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Abstract

Background: The aim of this study was to evaluate of the use of herbal products in patients in both pre- and post-surgery periods and during chemotherapy, and to determine the factors behind it.

Materials and Methods: This study was conducted as a descriptive study with 281 patients in 4 centers. The data of the study were collected by using a survey form prepared by the researcher, depending on literature and interview with the participants face-to-face.

Results: While the average age of the patients involved in the study is 49.1 ± 12.8 , 51.6% of them were females, 34.6% graduate of elementary school, and 34.5% were housewives. While the prevalence of the use of herbal product prior to surgical treatment is 38.9%, it was observed that this rate increased to 54.1% during chemotherapy. It was observed that the most frequently used product was garlic prior to surgical treatment (19.2%), that it was *urtica dioica* (13.8%) during chemotherapy. Before the surgical treatment, 94.3% of the patients, and during chemotherapy treatment, 81.7% of the patients, stated that the use of herbal product had not been questioned by the physician or nurse.

Conclusion: Analysis of the results indicates that health professionals need to obtain information regarding the use of herbal products by cancer patients during both pre- and post- surgery periods, as well as during chemotherapy. Patients should be provided with information and guidance about the advantages and disadvantages of using herbal products.

Keywords: Cancer, Phytotherapy, Herbal Product, Drug Interaction, Nursing

Introduction

Although there are many treatment modalities for cancer, such as surgery, radiotherapy, immunotherapy and chemotherapy, it has been noted that the use of complementary and alternative therapies (CAT) has been on the rise and that studies in several countries have found the incidence of these therapies to vary between 7% and 64% (with an average of 31.4%). While the use of CAT in cancer patients in the USA and Europe is 38.3% and 35.9%, respectively, a study that covered 14 European countries, including Turkey, has found an average rate of 36% (Molassiotis et al. 2005; Langhorne et al. 2007; Uğurluer et al., 2007; Kim and Karver, 2012; Kav et al., 2008, Barnes et al 2008). The patients resort to the CAT in order to fight against cancer and prevent recurrence, to minimize side-effects and to increase their quality of life (Block et al., 2004; Yazar and Yarış, 2009; Trogrlic et al., 2016).

In the use of herbal products, which is one of the CAT methods, toxic, allergic and carcinogenic effects can be observed in patients before chemotherapy and surgery, due to drug-drug and plant-drug interaction. The incidence of morbidity and mortality might be increased in the pre-operative period, due to polypharmacy and drug interactions (Bovil, 1997; Breidenbach et al., 2000). For example, *Echinacea purpurea-pallida-angustifolia* is the most frequently used herb by surgery patients, and its long-term use (generally eight weeks) may cause suppression of immune system, and increase the toxicity of barbiturates and the hepatotoxic effects of the steroids, amiodarone, methotrexate, ketoconazole and halothane. Likewise, garlic preparations whose most serious side-effect is increased bleeding, may change the pharmacokinetic variables of paracetamol if taken together, reduce the blood level of warfarin, and cause hypoglycemia when taken together with chlorpropamide (Kumar et al., 2005; Gratus et al., 2009; Aral et al., 2011).

If the herbal products are used after surgery, they may interact with the chemotherapy agents as well, causing serious side-effects, dramatically increasing the effects of the chemotherapy agent, or destroying its effectiveness completely. For example, St John's wort which has such side-effects as nausea and hypersensitivity, interacts with almost all chemotherapy agents, reduce the active metabolite of irinotecan and cause the reduction of the plasma concentration of cyclophosphamide. Senna (*Cassia Acutifolia* veya *C. Angustifolia*) is frequently used for the treatment

of constipation that arises as a side-effect of chemotherapeutic agents. If used in excess of the required doses, it may cause violent diarrhea and damage intestinal epithelia (Richardson et al., 2000; Yazar and Yarış, 2009).

The aim of this study was to evaluate the use of herbal products in cancer patients who had undergone surgery and received chemotherapy, and the factors involved.

Materials and Methods

Study design

This work has been carried out as a descriptive, cross-sectional study for the purpose of examining the use of herbal products in cancer patients who had undergone surgery and received chemotherapy, and the factors involved in the use of the said products.

