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Article

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Abstract

Ethnopharmacological relevance: Cancer patients in all cultures are high consumers of herbal medicines (HMs) usually as part of a regime consisting of several complementary and alternative medicine (CAM) modalities, but the type of patient, the reasons for choosing HM-CAM regimes, and the benefits they perceive from taking them are poorly understood. There are also concerns that local information may be ignored due to language issues. This study investigates aspects of HM-CAM use in cancer patients using two different abstracting sources: Medline, which contains only peer-reviewed studies from SCI journals, and in order to explore whether further data may be available regionally, the Thai national databases of HM and CAM were searched as an example.

Materials and Methods: the international and Thai language databases were searched separately to identify relevant studies, using key words chosen to include HM use in all traditions. Analysis of these was undertaken to identify socio-demographic and clinical factors, as well as sources of information, which may inform the decision to use HMs.

Results: Medline yielded 5,638 records, with 49 papers fitting the criteria for review. The Thai databases yielded 155, with none relevant for review. Factors associated with HM-CAM usage were: a younger age, higher education or economic status, multiple chemotherapy treatment, late stage of disease. The most common purposes for using HM-CAM cited by patients were to improve physical symptoms, support emotional health, stimulate the immune system, improve quality of life, and relieve side-effects of conventional treatment.

Conclusions: Several indicators were identified for cancer patients who are most likely to take HM-CAM. However, interpreting the clinical reasons why patients decide to use HM-CAM is hampered by a lack of standard terminology and thematic coding, because patients' own descriptions are too variable and overlapping for meaningful comparison. Nevertheless, fears that the results of local studies published regionally are being missed, at least in the case of Thailand, appeared to be unfounded.

Cancer patients taking herbal medicines: a review of clinical purposes, associated factors, and perceptions of benefit or harm

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Keywords: cancer patient, complementary and alternative medicine, herbal medicine, food supplement, review.

Introduction

Cancer patients in all parts of the world are high users of herbal medicines (HMs), which they choose for clinical reasons related to their cancer diagnosis (Poonthananiwatkul 2015)

and which they usually take as part of a regime consisting of several complementary and alternative medicine (CAM) modalities (Alsanad et al 2014; McLay et al 2012). The contribution of HMs cannot easily be separated from those of other forms of CAM, although they are more likely to possess pharmacological effects and/or interact with conventional medicines. The specific reasons why patients take HM-CAM regimes have not been completely identified but include trying to actively treat cancer, reduce symptoms of the disease, ameliorate side effects associated with conventional treatments, prevent further recurrence or metastasis of the cancer, and to enhance general health in order to deal with the disease and its treatment (Poonthananiwatkul 2015; Alsanad et al 2014; Ernst 2009). A recent study of cancer patients at a traditional medicine hospice in Thailand suggested that in general herbal medicines were perceived to provide more benefit than harm, and a preliminary assessment of the herbal regime, using changes in symptom burden after staying at the hospice, supported this (Poonthananiwatkul 2015). HMs can be registered as medicines in the European Union, but not in most other countries, and 'nutritional' products are poorly regulated everywhere. HMs are often sold as 'food' or 'dietary' supplements to circumvent the regulations; however, as they are taken for therapeutic purposes they are considered to be HMs for the purposes of this study. The first step to addressing the problem of uncontrolled use of HMs as self-medication is therefore to explore the reasons why patients feel the need to take them. Perceptions of the efficacy and safety of these medicines influence the products chosen, although patients are unlikely to consider the indirect consequences of taking these medicines, including their interaction with conventional medicines or other supplements (Goey et al 2014; Zeller et al 2013). The issues posed by combining herbal medicines with conventional drugs have been well documented over the last decade (e.g. Alsanad et al 2014; McLay et al 2012; Williamson et al 2013) and patients in many countries are now being advised to avoid taking herbal medicines during conventional cancer treatment, although no published evidence is available to confirm this as a policy. The objective of this review is to summarize the socio-demographic and other factors that influence HM-CAM use in cancer patients, and their perceptions towards their benefit or harm.

Materials and methods

Search strategy

Data collected in ethnobotanical research has well-documented weaknesses, as critically reviewed by Heinrich et al (2009), and one of these is that datasets compiled regionally in local languages may not be available internationally. In order to investigate whether any

such 'hidden studies' were available, two separate reviews were carried out: the first, a search of Science Citation Indexed, peer-reviewed journals in Medline; the second, a search of the national databases in Thailand. The purpose of the Thai review was to act as an example to investigate whether extra information could be gained by casting the net more widely, despite the unreliability of non-peer-reviewed sources. The Thai databases were used as a test case because Thailand is a very high user of herbal medicines, they are comprehensive and we had access to the full dataset. The searches were restricted to 2003 onwards to provide a contemporary context and also because as a preliminary search found very few relevant studies prior to this. Even peer-review cannot guarantee quality so as many details as possible about each study (method, sample size, other findings) are included in table 1 to add context.

Information sources and searches

The global database Medline and the Thai on-line databases [Thailand Library Integrated System (ThaiLIS), Library of National Research Council of Thailand, Health Systems Research Institute Library, Thai Theses Online, Institute of Thai Traditional Medicine, Journal of Thai Traditional and Alternative medicine] (Thai Government 2014) were searched to identify literature on the experiences, attitudes or perceptions of cancer patients who had taken herbal medicines, using the following terms or their Thai language versions:

- 1) Complementary
- 2) Alternative
- 3) Medicine
- 4) Herbs
- 5) 1 or 2 or 3 or 4
- 6) Cancer
- 7) Attitude
- 8) 5 and 6 and 7
- 9) Limited to English
- 10) Limited to 2003 and 2014

The off-line Khampramong research database was also searched using the same terms, as an example of an institutional data resources. All English language studies published between 2003 and 2014 identifying the experiences/ attitudes/ perceptions/ intended purposes of cancer patients regarding HM were included. Review articles, operational (e.g. clinical guidelines) and health services (e.g. cancer screening) research, case reports,

studies on CAM which did not include HM use or surveys of other parties (such as physicians and other healthcare providers), and laboratory and animal studies were excluded. Studies looking purely at prevalence, trends and costs of herbal medicines were also omitted, as were studies on herb-drug combinations or side effects.

