

The use of complementary medicines in cancer patients and their potential for drug interaction

Abstract

Objectives: To determine prevalence of complementary medicine (CAM) use by oncology patients and to establish the potential for drug interactions between CAMs and conventional medicines. To gain qualitative data from oncology patients and staff on their attitudes to CAMs.

Design: A patient questionnaire was devised and patients selected for a one-to-one interview. Nursing staff were involved in the screening, selection and consenting of patients who were suitable for inclusion in the study using a targeting tool. This study enabled the proportion of patients who took CAMs to be identified and gave an insight into their reasons for taking them. Qualitative interviews were then conducted with pharmacy and nursing staff providing medicines management to the patients in the study.

Setting: Oncology wards in three district general hospitals in Northumbria Healthcare NHS Trust.

Participants: Of 250 potential patients screened 44 chemotherapy patients were recruited as were 5 oncology nurses and 4 oncology pharmacists.

Main outcome measures: Proportion of patients using CAM and qualitative assessment of patient and staff attitudes to CAM usage.

Results: Twenty-seven percent of patients interviewed used CAM. No major interactions were found between any of the conventional and complementary medicines taken. Half of the patients did not mention that they were taking CAM to a health care professional.

Conclusions: Patients do not view CAMs as medicines and were not aware of potential interactions with conventional medicines. Pharmacists must be aware of and monitor CAM use in their patients and ensure they use their clinical skills to assess potential risk of CAMs when evidence in the literature is lacking.

Introduction

Patients self-administering complementary and alternative medicines (CAMs) is common, with an estimated 25% of the UK population using at least one form of CAM.¹ The definition of CAM can vary but has been quoted as 'a group of diverse medical and health care systems, practices, and products not considered part of conventional medicine.'^{2,3} Medication history taking by pharmacy staff is an established part of the medicines management of hospital patients, but the focus is on conventional treatments and, potentially, CAMs can be overlooked. The use of CAMs by cancer patients tends to be higher than in the population as a whole, with various studies finding a prevalence of between 31% and 73%.^{2,4-6}

Pharmacists should be actively seeking to record all use of CAMs by patients and monitor for potential interactions. The Royal College of Radiologists (RCR) Faculty of Clinical Oncology has provided

advice and encouraged its members to discuss CAMs with their patients. Their advice is: 'Interaction with treatment is an important issue for study and by opening up this growing field to discussion and formal recording of interactions, an increasingly reliable body of knowledge will develop.'⁶

Aims and objectives

Apart from one large European study,⁵ most research regarding CAM in oncology patients has been conducted in the USA. The primary aim of this investigation was to determine the prevalence of use of herbal and complementary medicines by oncology patients and to establish the potential for drug interactions with any conventional medicine the patients may be taking.

Method

Subject and settings

Approximately 250 chemotherapy patients passed through the oncology wards at Hexham, North Tyneside and Wansbeck General Hospitals during the study. A

targeting tool has been developed for nursing staff to refer oncology patients to a pharmacist for review if there are any perceived issues with their medicines during the patients' pre-assessment visit. The tool identifies patients who are taking four or more medicines; may have compliance issues; have an unclear medication history or are taking CAMs. All patients identified by the targeting tool were considered. Nursing staff were involved in consenting patients for inclusion, ensuring that patients had time to talk and were willing to be questioned. The selection process was monitored to ensure a range of patients with different cancer types (Table 1) representative of the local oncology patient population was interviewed. After screening and initial referral a total of 44 patients were recruited into the study.

A questionnaire was designed and used to interview patients about their use of CAM during their routine clinical medication review. The aim of the interview was to gain qualitative data about patients' knowledge and attitudes towards CAM. Adults who attended oncology clinics were eligible for interview. The same interviewer visited the clinics on several days over a 3-month period. This point-prevalence study enabled the proportion of patients who took CAMs to be identified, and gave an insight into their reasons for this.

