemia major cases.[14]

Thalassemia control strategies in the world

In areas in which thalassemia is common, different strategies for thalassemia control are recommended. These strategies include:

- *Identifying carriers:* carriers can be detected since the birth. In some countries, in which thalassemia is very prevalent, thalassemia is detected at the time of marriage or prior to pregnancy. Sometimes this is done in school age or in a similar period. The simultaneous administration of such tests and actions to raise awareness can reduce the incidence of thalassemia.
- *Genetic counseling:* before and after marriage and prior to pregnancy.
- *Population screening:* in specific populations and places where the disease is common.
- *Prenatal diagnosis:* Experience shows that the use of aforementioned interventions may not result in successful prevention. Therefore, PND is considered as one of the most important thalassemia control strategies all over the world.[2,21]

In addition to these strategies, there are some other important measures to be taken:

- Public training
- identifying target groups and covering them with important programs and measures to control the disease
- improving the methods of detecting carriers
- appropriate consultation
- Providing molecular diagnosis
- Diagnosis of mild disease phenotypes
- Increasing access to PND
- Facilitating the process of embryonic samples
- Increasing access to DNA analysis
- Promoting prevention programs, and
- Allocation of resources for disease control.[21]

A history of thalassemia control in Iran

Thalassemia program pilot was initiated in Iran in 1991 and pilot program was implemented in some districts. In that time, the main strategy of the program was to screen the couples prior to their marriage and to suggest separation of carriers and marrying a non-carrier. This strategy was carried out based on the following figure (Figure 1). In order to develop the program and since many carrier couples insisted on being married and were interested to have child, in 1997, it was suggested to promote prenatal diagnosis.[22].

The second strategy was established in 2001. Based on this strategy, patients' families were identified and consultation services were provided for them. If they had not have healthy children, they were referred to prenatal diagnosis centers to have healthy children; consequently, genetic testing and prenatal care were developed in Iran. This has led to a dramatic reduction in new cases of β-thalassemia major. In addition, since all the partners were referring to laboratories, it became possible to investigate and control the incidence of the disease via a strong system. Figure 2 represents the strategy.

The third strategy was started in provinces with high prevalence rates in 2005. Accordingly, the couples who had married prior to 1997 and