Setting and sample

The study cohort consisted of 300 patients, who had been diagnosed with cancer, had undergone surgery in one of the four research and education hospitals in the province of Ankara, and who had received at least 1 round of chemotherapy in the outpatient chemotherapy clinics of these hospitals. All patients were at least 18 years old, with open consciousness and no orientation problems, no issues of communication, and all had agreed to take part in the study. The sample size had been determined using the sampling formula as 281 before determining the cohort, and patients were then admitted into the study (Çingil, 1990).

Data Collection Methods and the Process of Data Gathering

The study data were obtained by using a survey form that had been prepared by literature, by conducting face-to-face interviews with the participants. The survey form consisted of three parts-demographic data such as age, gender, marital status, diagnosis, date of diagnosis, current situation of disease, treatment modes, chemotherapy situation, and whether patients had used herbal products before. During the interviews, the “word” cancer was not used, taking into account the possibility that some patients might not be aware of their diagnosis. Instead of the term “cancer,” the phrase “this disease” was used. The diagnosis, the level of cancer, chemotherapy received and such information were taken from the patient’s dossier.

Data analysis

The data of the study were collected by using the survey form prepared by the researcher, though depending on the literature and interview with the participants face-to-face. The data obtained in this study was analysed by using X-square analysis, Fisher’s Exact Test, and Pearson X-square analysis. In the interpretation of the results, value of $p < 0.05$ was considered statistically significant.

Variables of the Study

The control variable of the study is the patients’ use of herbal product. The independent variables are age, sex, education level, profession, marital status, geographical region of their residence, disease progression, trust in medical treatment, belief in the benefits of herbal products, reasons for and purposes of using herbal products, and sources of information for the patients.

Ethical consideration

Written consent was taken from the Ethical Committee of Yıldırım Beyazıt University, as well as from the hospitals through the Public Hospitals Institution of Turkey, which is established under the Turkish Ministry of Health.

Results

The sociodemographic distribution of the patients is shown in Table 1.

Table 1: Distribution of the patients according to their sociodemographic status (n=281)

Properties		n	%
Gender	Female	145	51.6
	Male	136	48.4
Age	20-34	41	14.5
	35-49	107	38.1
	50-64	97	34.3
	65-79	32	11.4
	80-94	5	1.7
Educational Attainment	Illiterate	34	12
	Literate (no degree)	43	15.3
	Primary&secondary school	97	34.6
	High school	80	28.5
	University graduate	27	9.6
Marital status	Single	29	10.3
	Married	252	89.7
Employment status	Employed	24	8.5
	Unemployed	159	56.6
	Forced to leave work	98	34.9
Occupation	Housewife	97	34.5
	Retired	79	28.2
	Student	4	1.4
	Freelance employment	62	22
	Salaried employment	39	13.9
Health Insurance	No	34	12.1
	Yes	247	87.9
Family Type	Nuclear	226	80.4
	Extended	42	15
	Divided	13	4.6
Income Level (monthly)	Less than 1000 TL	79	28.1
	Between 1000 TL and 3000 TL	191	68
	More than 3000 TL	11	3.9
Settlement Type of Residence	Village	32	11.4
	County center	184	65.5
	Provincial center	65	23.1

It was determined that 77.9% of the patients had primary cancer. Likewise, 71.2% of the patients had been operated due to an internal organ cancer. 75.5% of the patients had been operated on once, while 77.2% had been operated within 12 months. Moreover, it was determined that 81.1% of the patients did not have another chronic disease and that 79.7% of them did not use other drugs.

The use of herbal products before surgery was 38.9%. It was found that the most widely used herbal products were ginger (19.3%) and nettle (8.3%). The main reasons for which the patients used herbal products in this period were determined as follows: The patients believed that they are beneficial (40.7%), and they were influenced by their acquaintances (31.5%). The use of herbal products during chemotherapy was 54.1%. The most widely used herbal product in this period was nettle (13.7%). The main reasons for using herbal remedies in this period were to reduce patient complaints (41.1%), and to decrease the side-effects of chemotherapy (32.4%).