Table 1. Distribution of participants' cancer types

Cancer type	Number males	Number females
Colorectal	5	9
Breast		14
CNS (Brain)	1	
Lung	3	3
Haematological	3	2
Oesophageal	1	
Pancreatic	1	1
Renal	1	

Table 2. Summary of CAMs taken by patients in the study and reasons given for their use

Complementary medicine	Frequency of use	Reason for use
1 Cod liver oil	Every morning	Aches and pains
2 Cod liver oil	Daily (when remembered)	Joints and general health
3 Cod liver oil	Daily	Bones
4 Cod liver oil	Daily	Colds
5 Liquorice	One stick per day	Bowels, digestion and cancer
6 Selenium	Daily	None given
Echinacea	Daily	None given
7 Garlic capsules	Daily	Cancer
Chiorella	Daily	Cancer
Vitamin E	Daily	Cancer
8 Vitamin E	Daily	General health
Vitamin C	Daily (2 tablets)	General health
Cod liver oil	Daily	General health
Aloe vera juice plus	Twice daily	Mucous membranes
Omega fatty acids (combination)		
9 Primrose oil tablets/capsules	Daily (4 per day)	None stated
10 Effalex (fatty acids)	When remembered (one teaspoon)	To aid digestion
Osteocare calcium tablets	Daily (one tablet)	Bones
Herbal teas		None stated
Evening primrose oil		None stated
11 Caleb tree syrup	Usually every other day in tea or coffee	Bowels
Herbal soap		Acne and skin problems
12 Carktol		Cancer
Vitamin D		Cancer
Many more — cannot recall		Cancer

A staff questionnaire was designed and used across the Trust to interview oncology nursing staff and pharmacists who were responsible for medicines management to this group of patients. The interview was used to collect data on their knowledge of CAM and their attitudes towards it. There were 14 questions in total. Staff members were asked to estimate the prevalence of CAM use within oncology and to state what types of people they thought would be more likely to use CAM. They were also questioned about their experiences and confidence in dealing with CAM, how they compared CAM with conventional medicines and their awareness of potential interactions involving CAM.

Patient questionnaire

A medication history was taken from all participants. Those that did use CAMs were asked further questions about their use and their attitudes towards them. Patients who did not use any CAMs were asked if they had considered using CAMs, where they would find out information about CAMs, and if

they were aware that CAMs can sometimes interact with conventional medicines.⁷ For all patients, background information was obtained from patient medical notes to determine the type of cancer, past medical history, type of chemotherapy and date of diagnosis.

Results

The sample

Of the 44 patients interviewed across the trust (29 female) 12 attended North Tyne-

side oncology unit, 21 attended Wansbeck and 11 attended Hexham. The mean age of participants was 60 years. The most common cancer types were breast and colorectal cancer, followed by lung cancer (Table 1).

Prevalence of CAM use

CAMs were used by 12 (27%) patients, five of whom used a single CAM while seven used more than one. Table 2 lists the CAMs taken along with the frequency and reason for use. Cod liver oil was the most commonly used CAM (five patients regularly took cod liver oil). Others included vitamins, evening primrose oil and fatty acids. Interestingly not a single patient had any idea of the strength of their CAMs and at least three took their CAMs only when they remembered.

Interactions

Patients' conventional and complementary medicines were recorded and later analyzed to determine whether there were any known interactions between them. No interactions were found with the patient's chemotherapy although for many of the CAMs there was little or no information available. The challenges pharmacists face when monitoring for interactions and the need to use wider information resources than traditional references texts for interactions, such as *Summary of Product Characteristics* (SPCs) and *Stockley's Drug Interactions* is highlighted in the discussion.