Data extraction

Full papers were obtained for studies considered relevant (figs 1 and 2) and read through by BP. To ensure validity, they were checked by Dr Saud Alsanad (College of Medicine, Al-Imam Mohammad Bin Saud Islamic University, Riyadh, KSA). The following data were extracted from the selected papers: author, year of publication, country, method used, response rate (%), sample size or calculation reported, cancer type, factors related to use of herbal medicine, purposes and thematic concepts cited for use. Factors such as age, gender, education level, income, type of cancer, previous conventional treatment and HM use were recorded, and also sources of information, which may influence decisions to use these products. Perceptions of benefit or harm resulting from taking these products were evaluated, but it must be emphasised that these are the opinions of patients who voluntarily took part in the studies cited, and are reported without any corroboration by independent assessment, clinical examination or biochemical tests. This is an intrinsic but unavoidable weakness of such studies.

5,638 records were found in the Medline database, but only 170 were judged relevant based on the title, i.e. they specifically examined herbal medicine use in cancer patients. 49 papers were eventually included in the review, as shown in figure 1. The Thai database search initially found 155 records, and 14 studies of herbal medicine use in cancer patients were selected based on the title (Fig 2). Titles and abstracts were read through by author BP and validated by a Thai speaker, Dr Supaporn Bunsiriluck (Sirindhorn College of Public Health, Thailand). No Thai language studies were found which fulfilled the criteria for inclusion, so no further analysis was undertaken for these studies.

Insert figures 1 and 2 here

Figure 1: Flow chart of the study selection process from the Medline database

Citations identified from databases (n=5,638)

Studies not relevant based on the title of the

(These were review articles, operational rese not involving herbal medicines, those concer



Figure 2: Flow chart of the study selection process from the Thai national databases



Purposes cited by cancer patients for taking herbal medicines as part of a CAM regime The main reasons given by cancer patients as to why they use HM-CAM are illustrated in fig 3; which in fact shows that this type of analysis is not particularly useful, as there is so much overlap in potential meaning in the reasons cited by the patients themselves. We used the terms cited in the studies to try to avoid misinterpretation, but these are highly subjective. Not all studies used the same parameters, terminologies and methodologies, and more than one purpose was frequently cited by patients who also often used multiple types of CAM. Although all the studies reviewed included HM as a category of CAM, most could not differentiate findings from each modality, so it is not possible to ascribe all the findings to HM use. A further complication is that the line between HM and dietary supplements is not clear, and can depend on non-clinical issues such as legal classification.

CAM and HM in particular are to alleviate physical symptoms associated with cancer, but this category could easily include 'improving general health and the ability to fight the disease', as well as 'treating cancer' and 'improving quality of life', although these reasons were also described specifically. Similarly, 'supporting emotional or mental health' could include 'taking an active role in treatment', 'managing stress' and 'feeling in control'. 'Stimulating or boosting the immune system' was also considered very important, and whereas few studies reported that using HM was intended to achieve a longer life-span, this is implicit in most other categories such as preventing recurrence and treating or curing cancer. Only one study one suggested that 'dissatisfaction with conventional medicine', but the fact that so many cancer patients use HM-CAM suggests that they do not think that conventional medicine has all the answers. Fig 3 therefore also illustrates the importance of using standardised terminology or the use of thematic coding, rather than relying on patients' own descriptions verbatim for this kind of study. Despite this, almost all of the categories relate to the desire to be actively involved in treatment, and the impetus to use HM-CAM comes from patients, rather than practitioners.

Figure 3 Illustration of purposes cited by cancer patients for using herbal medicines as part of a CAM regime