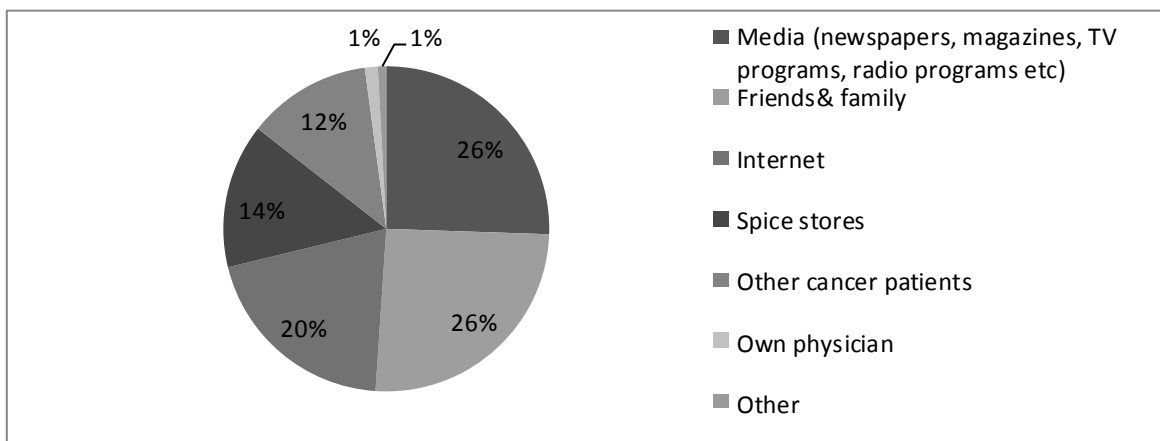
21% of the patients were found to use various herbal products for the complaints listed in Table 2. 5.9% of the patients using herbal products were found to use ginger for nausea, and 3.9% used flaxseed for constipation. 1.2% of the patients who had experienced side-effects of the herbal products stated that they had stomach ache while using nettle (Table 2).

Table 2: Herbal products used for complications due to chemotherapy and the distribution of side-effects due to their use (n=152).

Distribution of herbal products used for complications due to chemotherapy			
Complications	Herbal products employed against these complications	N	%
Nausea	Ginger	9	5.9
Constipation	Flaxseed	6	3.9
Mouth sores	Echinacea	4	2.6
Fatigue	Green tea	4	2.6
Coughing	Ginger	3	2
Diarrhea	Camomile tea	2	1.3
Indigestion	Licorice root	2	1.3
Anxiety	St John's wort	1	0.7
Loss of appetite	Licorice root	1	0.7
Side effects of the herbal products			
Observed side effect	Herbal product responsible	N	%
Stomach ache	Nettle	2	1.3
Nausea	Licorice root	1	0.7
Hypotension	Goldenseal root	1	0.7
Indigestion	Grapeseed	1	0.7
Diarrhea	Green tea	1	0.7

It was evident from the study that 39.8% of the patients were influenced by the media, and 20% by the internet (Figure 1).

Figure 1: Distribution of the factors that influence the use of herbal products (n= 156)



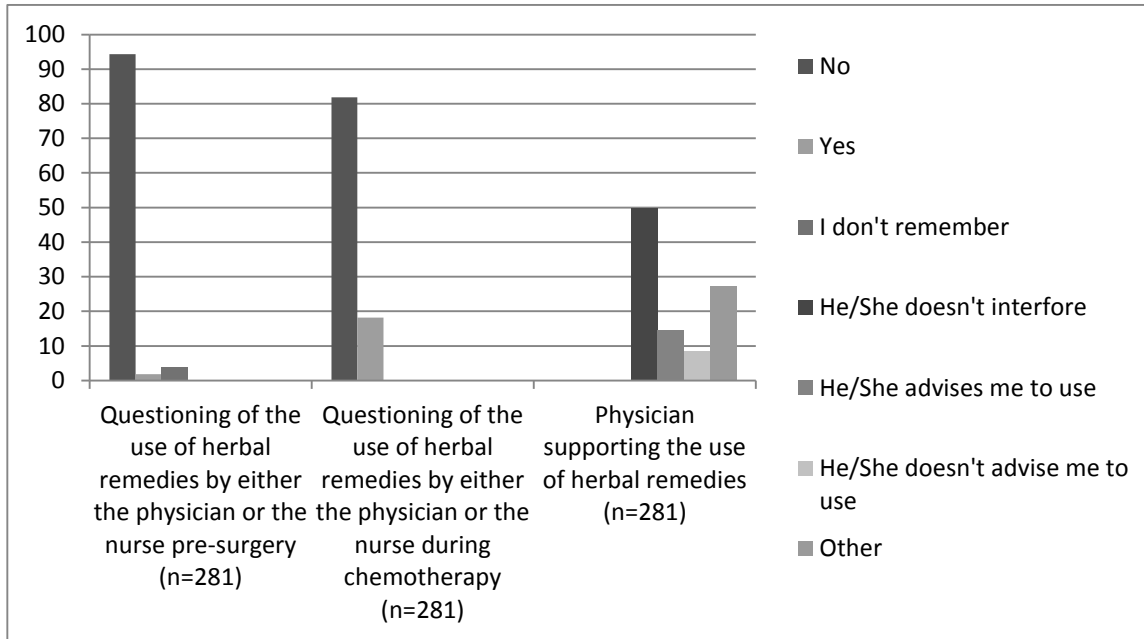
83% of the patients revealed that they obtained herbal products from the spice stores. 63.4% of the patients stated they spent less than 100 TL monthly, while 22.4% reported spending between 100 and 250 TL (Table 3).