Patient attitudes about CAM

Several of the 12 patients had taken CAMs for many years: five patients had been taking their CAMs for at least 10 years and

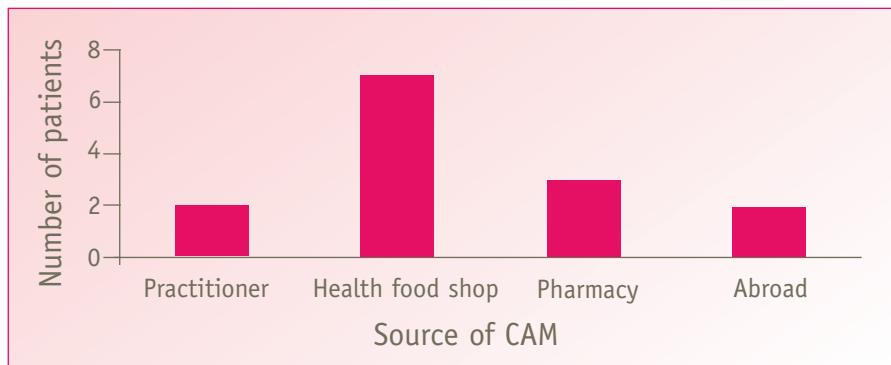


Figure 1. Sources of complementary medicines (CAMs)

two patients had been using them for at least one year. The other five patients who were using CAMs started taking them after they were diagnosed with cancer, one of whom was planning to stop. Cost was an issue for some patients who were spending between £5 and £30 on CAMs per month. Seven of these patients thought that CAMs helped them, three weren't sure and two thought CAMs probably didn't work. Two patients said that they had experienced adverse effects after taking CAM (slippery elm causing migraine and sickness; Saint John's Wort causing sickness; Echinacea causing diarrhoea).

Source of information about CAMs and supply sources

The source of CAMs supply is shown in Figure 1. The main source of information about CAM was the media — other sources included word-of-mouth, the source of the CAM, conventional practitioner, complementary practitioner and relatives.

When asked about whether the participants informed medical staff that they were taking CAM, six patients confided in a doctor or nurse, while six patients did not mention it at all. One patient said that she did not mention it because she was going to stop taking it. Another said that nothing had really been mentioned about it. The remaining four patients felt that it was not important or relevant. When asked what they would do if they were told that their CAMs interacted with their conventional treatment, 10 patients said they would stop taking it, one said they would consult their GP and one said they would consult their CAM practitioner.

A total of 17 patients said they would not consider taking CAMs. Of these patients two had tried some form of CAM previously and felt it did not benefit them and four people additionally said they tried to take as few medicines as possible. The most common reason given (n = 15) was that they did not believe CAMs would be of benefit. Some patients (n = 11) were not taking CAMs but would consider them in the future, three of whom said they would only consider them with medical

advice. Every patient was asked if they were aware that some CAMs can interact with conventional medicines — 27 patients said they were aware while 17 were not.

Staff attitudes about CAM

The most commonly estimated prevalence of patients' CAM use by staff members was 30 to 40% — the majority of staff interviewed thought that women would be more likely to use CAM than men.

Most staff members thought that patients 'only sometimes confided' in them about their use of CAM. One of the nursing staff suggested that this was because patients don't always think of things as being CAMs (for example, cod liver oil) and so forget to mention it.

When asked if they would tend to encourage or discourage use of CAMs, most staff said that this would depend on the particular medicine. Additionally they mentioned that if they did not consider that it would do any harm then they would neither encourage nor discourage use. The majority of staff (8) said they had concerns over safety and use of CAMs alongside conventional medicines.

Each member of staff was asked if they were aware of any interactions between CAM and conventional medicines. The

majority was aware of some interactions, but few could name specific examples, although St. Johns Wort was noted as having several interactions. All staff questioned thought that there was an inadequate awareness of potential interactions of CAM with conventional medicines.

Discussion Use of CAMs

This study gives an insight into the use of CAM by oncology patients within the Northumbria Healthcare NHS Trust, but more importantly it highlights the need for pharmacists to take a more active role in the identifying and managing patients using CAMs.