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Other study findings, if stated	Study in advanced cancer patients.	66% used spiritual therapies/ meditation in addition to HM; did not discuss with GPs.	79% discussed with doctor; 57% encouraged patients (none discouraged them). Mistletoe therapy most common by far.	Traditional Chinese medicine (TCM) most important modality (86.4%)	Dietary changes: reduced sugar, animal fat, red meat; increased fruit and vegetable intake.	A wide variety of other CAM used, mostly vitamins, minerals.	Patients were cancer survivors, >5 years post treatment.	25% took HMs that may interact with CT; 52.6% did not tell a healthcare professional.	~49% used HM with 'high levels of satisfaction; 3.2% reported no change; 4.4% adverse effects.	68% said 'beneficial with conventional treatment'; 28% said 'equal or better for cancer'	60% had taken 'supplements', 88% along with conventional drugs; 12% said HM and DS could replace them.		
Factors associated with herbal medicine use where identified	Higher anxiety and pain levels, lower satisfaction with conventional medicine	Younger age, higher education, private health insurance to cover CAM.	Females, breast cancer, longer time since diagnosis.	Younger, married, higher education or income, CT or RT, recurrence or metastasis.	Younger age, higher education, time from diagnosis.	Younger, more educated, more likely to use HM	Married, higher education.	Colorectal and breast cancer, later stages of cancer; previous experience of CT	Dramatic increase in CAM use after cancer diagnosis.	Not assessed; study was in a random sample of 438 adults.	Many factors: e.g. married, younger, Asian ethnicity, higher socioeconomic class.		
Clinical purpose for herbal medicine use and/or thematic analysis findings	Not assessed.	Improve physical and mental health, control symptoms, boost immune system.	Assist conventional treatment, especially by using mistletoe therapy; 'maintaining hope', taking an active role in self-care.	Treat cancer (81.5%), enhance immune system, prevent metastasis and reduce menopausal symptoms.	HMs part of an improvement in diet and lifestyle which were thought to cause cancer	Manage symptoms, improve quality of life and enhance immune system.	Reduce recurrence, manage stress and play an active role in treatment.	Not assessed.	Improve physical ability to fight disease and improve psychological health.	Not assessed.	'Cure' cancer, help the body to heal, boost the immune system and feel in control of treatment. Anxiety and depression found to be reduced		
Cancer type	Mixed	Breast	Mixed	Breast	Breast	Breast	Breast	Mixed	Mixed	Not cancer patients	Breast		
Sample size	111	551	108	1065	354	67	809	242	956	689	36		
Response Rate (%)	C	-	1		33.6	1	1	93.8	1	68	89		
Method*	RAQ	TQ	RAQ	SAQ	SAQ	FGI	SAQ	SAQ	SAQ	ТQ	SAQ		
Country	Australia	USA	Switzer- land	China	Finland and Australia	Turkey	USA	USA	14 EU countries	New Zealand	Canada		
Author (year published)	Correa-Velez et al. (2003)	Henderson & Donatelle (2003)	Van der Weg & Streuli (2003)	Cui Y et al. (2004)	Salminen et al. (2004)	Astin et al. (2005)	Hann et al. (2005)	Gupta et al. (2005)	Molassiotis et al. (2005)	Trevena and Reeder (2005)	Helyer et al. (2006)		
No	-	7	ς	4	S	9	7	×	6	10	11		

Table 1: Summary of research investigating related factors, reasons and study results of why cancer patients use herbal medicines

	ſ	ſ	ſ	AC	CEP	TED	MA	NUS	CRIP		Γ	T	
Other study findings, if stated	The majority had discussed with their doctors.	DS also used frequently.	HM used by 46.4%; most found benefit. Information from media, friends, family, practitioners.	Conventional drugs also used for same purposes.	CAM/HM thought viable for pain but cost prevented regular use.	75% used for 'boosting the immune system'. 66.7% considered it effective.	34% used conventional treatment and other CAM with HM.	HM used by 18.7%: 'vitamins' by 54.2%; diet by 23.7%, juicing 6.2%, TCM 5%.	CAM users expressed practical concerns and wanted oncologists to be more informed about CAM.	Self-care with CAM adjunct may help patients deal with the side effects of CT and RT	65% used at least one form of CAM; < 3% experienced adverse effects from HM/any CAM.	Very high prevalence rate. Most described particular benefits and will continue to use.	Some described CAM as 'instrument of God'.
Factors associated with herbal medicine use where identified	Cancer diagnosis or end of conventional treatment prompted CAM use.	Higher level of education; dissatisfaction with medical treatment; CT	Younger, higher education, previous combination treatments for their cancer.	DS cited more commonly than HM.	Not assessed.	Chinese HM linked to younger age and severe menopausal symptoms	Previous use; younger age, being married, RT.	HM associated with younger age; increase in all CAM in advanced stages of disease.	Themes found: coping with psychological and physical distress, lifestyle disruption.	Not assessed.	Most (83%) would be happier to accept CAM if offered by the hospital.	Expenses for CAM paid for 40% of total medical cost, Western medicine only 20%.	Kinship, social, educational, economical, and beliefs.
Clinical purpose for herbal medicine use and/or thematic analysis findings	Boost immune system, prevent cancer recurrence, and improve physical and emotional health.	To reduce symptoms; especially 'psychological' distress.	HM mainly used to improve physical ability to fight cancer.	Pain or nausea of CT.	Pain management.	To alleviate menopausal symptoms and side effects of CT and tamoxifen	To support their general health status.	Improving wellbeing, boosting immune system, assist in treating cancer, educe recurrence.	'Cure' disease, boost immunity, improve overall health, prolong life, and peace of mind.	CAM used: diet/life-style; mind and body control; HM 'for hair loss'	Not assessed.	'Cure' cancer, boost immune system, increase quality of life, relieve cancer symptoms, and others.	Cope with disease and treatment, emotional support.
Cancer type	Mixed	Breast	Lung	Mixed	Breast	Breast	Breast	Breast	Mixed	Mixed	Mixed	Mixed	Breast
Sample size	19	105	H	37	30	5046	129	367	7	202	1,323	121	6
Response Rate (%)		C	-	I	ı	1	ı	I	,	1	28.8	1	ı
Method*	IDI	RAQ	QAQ	SAQ	ISS	RAQ	SAQ	QAQ	IDI	RAQ	SAQ	SSI	ISS
Country	Australia	USA	8 EU countries	NSA	USA	China	Turkey	Australia	Taiwan	Thailand	Australia	China	USA
Author (year published)	Humpel and Jones (2006)	Lengacher et al. (2006)	Molassiotis et al. (2006)	Williams et al. (2006)	Wong-Kim & Merighi (2007)	Chen et al. (2008)	Gulluoglu et al. (2008).	Kremser et al. (2008)	Lu et al. (2010)	Piamjariyakul et al. (2010)	Oh et al. (2010)	Teng et al. (2010)	Wanchai et al. (2010)
No	12	13	14	15	16	17	18	19	20	21	22	23	24