Table 3: Acquisition methods for the herbal products and the expenditures incurred (Monthly) (n=156)

Mode of acquisition and the monthly expenditures incurred for the herbal products used		n	%
Mode of acquisition for the herbal products	Spice stores	130	83.3
	Gathering from the nature	46	29.5
	Through social relations (friends and family)	44	28.2
	Internet (online purchases)	41	26.2
	Pharmacies	10	6.4
	Other	10	6.4
Monthly expenditure for the herbal products	Less than 100 TL	99	63.4
	Between 100 and 250 TL	34	21.8
	Between 250 and 500 TL	11	7.1
	Did not pay any money, obtained through other means	9	5.8
	More than 500 TL	3	1.9

While the use of herbal products before surgery was not questioned by the physician or the nurse at a rate of 94.3%, the same rate was found to be 81.8% during chemotherapy. 49.8% of the patients stated that their doctor did not interfere with the use of herbal products, while 27.2% said they did not talk about this issue with their doctors at all (Table 2).

Table 2: Questioning of the use of herbal products, either by the physician or the nurse, before surgery or during chemotherapy



A statistically significant relationship was found between the employment status and the use of herbal products in the pre-surgery period. It was seen that patients who were employed were more likely to use herbal products ($p < 0.05$). In addition, family type and the settlement type of residence were both seen to be correlated to the use of herbal products in the pre-surgery period as well as during chemotherapy. The majority of the patients using herbal products belonged to nuclear families and lived in provincial centers ($p < 0.05$). There is a statistically significant correlation between the educational attainment level and the use of herbal remedies during chemotherapy ($p < 0.05$). The highest rate of herbal product use was observed among college graduates (63%), and the least among illiterate patients (32.4%) (Table 4).

Table 4: Socio-demographic characteristics of the patients and their use of herbal remedies before surgery and during chemotherapy

Socio-demographic Characteristics		Use of herbal remedies before surgery (N=109)						Qi Square Test	
		No		Yes		Total		Qi Square	p
		n	%	n	%	N	%		
Employment status	Employed	7	28.2	17	70.8	24	100	9.461	0.009
	Unemployed	97	61	62	39	159	100		
	Forced to leave work while employed	68	69.4	30	30.6	98	100		
Family type	Nuclear	128	56.7	98	43.3	226	100	10.471	0.005
	Extended	34	81	8	19	42	100		
	Divided	10	76.9	3	23.1	13	100		
Settlement type of residence	Village	23	71.9	9	28.1	32	100	13.455	0.001
	County center	121	65.8	63	34.2	184	100		
	Provincial center	28	42.6	37	57.4	65	100		

Characteristics		Use of herbal remedies during chemotherapy (N=152)						Qi Square Test	
		No		Yes		Total		Qi Square	p
		n	%	n	%	N	%		
Educational attainment	Illiterate	23	67.6	11	32.4	34	100	10.516	0.033
	Literate (no degree)	25	58.1	18	41.9	43	100		
	Primary-secondary	41	42.2	56	57.8	97	100		
	Highschool	30	37.5	50	62.5	80	100		
	College	10	37	17	63	27	100		
Family type	Nuclear	93	41.1	133	58.9	226	100	11.37	0.003
	Extended	27	64.2	15	35.8	42	100		
	Divided	9	69.2	4	30.8	13	100		
Settlement type of residence	Village	16	50	16	50	32	100	7.691	0.021
	County center	92	50	92	50	184	100		
	Provincial center	21	32.3	44	67.7	65	100		

The use of herbal remedies is correlated to the use of other drugs and the existence of other sicknesses in both the pre-surgery and chemotherapy periods in a statistically significant way ($p < 0.05$). While the use of herbal products was higher in patients who had another disease accompanying cancer and used multiple drugs, it was lower in patients who did not have another chronic disease and who did not use other drugs (Table 5).