The definition of CAM can vary slightly but has been quoted as 'a group of diverse medical and health care systems, practices, and products not considered part of conventional medicine'.³ Researchers have found that typical CAM users tend to be educated, younger people with a higher socio-economic status, and are more commonly female.^{2,4} Reasons for the increasing use of CAM within oncology are thought to be a result of limitations of conventional treatment, a desire to gain personal control, or an increased awareness of CAM due to media and advertising.^{1,2,4}

The prevalence of CAM use determined

Table 3. List of common CAM interactions*

CAM	Potential interaction/ Problems
Co-enzyme Q10:	Doxorubicin and general reduction of effect of chemotherapy and radiotherapy
Echinacea	Avoid in Hodgkin's disease, leukaemia, myeloma or lymphoma
St John's Wort:	Reduced effectiveness of chemotherapy increase side-effects associated with radiotherapy
Mistletoe:	No proven to be a safe and effective cancer treatment
Co-enzyme Q10	Warfarin and oral anticoagulants
Gingko Biloba	Warfarin and oral anticoagulants
St John's Wort	Warfarin and oral anticoagulants
Cranberry Juice	Warfarin and oral anticoagulants
Black Cohosh	Avoid in breast or endometrial cancer patients
Red Clover	Avoid in breast or endometrial cancer patients
Wild Yam	Avoid in breast or endometrial cancer patients
Saw palmetto	Avoid in prostate cancer patients

*adapted from Interactions between cancer treatment and herbal and nutritional supplements and medicines produced by the RCR⁷

in this study (27%) is similar to the estimated total prevalence of CAM use in the UK (25%)¹ but lower than that reported for other oncology patient populations studied. One systematic review of the available evidence on the use of CAM in cancer patients concluded that the large differences in prevalence found between studies are likely to be due to different understanding and definitions of CAM.⁸

A key finding was that patients were unable to state the strength of the CAM they took. This could cause problems, for example chronic consumption of high dose vitamin E (400–800 IU per day) can lead to toxicity, causing symptoms such as fatigue, weakness, headache, blurred vision and rash.⁸ Because patients self-medicate with CAM, it is important that pharmacists educate patients on accepted dose ranges and the strength of medicines that they are taking and on choosing supplements where the strengths are clearly stated.

Interactions

The potential for interactions between complementary and conventional medicines for the patients in this study was low. The study showed the targeting tool used by nursing staff to identify patients for pharmacy assessment was successful in alerting pharmacy to patients who were taking CAMs enabling pharmaceutical input to be provided. For many of the CAMs used there is little or no evidence available on potential interactions, so problems may not be highlighted. It would therefore be prudent to use all CAMs with a degree of caution when combining them with conventional therapies. Many chemotherapy drugs have a narrow therapeutic window, and therefore potential interactions with CAMs are particularly important. With relatively little information on interactions with CAMs, pharmacists must use their training and expertise in pharmacology to help assess patients for potential interactions. Interactions and adverse effects are more likely to occur in people who have chronic medical conditions, such as liver or kidney disease. Pharmacokinetic interactions with effects on absorption, distribution, metabolism or excretion are most common.²

This can result in a patient receiving either a sub-optimal dose or an overdose of their conventional medicine.^{9,10} One of the most common causes of drug interaction is from the inhibition or induction of cytochrome P450 enzymes, which are involved in the oxidation of many drugs. There is evidence to suggest that co-enzyme Q10 might reduce the activity of chemotherapy drugs that generate free radicals, such as doxorubicin.¹¹

There may also be problems with the use of CAMs because of interactions with disease. For example, the RCR recommend that patients with hormone-sensitive cancers should avoid certain treatments, such as saw palmetto in prostate patients and black cohosh in breast cancer.⁷ Some of the more common CAM interactions highlighted by RCR are listed in Table 3. It is thought that antioxidants may cause problems by protecting harmful tumour cells from oxidative damage.^{4,9,10} Pharmacists should be encouraged to record any possible adverse interactions that they observe and report them through the Yellow Card Scheme (www.mhra.gov.uk).¹²