						T			40)(CE	P	T	E	D	Ν	A	Ν	U	S	CF	RI	P											
Other study findings, if stated	14 patients refused Western	medicine, used only TCM.	Improvement in sleep, fatigue, annetite and emotional health	HM used as recommended by	family members (43.5%).	Only 19.7% of patients reported	HM use; remainder used other	types of CAM.	TCM used in addition to	conventional medicine.	Patients believed that using HM	after being diagnosed helped with	prognosis.	CAM users active in developing	treatment plans, which improved	their quality of life.	Patients expected doctors to refer	them or participate in building a	CAM treatment plan	44 % of parents used DS for their	child; most used organic food.		38% potential interactions with	hormone therapy (letrozole,	anastrazole, tamoxifen etc).	Over 60% used TCM for 'curing'	cancer.	Most patients used CAM; mainly	herbal (90%). 56.1% discussed	CAM with GP.	51% reported benefit, 9.4% side	effects; 58.3% did not tell their	doctors.	Information from family and friends, GP, media. Some
Factors associated with herbal medicine use where identified	Being male, advanced	disease.	This was a clinical study on a particular combination	Most >40 vrs female in	rural areas.	Fewer than $20\% < 50$ yrs	old, most ($\sim 60\%$) HM users	between 50 - 69 years.	Not assessed.		'Learning new CAM	methods' as a positive step	for self-help	Optimism and a belief that	one has the ability to act to	achieve a good outcome.	Younger age, Jewish	religion, but lesser degree of	religiosity.	No difference in parents who	used CAM in age, income,	education or faith.	Use by friends and family,	higher educational	attainment.	Cultural acceptance of TCM	is high in China.	No significant differences in	demographics between	users and non-users	High income; cancer type.			Higher formal education and younger age.
Clinical purpose for herbal medicine use and/or thematic analysis findings	Longer life, better quality of life,	improved immunity.	Improve quality of life in several	wicus. Not assessed		Not assessed.			Themes identified: HM benefits were	medical, social and psychological	Themes identified: 'maintaining	control' and 'valuing wellness' as	form of self-help.	To cope with disease; improve	quality of life.		Cope with CT effects and disease,	provide emotional support.	2	Not assessed, but parents felt it had	benefitted children and not caused	further suffering.	Improving general health, boosting	the immune system further cancer	prophylaxis.	Cure cancer, improve the immune	system.	Boost the immune system.			Alleviate symptoms, treat cancer,	assist conventional treatment,	improve physical and mental health	Not assessed.
Cancer type	Mixed		Breast	Mixed		Mixed			Mixed		Lung	2		Mixed			Breast /	Gyn.		Mixed			Breast			Mixed		Gynaec	ologic		Mixed			Breast
Sample size	65		82	12.60		1498	C		9		12			23			275			96			453			352		67			248			211
Response Rate (%)			97.5		5	75.7			ı		-			92						1			79.5%			82.2		I			I			81
Method*	RAQ		RAQ	RAO	Y	SAQ			ISS		ISS			ISS			SAQ			RAQ			SAQ			SAQ		SAQ			SAQ			SAQ
Country	Singapor	e	China	Palestine		UK			China		Canada			NSA			Israel			Australia			UK			China		Turkey			Thailand			Germany
Author (year published)	Wong et al.	(2010a)	Wong et al.	Ali-Shtaveh et	al. (2011)	Damery et al.	(2011)		Liu et al. (2011)		Amichai et al.	(2012)		Arthur et al.	(2012)		Ben-Arye et al.	(2012)		Heath et al.	(2012)		McLay et al.	(2012)		McQuade et al.	(2012)	Nazik et al.	(2012)		Puataweepong	et al. (2012)		Tautz et al. (2012)
No	25		26	77	i	28			29		30			31			32	_		33			34			35		36			37	_		38

_							-		A	C	CE		T	Ε	D	Ν		<u>N</u>	U	S	C	R	P		-		-				
Other study findings, if stated	disclosed use to doctors.	Study restricted to use TCM in Chinese immigrant parents of	children with cancer.	HM and DS provided benefits,	unlike yoga, HOM or	acupuncture	DS widely used; many did not	tell their oncologist.	Most (68.2%) used HMs, few	(24%) discussed with a doctor.	42% reported use of more than	one type of CAM.	DS and HMs mainly used; 66.3%	discussed with doctor; 89.6%	reported benefits.	66% 'benefitted' from CAM; 5	patients reported side effects. $\sim 30\%$	discussed with physician.	50% used HM; most (70%)	thought their physician would	'not take time to discuss'.	Most parents of child patients	used at least one type of CAM	and reported it beneficial.	37.5% used CAM; mainly HM or	HOM; \sim 79% reported benefits.	50% used CAM; mainly HM.	77% 'intended' to discuss with	their physician.	on-line questionnaire	-
Factors associated with herbal medicine use where identified		Themes: extent of trust in conventional medicine,	interaction with practitioners.	Female, higher education,	breast cancer, length time	after diagnosis.	Higher level of education		Influence of media (66%),	friends and relatives (64%).	Being fearful regarding	future.	Female; having experienced	and used CAM in past.		Influence of family and	friends.		Breast cancer.			Not assessed.			Higher education level and	younger age.	Not assessed.			telephone questionnaire; OQS=	-
Clinical purpose for herbal medicine use and/or thematic analysis findings		The use of food as therapy is part of their daily cultural practice	•	Not assessed.			To improve physical health.	1	Not assessed.		Improve general, emotional or	spiritual health, boost immunity.	Improve general health post-	conventional treatment.		Enhance physical well-being and	improve wound-healing.		To reduce unpleasant symptoms,	support immune system and maintain	health.	About a third reported using HM and	CAM for 'curative' purposes.		Improve cancer-related symptoms and	support general health.	Not assessed.			Self- administered questionnaire; TO= t	is group interview.
Cancer type		Mixed		Mixed			Mixed		Mixed		Lung		Mixed			Ortho-	paedic	1	Mixed			Mixed			Breast		Mixed			re; SAO =	GI= Focu
Sample size		25		316			220		472	R	108		803			274			1			100			184		320			questionnai	interview;]
Response Rate (%)					5		43		-		59		82%									-					89			Iministered o	i-structured
Method*		IDI		RAQ			SAQ		RAQ		SAQ		ISS			RAQ.			SQO	I		RAQ			SAQ		SAQ			esearcher-ad	; SSI = Semi
Country		Canada		USA			UK		Turkey		USA		Italy			Malaysia			Germany			USA			France		Australia			s: *RAO = R	oth interview
Author (year published)		Watt et al. (2012)		Garland et al.	(2013)		O'Connor et al.	(2013)	Tuna et al.	(2013)	Bismark et al.	(2014)	Bonacchi et al.	(2014)		Dhanoa et al.	(2014)		Huebner et al.	(2014)	n.	Ladas et al.	(2014)		Saghatchian et	al. (2014)	Wilkinson and	Stevens (2014)		Key to abbreviation:	survey; IDI = in-def
No		39		40			41		42		43		44			45			46			47			48		49				