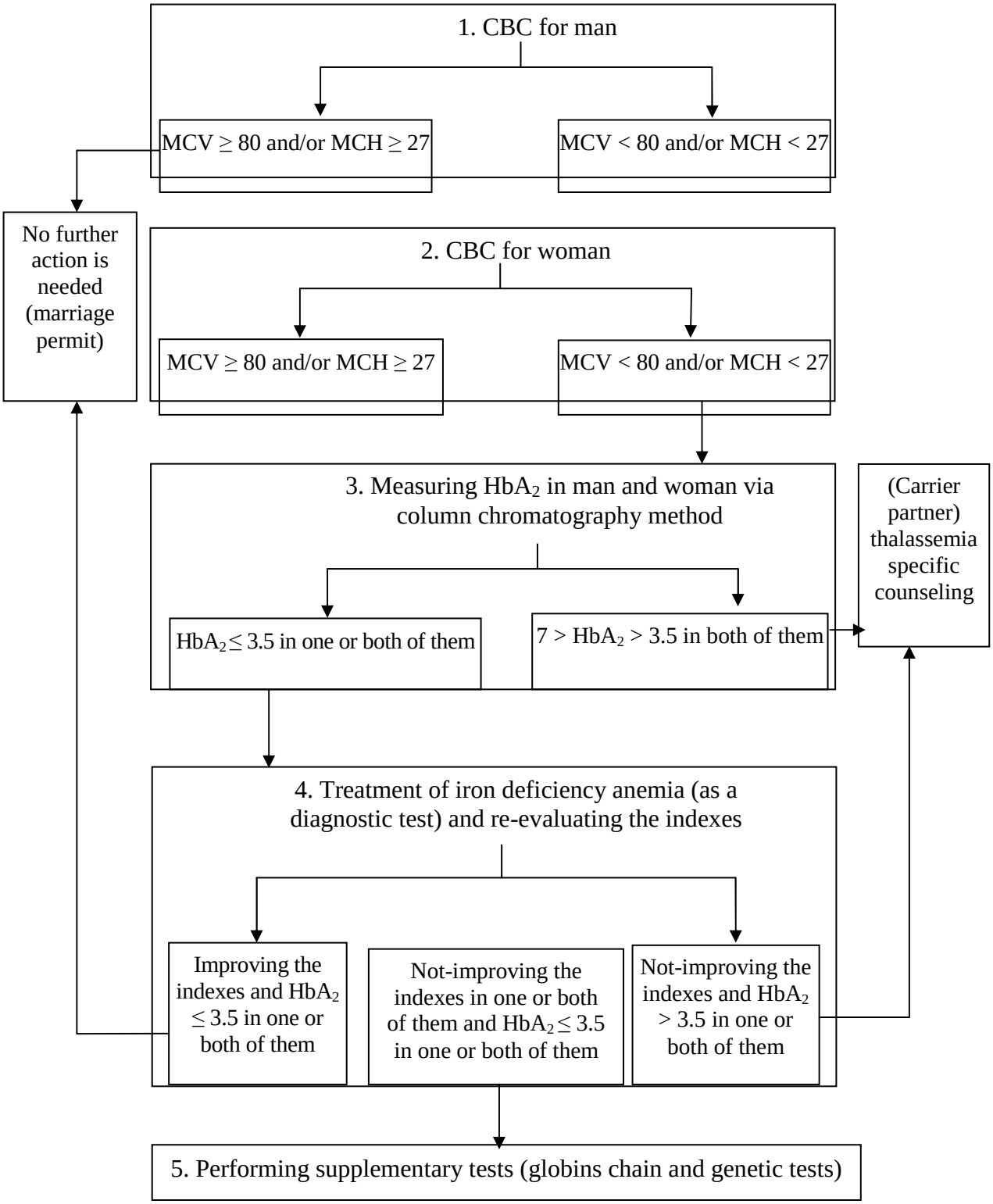

Figure 1. National algorithm of the steps of thalassemia tests (to detect β-thalassemia carrier couples)
CBC: Complete blood count; MCV: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin; HbA_2: Hemoglobin, alpha $_2$.