Table 5: The medical status of the patients and their use of herbal remedies before surgery and during chemotherapy.

Characteristics		Use of herbal remedies before surgery (N=109)						Qi Square Test	
		No		Yes		Total		Qi Square	p
		n	%	n	%	N	%		
Other drugs used	No	146	65.1	78	34.9	224	100	7.159	0.007
	Yes	26	45.6	31	54.4	57	100		
Any other accompanying chronic disease	No	147	65	79	35	226	100	7.698	0.006
	Yes	25	45.5	30	54.5	55	100		
	Yes	17	30.9	38	69.1	55	100		
Characteristics		Use of herbal remedies during chemotherapy (N=152)						Qi Square Test	
		No		Yes		Total		Qi Square	p
		n	%	n	%	N	%		
Other drugs used	No	113	50.4	111	49.6	224	100	7.159	0.007
	Yes	16	28	41	72	57	100		
Any other accompanying disease	No	112	49.5	114	50.5	226	100	6.988	0.008
	Yes	17	30.9	38	69.1	55	100		
	Yes	113	50.4	111	49.6	224	100		

Discussion

In literature, patients with chronic disease are identified as patients who use multiple drugs, who are generally in advanced age, and who prefer alternative treatments in high percentages. This situation could be due to the patient taking a more active role in his or her health, as a result of having a chronic disease and suffering due to that disease. Hence, the possibility of alternative products interacting with drugs increases (Akyürek, 2005; Adams and Jewell,

2007; Sarınca, 2012; Oğur, 2015). In accordance with the literature, it has been found that there is a statistically significant correlation between the use of herbal products and the condition of having a chronic disease, for both before and after surgery periods. In those patients who suffered from another disease and use multiple drugs, the use of herbal product was found to be higher, both before surgery and during chemotherapy. Unlike medical drugs, herbal products contain a lot of active ingredients. For that reason, interactions between herbal products and drugs can be more numerous and frequent than those between drugs. (Block et al., 2004; Aşçı, 2007; Aydos, 2011). The finding that the use of herbal products is at a higher level in patients using multiple drugs implies that health professionals must be more careful for the herbal product-drug interactions that may arise in these patients, it is vital to explain to the patient that he/she might experience different complications instead of beneficial effects, and the critical role the nurse should play at every step of the treatment (Teng et al., 2010).

In the data published in 2008 by NCCAM and the US National Health Statistics Center on the use of CAT in the US, the most frequently used CAT agents were natural products other than minerals and vitamins (Barnes et al., 2007). In a study that was carried out in 14 European countries, including Turkey, on the use of CAT agents by Molassiotis et al (2005), herbal treatments were found to be the most widely used method. There are a number of studies in Turkey on this topic, too. In the studies conducted until now, the use of at least one CAT agent was found to vary between 36% and 60.1% (Gözüm et al., 2003; Kav et al., 2008; Oğur, 2015). In a literature survey conducted by Kav et al in 2008, 14 research articles and 7 studies presented at national conferences were compiled and a combined dataset of 5252 patients were constructed. It was found in this literature survey that the prevalence of CAT use varied between 22.1% and 84.1%, and nettle was the most widely used herb. In our study, the use of herbal products before surgery was 38.9%, while the corresponding rate after surgery and during chemotherapy was 54.1%. The most widely used herb was garlic for the period before surgery (19.3%), and nettle during chemotherapy and after surgery (13.7%). Some possible reasons behind these choices may be as follows: Garlic and nettle are known with their antioxidant properties, they are suitable to the palate of the people in Turkey, and they are easily obtained and cheap (Kucukoner et al., 2013).