Key to treatments and CAM modalities: HM = herbal medicine(s); HOM = homoeopathy; RT = radiotherapy; CT = chemotherapy; DS = dietary supplements (may sometimes include HM); TCM traditional Chinese medicine.

Factors associated with herbal medicines use as part of a CAM regime

In general, the results supported other studies investigating the frequency of general CAM use which have found that a younger age, higher level of education and income, ethnicity and being female, were linked to HM-CAM use, as detailed in table 1. As far as cancer patients are concerned, this diagnosis appears to act as an impetus to using HM-CAM, with the intention of improving general health to 'fight disease' as well as cope with side effects of conventional drug treatment, in a way not usually associated with other disease states.

The more serious disease states were associated with CAM which included HM and dietary supplements (HM-CAM). Multiple chemotherapy treatment was related to higher HM-CAM usage and many patients started using CAM (of any type) only after being diagnosed with cancer. However, those who had used HM-CAM for other purposes were also more likely to be associated with its use in cancer. A greater use of HM-CAM was noted in cancer patients who were in a recurrent or metastatic stage (e.g. Cui et al., 2004) and the longer the time since the initial cancer diagnosis, the more likely patients were to use HMs (Salminen et al., 2004). These reasons may be related to other factors such as 'fearfulness about the future' and 'anxiety about possible recurrence', which were also linked with a greater tendency to use HM-CAM (Correa-Velez et al., 2003, Bismark et al., 2014).

Experiences reported by patients after taking herbal medicines

The recorded incidence of herbal use varies widely, i.e. between 10.8% and 90.2%, but all the studies reviewed showed that at least 55% of patients believed they had had benefited, whereas few patients (8% to 18%) reported negative effects (Damery et al., 2011, Nazik et al., 2012, Molassiotis et al., 2006, Chen et al., 2008, Tuna et al., 2013, Bonacchi et al., 2014).

Perceived beneficial experiences: Previous studies have reported positive effects after HM-CAM use but results varied greatly. Between 22% and 90% of patients said they had experienced benefits, the most common being relief of pain, dyspepsia and fever, and improved appetite and patterns of sleep (Oh et al., 2010, Molassiotis et al., 2005, Puataweepong et al., 2012, Hyodo et al., 2005, Teng et al., 2010, Ladas et al., 2014, Trevena and Reeder, 2005). Other perceived benefits were a greater ability to cope with the illness and its treatment or specific effects in relieving pain and adverse effects of conventional medicine including chemotherapy (i.e. nausea), as well as alleviating severe depression or anxiety and improving emotional health, as shown in table 1.

Perceived negative experiences reported by patients after taking HMs: Negative effects from HM-CAM reported by cancer patients ranged from 3% to 9.4% and included pain, dyspepsia, abdominal pain and fatigue (Oh et al., 2010, Molassiotis et al., 2005, Puataweepong et al., 2012, Hyodo et al., 2005, Trevena and Reeder, 2005). As with perceived benefit, it is not possible to ascribe all of these to the HM-CAM treatment and some may be due to progression of the disease.

Other findings of the review

Concurrent use with conventional therapies: most studies found that over 50% of patients who used HM-CAM did so along with conventional medicines (e.g. Nazik et al., 2012, Gupta et al., 2005, Helyer et al., 2006), many to treat specifically the adverse effects of conventional treatment (e.g. Gupta et al., 2005, McLay JS et al., 2012).

Informing medical practitioners of HM use: differences were noted between countries but the number of studies cited was insufficient to draw any conclusions. Most strikingly, two US and two UK studies reported that the majority of patients surveyed did not tell their doctor of their HM-CAM use, whereas in two Australian studies, the majority either informed or intended to inform their doctor. In Turkey, Italy, Israel and Germany (1 study each), most patients discussed their HM-CAM use with their GP, but in Thailand, most did not (1 study).

Discussion

Many studies have investigated the use of CAM generally in cancer patients, which is commonplace (e.g. Teng et al 2010), and in some cases this has included HM (including dietary supplements). HM is the main form of CAM which can interact with conventional drugs, so the implications of HM use are more serious (e.g. Alsanad et al 2014) and therefore formed the focus of this investigation. As most users of CAM use more than one modality, we have examined all studies which specified the HM as part of their regime. Although in traditional Chinese medicine (TCM) for example, combining conventional with herbal medicine in cancer treatment is endorsed by physicians and may be beneficial (e.g. Hu et al 2015; Cui et al 2004), patients usually used HM-CAM on their own initiative and without informing their doctor, and many considered it was not necessary to do so.