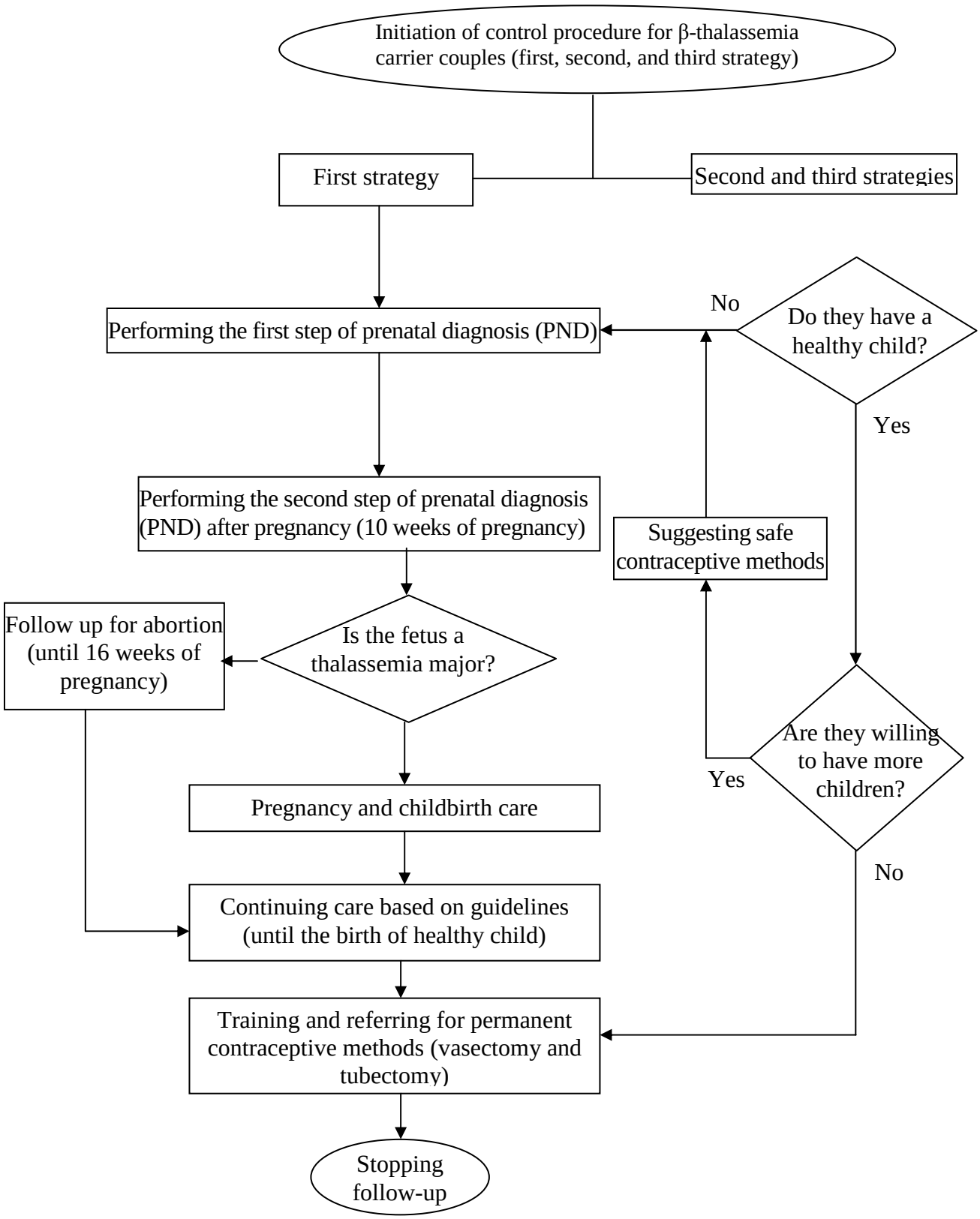

Figure 2. Controlling β-thalassemia carrier couples

had children/healthy children were tested to determine if they are carriers; the carriers were counseled to prevent the birth of children with thalassemia major (Figure 3).

Genetic counseling and genetic diagnostic laboratory network was established in 2008 and was incorporated in the network system. The main tasks of the network were to counsel people and refer them for genetic testing and prenatal diagnosis of thalassemia. Each genetic counseling team was consisted of a physician and an expert. Teams were trained in real and virtual classes. The network was responsible for counseling couples who were both carriers. After counseling, if couples insisted on marriage, they would be referred to prenatal diagnosis centers and epidemiologic control departments in nearby health centers.[11,23]

Preventing the birth of children with thalassemia major in Iran health system

Currently, prevention of the birth of children with thalassemia major in Iran health system is performed through the following options:

- *First option:* motivating carrier couples to cancel their marriage;

Only couples who are both thalassemia carriers (minor) will have children with thalassemia major, so the easiest way to prevent the birth of children with thalassemia major is to motivate them not to marry each other. It was the basis of the first strategy of thalassemia major prevention at the beginning of the program.

- *Second option:* Avoiding thalassemia couples from having children;

The second option to prevent the birth of thalassemia major children included avoiding thalassemia couples from having children and motivating them to adopt a child if they were eager to have children. This was the basis for further development of thalassemia program in later phases.