© Christine Knott

Although most patients were aware that CAMs could interfere with conventional medicine a large proportion of patients (n=17) did not know this could be a problem. This is consistent with the common public perception that because CAM is natural it is safe.¹³ Patient education is definitely an issue here and a better understanding of CAM by patients and staff could reduce the risk of potentially serious adverse effects from occurring. Most people said they would stop taking their CAM if they were told it could interfere with their conventional treatment.

Following a European Directive on traditional herbal medicinal products, many CAMs will need to be licensed or

comply with the MHRA Traditional Herbal Medicines Registration Scheme by April 2011. This is to be welcomed because it will ensure the quality of the CAMs that are available to the public and increase our knowledge about these medicines.

The most common source of CAM was health food shops and the most common source of information was the media — in particular the internet. The scenario of the patient presenting with a print-out of information on a CAM from the internet is increasingly common. Pharmacists are often required to advise patients on these medicines, particularly because the patient may have neglected to mention them to their doctor. There are many internet sites that provide advice and information on complementary and alternative medicines in cancer. Some of these use an evidence-based approach towards CAM¹⁴ and some promote complementary therapies in combination with conventional treatment.¹⁵ Unfortunately, there are many sites that sensationalize the benefit of alternative medicines. The scope of information available on the internet is huge, and varies widely in its credibility, which is a concern.

A large proportion of patients failed to inform their doctor of their CAM use and did not consider it to be relevant or important to do so. More awareness of potential interactions with conventional medicines should be raised, and staff should ensure that full drug histories are taken from every patient, to include CAMs.¹⁶ Patients should be encouraged to bring in their medicines, including herbals from home and to remember to inform staff if medicines change. The importance of providing a full drug history and the potential for drug interactions should be conveyed to patients, and their use of CAM should be clearly documented.

Conclusions

In our study we found that patients did not view CAMs as medicines and were not aware of their potential interactions with conventional medicines. Pharmacists must be aware of and monitor CAM use in their patients, and should ensure they use their

clinical skills to assess for potential risks of CAM use when evidence in the literature is lacking. ❀

Declaration of competing interests

The authors declare that they have no competing interests.

Steve Williamson, consultant pharmacist for cancer services, Northumbria Healthcare NHS Trust, **Louise Maguire**, clinical pharmacist, Newcastle Hospitals NHS Trust [Ms. Maguire was a pre-registration pharmacist at Northumbria Healthcare NHS Trust at the time of the research]. Correspondence to: Steve Williamson at Northumbria Healthcare NHS Foundation Trust, Pharmacy, North Tyneside Hospital, Rake Lane, North Shields, Tyne and Wear, NE29 8NH. Email: steve.williamson@nhct.nhs.uk