The most common reasons for taking HM-CAM found in this study were linked to the desire to improve physical and mental symptoms and quality of life, and to help deal with the disease and its unpleasant treatment. As CAM is not sanctioned officially by most medical

authorities, and not usually covered by public insurance schemes, it requires independent research into self-care health options, for example by using the internet and media. This may be a reflection of the findings that younger patients and those of a higher educational and financial status were associated with a higher use of HM-CAM.

This study also showed that most of the relevant information on HM-CAM is available in the mainstream, peer-reviewed literature. A comprehensive set of Thai databases compiled from local studies was used as an example for exploration; however, it provided no new information and did not even identify two Thai clinical studies published internationally (Piamjariyakul et al 2010; Puataweepong et al. 2012). This is understandable since authors prefer to publish in SCI journals, although the results cannot be extrapolated elsewhere until further studies have been done.

Conclusions

This review identified several indicators for cancer patients who are most likely to take HM-CAM, using information taken from Medline. Fears that the results of local studies published regionally are being missed, at least in the case of Thailand, appeared to be unfounded. In addition to patient characteristics as described above, the use of HM-CAM was also associated with the type and stage of cancer and the side-effects of conventional treatment experienced. However, interpreting the specific clinical purposes why patients decide to use HM-CAM, and what they expected of and experienced from the treatments, is hampered by a lack of standard terminology and thematic coding. Patients' own descriptions are too variable and overlapping for meaningful comparison, but even so, most the categories relate to a desire to be actively involved in treatment, to improve general health and aid recovery. The impetus to use HM-CAM comes mainly from patients, rather than practitioners, except in China where integration of TCM and conventional medicine for cancer treatment is more common.

References

Ali-shtayeh, M., Jamous, R. 2011. Herbal preparation use by patients suffering from cancer in Palestine. Complementary Therapies in Clinical Practice, 17, 235-240.

Alsanad S. M., Williamson E. M., Howard R. L. 2014. Cancer patients at risk of herb/food supplement-drug interactions: A systematic review. Phytotherapy Research 28:1749-1755

Amichai, T., Grossman, M. Richard, M. 2012. Lung cancer patients' beliefs about complementary and alternative medicine in the promotion of their wellness. European Journal of Oncology Nursing, 16, 520-527.

Arthur, K., Belliard, J., Hardin, S., Knecht, K., Chen, C., Montgomer, S. 2012. Practices, attitudes, and beliefs associated with complementary and alternative medicine (CAM) use among cancer patients. Integrative Cancer Therapies, 11, 232-242.

Astin, J., Reilly, C., Perkins, C., Child, W. 2005. Breast cancer patients' perspectives on and use of complementary and alternative medicine: a study by the Susan G. Komen Breast Cancer Foundation. Journal of the Society for Integrative Oncology, 4, 157-169.

Ben-arye, E., Schiff, E., Steiner, M., Keshet, Y., Lavie, O. 2012. Attitudes of patients with gynecological and breast cancer toward integration of complementary medicine in cancer care. International Journal of Gynecological Cancer, 22, 146-153.

Bismark, R., Chen, H., Dy, G., Gage-bouchard, E., Mahoney, M. 2014. Complementary and alternative medicine use among patients with thoracic malignancies. Supportive Care in Cancer, 22, 1857-1866.

Bonacchi, A., Fazzi, L., Toccafondi, A., Cantore, M., Mambrini, A., Muraca, M., Banchelli, G., Panella, M., Focardi, F., Calosi, R. 2014. Use and Perceived Benefits of Complementary Therapies by Cancer Patients Receiving Conventional Treatment in Italy. Journal of Pain and Symptom Management, 47, 26-34.

Chen, Z., Gu, K., Zheng, Y., Zheng, W., Lu, W., Shu, X. 2008. The use of complementary and alternative medicine among Chinese women with breast cancer. The Journal of Alternative and Complementary Medicine, 14, 1049-1055.

Correa-velez. I., Clavarino, A., Barnett, A, Eastwood, H. 2003. Use of complementary and alternative medicine and quality of life: changes at the end of life. Palliative Medicine, 17, 695-703.

Cui, Y., Shu, X., Gao, Y., Wen, W., Ruan, Z., Jin, F., Zheng, W. 2004. Use of complementary and alternative medicine by Chinese women with breast cancer. Breast Cancer Research and Treatment, 85, 263-270.

Damery, S., Gratus, C., Grieve, R., Warmington, S., Jones, J., Routledge, P., Greenfield, S., Dowswell, G., Sherriff, J., Wilson, S. 2011. The use of herbal medicines by people with cancer: a cross-sectional survey. British Journal of Cancer, 104, 927-933.

Dhanoa, A., Yong, T., Yeap, S., Lee, I., Singh, V. 2014. Complementary and alternative medicine use amongst Malaysian orthopaedic oncology patients. BMC Complementary and Alternative Medicine, 14, 404.

Ernst, E. 2009. Complementary and alternative medicine (CAM) and cancer: the kind face of complementary medicine. International Journal of Surgery, 7, 499-500.

Garland, S., Valentine, D., Desai, K., Li, S., Langer, C., Evans, T., Mao, J. 2013. Complementary and Alternative Medicine Use and Benefit Finding Among Cancer Patients. The Journal of Alternative and Complementary Medicine, 19, 876-881.

Goey AK, Beijnen JH, Schellens JH (2014). Herb-drug interactions in oncology. Clinical Pharmacology and Therapeutics. 95, 354-355

Gulluoglu, B., Cingi, A., Cakir, T., Barlas, A. 2008. Patients in northwestern Turkey prefer herbs as complementary medicine after breast cancer diagnosis. Breast Care, 3, 269-273.