In the literature, among the reasons that lead patients to use CAT methods, the following are listed: Having done everything possible against the disease, desperation, increasing the resilience of the body in the struggle against cancer, desire to feel better, and just hoping that it may work (Paltiel et al., 2001; Block et al., 2004; Cui et al., 2004; Hyodo et al., 2005; Scott et al., 2005; İnanç et al., 2006; Kav et al). Likewise, our study's findings were consistent with the literature. In the period before surgery, top reasons for which patients used herbal products were: belief that herbal products would be beneficial (40.7%), influence of family and friends (31.5%), and the desire to try anything that could be of help (27.8%). Top reasons for the use of herbal products after surgery were: reducing complaints (41.1%), reducing the side-effects of chemotherapy (32.4%), strengthening the immune system (25.2%), and supporting the treatment prescribed by the physician (25.2%). The most widely used herbal products in this period were ginger (5.9%) for nausea and flaxseed for constipation (3.9%). Besides their effect on healing, chemotherapeutic agents have certain side-effects, such as nausea, vomiting, hair loss, diarrhea, and suppression of bone marrow. When patients receive cancer diagnosis, they think they have come to the end of their lives, they would be separated from their loved ones, and they would suffer terrible pain. The outcome of this study is in harmony with these feelings of the patients in that in the post-surgery phase, they prefer using a variety of herbal products in order to reduce the side-effects of chemotherapy, and increase their comfort level and the quality of life.

The cytotoxic drugs employed during chemotherapy may interact with other drugs and herbal products being used. These interactions affect the healing process of the patients in undesirable ways, cause side-effects and reduce the efficacy of the cytotoxic drugs. In a study conducted by the US Department of Health (2001), a number of findings were reported regarding the side effects that arise out of drug-herbal product interactions. In a study by Bilge (2010) 37.9% of the patients reported having seen benefits of the herbal products, while 42.8% said they did not see any benefits and 6.70% said they experienced harmful effects. 5 patients reported nausea, 2 patients reported skin burns, 1 patient reported mouth sores, 1 patient reported skin rashes and 2 patients reported gastric bleeding. Our study's findings are in agreement with the literature, as 4.1% of the patients reported having experienced side effects of the herbal product that they used during chemotherapy. 1.2% of the patients using herbal products stated that they experienced stomach aches when using nettle. Besides, there was one patient each that linked licorice root to nausea, goldenseal root to hypotension, grape seed to indigestion and green tea to diarrhea.

In a study by Yazar (2014), physicians were asked what they knew about their patients' use of herbal products, in which dosages these herbal products were used by them, how they were taken, and their side-effects. Responses of 194 physicians (92.4%) were then evaluated. 4.6% of the respondents stated they knew about the patients using herbal products, while 29.4% had partial information and 66% did not have any information. In a study conducted by Barnes et al (1998), 69% of the herbal product users would not inform their physicians if a side-effect arose. In another study by Bacchini et al (2008) 58% of the individuals purchasing herbs and herbal products kept it secret from their physicians. In our study, 81.8% of the patients said that if they used herbal products they would not share this information with their doctors. 49.8% of the patients stated that their doctors did not interfere with herbal product use. Moreover, neither the nurses nor the physicians questioned the use of herbal products in 94.3% of the patients in the

pre-surgery period, while the corresponding rate for the post-surgery period 81.8%. This shows why it is important to take the patients' medical history of drug and herbal product use in a very careful way, to question if new symptoms or drug-drug or drug-herbal product interactions arise in patients using herbs or herbal products alongside drugs, and to take record of potential side effects.

It is seen in the literature that patients using alternative products are generally influenced by TV programs or the internet. It is thought that media exposure is increasing the frequency of usage for these products. Some of the reasons for the increasing use of the herbal products among the alternative treatments are the lack of a standardized supervision, and hence ease of access for these products, increased exposure to the masses thanks to the visual and printed media TV channels and the press (Dedeoğlu, 2014; Oğur, 2015). In a study carried out by Barnes et al (2008) in the US, patients requested information on herbal products, either from the books or brochures about them (90.4%) or from their doctors (50%). In a study conducted by Kav et al (2008), patients are seen to head towards CAT treatments through the guidance of their close acquaintances such as family and friends. Our study parallels the findings in the literature. It was found that the media and the patients' acquaintances were influential at a rate of 39.8%. This shows the importance of effective and correct public communications on health issues and the necessity of reorganizing the health programming in the media that informs the public in an unbiased and correct way.

Conclusion and Recommendations

In the light of the data that this study produced, it is recommended that CAT should be included in the curricula of the schools of nursing and medicine, courses should be created for the nurses and physicians to increase their knowledge about CAT, medical history forms of the patients should be redesigned to identify their use of CAT, and more studies should be undertaken to determine the level of information and the opinions of patients, nurses and physicians regarding herbal products.

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