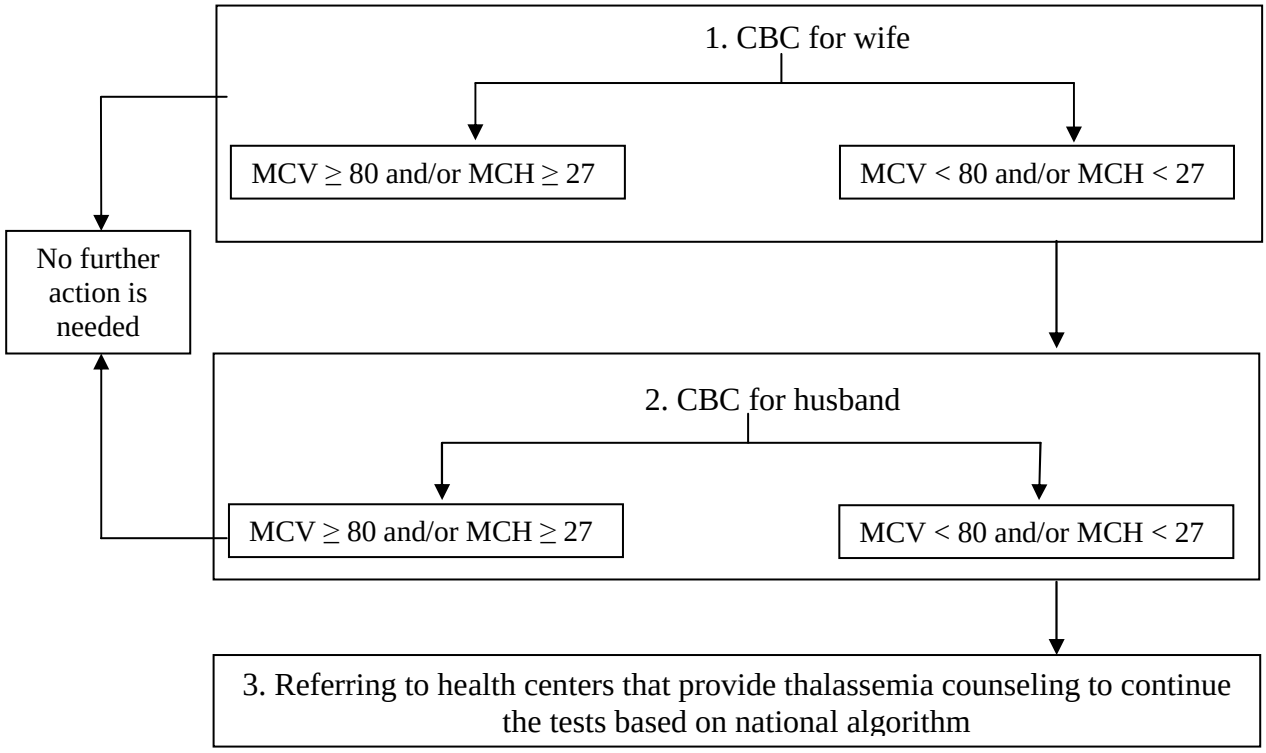

Figure 3. Detecting thalassemia major couples who married prior to 1997 (for regions with high prevalence rates)

CBC: Complete blood count; MCV: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin; HbA_2

• *Third option:* prenatal diagnosis (PND);

PND and determining how genes are inherited from parents to embryos is the third option to prevent the birth of children with thalassemia major. The type of genes, their position, mutation type, and the inheritance status of the fetus from each couple should be determined. If defective genes are from both parents, the fetus will be a thalassemia major type and abortion will be the only alternative to prevent the birth of a thalassemia major child. This was the basis of the third strategy. Accordingly, in case of diagnosis of thalassemia major in the fetus, parents will be referred to coroners to receive permission for legal abortion. After authorization by gynecologists abortion is performed in a hospital. Legal limit for abortion is up to 16 weeks of pregnancy. Genetic tests and diagnostic procedures for prenatal diagnosis (PND) are as follows:

First: In order to identify the gene and its mutation type, couple and sometimes some other family members are invited to do blood test.

Second: After about 10 weeks of pregnancy, fetal tissue samples are prepared and the status of gene transfer is tested from parents to fetus.[24]

The main objective is to assess the abnormalities at birth or chromosomal diseases (such as Down syndrome) or other genetic diseases. In many countries, if fetus is affected by diseases or if parents are not willing to have the baby, families are allowed to terminate pregnancy and do abortion.

In cases where the family does not wish to do an abortion, prenatal diagnosis helps the treatment team and the family to become ready to deal effectively with birth of an infant who will have the disease. The other goal of prenatal diagnosis is to ensure parents who are concerned about their fetus. This is especially true in families who already had children with the disease. In Iran, in the case of early diagnosis of some diseases and following some legal observations, it is possible to do abortion. Prenatal diagnosis of thalassemia in Iran has become available since 1993. However, it was officially started in 1996, when abortion therapy was introduced.[11,22]

Discussion

Thalassemia program is appropriately structured and has been achieved successes especially in reduction in β-thalassemia major in Iran but in some areas thalassemia program has some defects and the program faced some cultural barrier.[10,22,25] The age of the patients has elevated because of good management of the diseases so we should note this situation in the surveillance program. Given the conditions in Iran, it may become necessary to use new methods of prenatal diagnosis. One of the other genetic approaches for prenatal diagnosis which is called PND is used to detect chromosomal abnormalities of the fetus before birth. However, when abnormalities in the fetus are detected, it is very difficult for the couple to make a decision for doing the abortion and it may lead to physical and psychological complications for them. Using [re-implantation genetic diagnosis (PGD) can avoid such problems.

A new method has been developed to replace PND which can decrease its problems[2]. Pre-implantation genetic diagnosis technique (PGD) is even one of the methods to determine of fetal sex as well by DNA analysis. This procedure can be done at approximately 15-18 weeks of gestation by amniocentesis, or at approximately 10-12 weeks of gestation by chorionic villus sampling (CVS).[26] The main purpose of using PGD is to prevent the transmission of genetic diseases from carrier parents to their children.

Some PGD applications are as follows; for patients who underwent IVF (In vitro fertilization) or microinjection surgery more than 3 times, but the surgeries did not result in pregnancy; when women are over 35 years of age; in case of structural anomalies such as trans-location (displacement of chromosome fragments) found in couples' cerotype test; in case of multiple abortions when there is not any other reason for abortion; diagnosis of sex-linked diseases such as hemophilia which is particularly more prevalent in boys than girls; monogenic diseases such as

thalassemia, which may occur in the newborn. PGD can be used to separate a cell from a developing embryo and perform genetic experiments on it, and then the embryos that are free of genetic abnormalities are transferred to the womb, and expect a healthy baby without the need for abortion which was necessary in the older methods.[27] This approach not only is more ethical but also will reduce psychological complications of couples. Furthermore, this method would be very helpful for people with religious attitudes who may not accept abortion.[28]

Conflict of Interests

Authors have no conflict of interests.

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