Gupta, D., Lis, C., Birdsall, T., Grutsch, J. 2005. The use of dietary supplements in a community hospital comprehensive cancer center: implications for conventional cancer care. Supportive Care in Cancer, 13, 912-919.

Hann, D., Baker, F., Denniston, M., Entrekin, N. 2005. Long-term breast cancer survivors' use of complementary therapies: perceived impact on recovery and prevention of recurrence. Integrative Cancer Therapies, 4, 14-20.

Heath, J., Oh, L., Clarke, N., Wolfe, J. 2012. Complementary and alternative medicine use in children with cancer at the end of life. Journal of Palliative Medicine, 15, 1218-1221.

Heinrich M, Edwards S, Moerman DE, Leonti M (2009). Ethnopharmacological field studies: a critical assessment of their conceptual basis and methods. Journal of Ethnopharmacology, 124, 1-17.

Helyer, L., Chin, S., Chui, B., Fitzgerald, B., Verma, S., Rakovitch, E., Dranitsaris, G., Clemons, M. 2006. The use of complementary and alternative medicines among patients with locally advanced breast cancer--a descriptive study. BMC Cancer, 6, 39.

Henderson, J., Donatelle, R. 2003. Complementary and alternative medicine use by women after completion of allopathic treatment for breast cancer. Alternative Therapies in Health and Medicine, 10, 52-57.

Hu YC, Wu CT, Lai JN, Tsai YT (2015). Detection of a negative correlation between prescription of Chinese herbal products containing coumestrol, genistein or daidzein and risk of subsequent endometrial cancer among tamoxifen-treated female breast cancer survivors in Taiwan between 1998 and 2008: A population-based study. J Ethnopharmacol. 169:356-62

Huebner, J., Muenstedt, K., Prott, F., Stoll, C., Micke, O., Buentzel, J., Muecke, R., Senf, B. 2014. Online Survey of Patients with Breast Cancer on Complementary and Alternative Medicine. Breast Care, 9, 60-63.

Humpel, N., Jones, S. C. 2006. Gaining insight into the what, why and where of complementary and alternative medicine use by cancer patients and survivors. European Journal of Cancer Care, 15, 362-8.

Hyodo, I., Amano, N., Eguchi, K., Narabayashi, M., Imanishi, J., Hirai, M., Nakano, T., Takashima, S. 2005. Nationwide survey on complementary and alternative medicine in cancer patients in Japan. Journal of Clinical Oncology, 23, 2645-2654.

Kim, S., Kim, K., Park, J., Shin, J., Kim, S., Park, J., Park, E., Seo, H. 2013. Factors Associated with Discontinuation of Complementary and Alternative Medicine among Korean Cancer Patients. Asian Pacific Journal of Cancer Prevention, 14, 225-230.

Klepser, T., Doucette, W., Horton, M., Buys, L., Ernst, M., Ford, J., Hoehns, J., Kautzman, H., Logemann, C., Swegle, J. 2000. Assessment of patients' perceptions and beliefs regarding herbal therapies. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy, 20, 83-87.

Kremser, T., Evans, A., Moore, A., Luxford, K., Begbie, S., Bensoussan, A., Marigliani, R., Zorbas, H. 2008. Use of complementary therapies by Australian women with breast cancer. Breast, 17, 387-94.

Ladas, E., Rivas, S., Ndao, D., Damoulakis, D., Bao, Y., Cheng, B., Kelly, K., Antillon, F. 2014. Use of traditional and complementary/alternative medicine (TCAM) in children with cancer in Guatemala. Pediatric Blood and Cancer, 61, 687-692.

Lengacher, C., Bennett, M., Kip, K., Gonzalez, L., Jacobsen, P., Cox, C. 2006. Relief of symptoms, side effects, and psychological distress through use of complementary and alternative medicine in women with breast cancer. Oncology Nursing Forum, 33, 97-104.

Liu, C., Tang, W., Wang, H., Lee, K. 2011. Cancer patients' experience of combined treatment with conventional and traditional Chinese medicine: A biopsychosocial phenomenon. Cancer Nursing, 34, 495-502.

Lu, J., Tsay, S., Sung, S. 2010. Taiwanese adult cancer patients' reports of using complementary therapies. Cancer Nursing, 33, 320-326.

Mao, J., Palmer, S., Desai, K., Li, S., Armstrong, K., Xie, S. 2012. Development and validation of an instrument for measuring attitudes and beliefs about complementary and alternative medicine (CAM) use among cancer patients. Evidence-Based Complementary and Alternative Medicine, 2012:798098.

McLay, J., Stewart, D., George, J., Rore, C., Heys, S. 2012. Complementary and alternative medicines use by Scottish women with breast cancer. What, why and the potential for drug interactions? European Journal of Clinical Pharmacology, 68, 811-819.

McQuade, J., Meng, Z., Chen, Z., Wei, Q., Zhang, Y., Bei, W., Palmer, J., Cohen, L. 2012. Utilization of and attitudes towards traditional Chinese medicine therapies in a Chinese cancer hospital: a survey of patients and physicians. Evidence-Based Complementary and Alternative Medicine, 2012 :504507.

Molassiotis, A., Fernadez-ortega, P., Pud, D., Ozden, G., Scott, J., Panteli, V., Margulies, A., Browall, M., Magri, M. Selvekerova, S. 2005. Use of complementary and alternative medicine in cancer patients: a European survey. Annals of Oncology, 16, 655-663.

Molassiotis, A., Panteli, V., Patiraki, E., Ozden, G., Platin, N., Madsen, E., Browall, M., Fernandez-ortega, P., Pud, D., Margulies, A. 2006. Complementary and alternative medicine use in lung cancer patients in eight European countries. Complementary Therapies in Clinical Practice, 12, 34-39.