References

1. Cassileth BR, Vickers AJ. High prevalence of complementary and alternative medicine use among cancer patients: implications for research and clinical care. *J Clin Oncol* 2005; **23**(12): 2590–2592.
2. Cassileth BR, Ernst E. The prevalence of complementary/alternative medicine in cancer — a systematic review. *Cancer* 1998; **83** (4): 777–782.
3. Richardson MA, Sanders T, Palmer L, Greisinger A, Singletary SE. Complementary/alternative medicine use in a comprehensive cancer centre and the implications for oncology. *J Clin Oncol* 2000; **18**: 2505–2514.
4. Sparreboom A, Cox MC, Acharya MR, Figg W. Herbal remedies in the united states: potential adverse interactions with anticancer agents. *J Clin Oncol* 2004; **22**(12): 2489–2503.
5. Molassiotis A, Fernandez-Ortega P, Pud D *et al.* Use of complementary and alternative medicine in cancer patients: a European survey. *Annals of Oncology* 2005; **16**: 655–663.
6. Royal College of Radiologists. *Interactions between cancer treatment and herbal and nutritional supplements and medicines: Information for doctors*, 2006. Ref No: BFCO(06)3.
7. Zollman C, Vickers A. ABC of complementary medicine: what is complementary medicine? *BMJ* 1999; **319**: 693–696.
8. Cassileth BR, Lucarelli CD. *Herb-drug interactions in oncology*, BC Decker Inc. 2003.
9. Lee CO. Integrated care. Herbs and cytotoxic drugs: recognising and communicating potentially relevant interactions. *Clin J Oncol Nurs* 2005; **9**(4).
10. McCune JS, Hatfield AJ, Blackburn AR *et al.* Potential of chemotherapy-herb interactions in adult cancer patients. *Support Care Cancer* 2004; **12**: 454–462.
11. Portakal O, Ozkaya O, Erden Inal M *et al.* Coenzyme Q10 concentrations and antioxidant status in tissues of breast cancer patients. *Clin Biochem* 2000; **33**: 279–84.
12. Tricky Wort. Onlooker, *Pharm J* 2000; **264**(7101): 896.
13. Medicines and Healthcare products Regulatory Agency. *Herbal medicines regulation and safety* available at <http://www.mhra.gov.uk/Howweregulate/Medicines/Herbalandhomeopathicmedicines/Herbalmedicines/index.htm>
14. National Cancer Institute website <http://www.cancer.gov/>
15. Penny Brohn Cancer Care www.pennybrohncancercare.org (formerly Bristol Cancer Help Centre <http://www.bristolcancerhelp.org>)
16. Markman M. Safety issues in using complementary and alternative medicine. *J Clin Oncol* 2002; **20**(18): 395–415.

Breast cancer diagnosis and treatment: an update

Epidemiology

Breast cancer is the most common cancer in the UK.¹ There are approximately 44,600 women and 300 men diagnosed each year in the UK.¹ More than 12,000 women and approximately 100 men die from breast cancer in the UK each year, making it the second most common cause of death in women after lung cancer.¹

Types of breast cancer

An early form of breast cancer in which there is evidence of cancerous cells within the ducts (ductal cancer *in situ*) is highly localised with no spread to the surrounding breast tissue.¹ If left untreated, however, this can develop into invasive ductal breast cancer — the cause of around 70–80% of cases. Similarly, carcinomatous cells can develop in cells lining the lobules, without spread, but around 10% of breast cancers are invasive lobular cancers, and these are

more common in women aged 45–55 years but rare in men.

Familial breast cancer, accounting for 5–10% of all cases, is caused by the inheritance of one of the mutated genes; *BRCA1*, *BRCA2*, *TP53* or *PTEN*.¹ Around two-thirds of women have hormone-receptor positive tumours, in which endogenous oestrogen and progesterone promote tumour growth.¹ Some cancers test positive for human epidermal growth factor receptor-2 (HER2), which also promotes cancerous growth.¹ Inflammatory breast cancer in which cancer cells accumulate in lymph channels and ducts to cause blockage and acute inflammation, is rare.¹ Paget's disease is associated with 1–2% of cases.¹ It starts with an eczema-like rash, usually affecting the skin around one nipple. In 90% of such cases an underlying mass is present, which can be invasive.¹

Presentation

Breast cancer is most commonly diagnosed by breast screening in asymptomatic women or by self-examination. Warning signs may include any of the following:¹

- change in size, shape or feel of breasts
- the presence of a new lumpy mass that cannot be moved independently from overlying skin
- thickening in one breast or armpit
- any puckering, dimpling or redness of the skin
- changes in the position of nipple, nipple inversion, nipple rash or discharge
- a new one-sided pain or discomfort.

The NHS Breast Screening programme is perhaps one of the most successful in Europe, saving an estimated 1400 lives each year.² The programme has contributed