Nazik, E., Nazik, H., Api, M., Kale, A., Aksu, M. 2012. Complementary and alternative medicine use by gynecologic oncology patients in Turkey. Asian Pacific Journal of Cancer Prevention 13, 21-25.

O'Connor, N., Graham, D., O'Meara, A., Devins, M., Jennings, V., O'leary, D., O'Reilly, M. 2013. The use of complementary and alternative medicine by Irish pediatric cancer patients. Journal of Pediatric Hematology/Oncology, 35, 537-542.

Oh, B., Butow, P., Mullan, B., Beale, P., Pavlakis, N., Rosenthal, D., Clarke, S. 2010. The use and perceived benefits resulting from the use of complementary and alternative medicine by cancer patients in Australia. Asia-Pacific Journal of Clinical Oncology, 6, 342-349.

Piamjariyakul, U., Williams, P., Prapakorn, S., Kim, M., Park, L., Rojjanasrirat, W., Williams, A. 2010. Cancer therapy-related symptoms and self-care in Thailand. European Journal of Oncology Nursing, 14, 387-394.

Puataweepong, P., Sutheechet, N., Ratanamongkol, P. 2012. A survey of complementary and alternative medicine use in cancer patients treated with radiotherapy in Thailand. Evidence-Based Complementary and Alternative Medicine, 2012:670408.

Saghatchian, M., Bihan, C., Chenailler, C., Mazouni, C., Dauchy, S., Delaloge, S. 2014. Exploring frontiers: Use of complementary and alternative medicine among patients with early-stage breast cancer. The Breast, 23, 279-285.

Salminen, E., Bishop, M., Poussa, T., Drummond, R., Salminen, S. 2004. Dietary attitudes and changes as well as use of supplements and complementary therapies by Australian and Finnish women following the diagnosis of breast cancer. European Journal of Clinical Nutrition, 58, 137-144.

Tautz, E., Momm, F., Hasenburg, A. & Guethlin, C. 2012. Use of complementary and alternative medicine in breast cancer patients and their experiences: a cross-sectional study. European Journal of Cancer, 48, 3133-3139.

Teng, L., Jin, K., He, K., Bian, C., Chen, W., Fu, K., Zhu, T., Jin, Z. 2010. Use of complementary and alternative medicine by cancer patients at Zhejiang University Teaching Hospital, Zhuji Hospital, China. African Journal of Traditional, Complementary and Alternative Medicines, 7, 322-330.

Thai Government (2014) http://arcbs.bsru.ac.th/web2009/database/thedb.html (accessed August 2015)

Tovey, P., Broom, A., Chatwin, J., Hafeez, M., Ahmad, S. 2005. Patient assessment of effectiveness and satisfaction with traditional medicine, globalized complementary and alternative medicines, and allopathic medicines for cancer in Pakistan. Integrative Cancer Therapies, 4, 242-8.

Trevena, J., Reeder, A. 2005. Perceptions of New Zealand adults about complementary and alternative therapies for cancer treatment. New Zealand Medical Journal, 118, U1787.

Tuna, S., Dizdar, O., Calis, M. 2013. The prevalence of usage of herbal medicines among cancer patients. Journal of BUON (Balkan Union of Oncology), 18, 1048-51.

Van der weg, F. & Streuli, R. A. 2003. Use of alternative medicine by patients with cancer in a rural area of Switzerland. Swiss Medical Weekly, 133, 233-40.

Wanchai, A., Armer, J., Stewart, B. Breast cancer survivors' perspectives of care practices in western and alternative medicine. Oncology nursing forum, 2010. Oncology Nursing Society, 494-500.

Watt, L., Gulati, S., Shaw, N., Sung, L., Dix, D., Poureslami, I., Klassen, A. 2012. Perceptions about complementary and alternative medicine use among Chinese immigrant parents of children with cancer. Supportive Care in Cancer, 20, 253-260.

Wilkinson, J., Stevens, M. 2014. Use of complementary and alternative medical therapies (CAM) by patients attending a regional comprehensive cancer care centre. Journal of Complementary and Integrative Medicine, 11, 139-145.

Williams PD, Piamjariyakul U, Ducey K, Badura J, Boltz KD, Olberding K, Wingate A., Williams A. R. 2006. Cancer treatment, symptom monitoring, and self-care in adults: pilot study. Cancer Nursing, 29, 347-55.

Williamson, E. M., Driver, S. B., Baxter, K. Lee, C. R. 2013. Stockley's Herbal Medicines Interactions : a guide to the interactions of herbal medicines, London, Pharmaceutical Press.

Wong-kim, E., Merighi, J. 2007. Complementary and alternative medicine for pain management in US-and foreign-born Chinese women with breast cancer. Journal of Health Care for the Poor and Underserved, 18, 118-129.

Wong, L., Chan, E., Tay, S., Lee, K., Back, M. 2010a. Complementary and alternative medicine practices among Asian radiotherapy patients. Asia Pacific Journal of Clinical Oncology, 6, 357-63.

Wong, L., Wong, C., Leung, P., Lam, W. 2010b. The efficacy of herbal therapy on quality of life in patients with breast cancer: self-control clinical trial. Patient Preference and Adherence, 4, 223.

Zeller, T., Muesnstedt, K., Stoll, C., Schweder, J., Senf, B., Ruckhaeberle, E., Becker, S., Serve, H., Huebner, J. 2013. Potential interactions of complementary and alternative medicine with cancer therapy in outpatients with gynecological cancer in a comprehensive cancer center. Journal of Cancer Research and Clinical Oncology, 139, 357-365. Graphical Abstract Cancer patients taking herbal medicines: a review of clinical purposes, associated factors, and perceptions of benefit or harm

