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Is there a role for complementary therapy in the management of leukemia?

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Abstract

Patients with leukemia often seek additional treatments not prescribed by their oncologist in an effort to improve their cancer treatment outcome or to manage symptoms. Complementary therapies are used in conjunction with traditional cancer treatments to decrease symptoms and side effects associated with cancer or cancer treatment, and to improve patients' overall quality of life. Complementary therapies are distinct from so-called 'alternative' therapies, which are unproven, ineffective and may postpone or interfere with mainstream cancer treatment. Complementary therapies are pleasant, inexpensive, nonpharmacologic and effective. For patients with leukemia, the complementary therapies that are always appropriate include mind–body interventions, such as self-hypnosis, meditation, guided imagery and breath awareness. Massage and reflexology (foot massage) decrease symptoms with effects lasting at least 2 days following treatment. Acupuncture is very beneficial for symptom management without adverse consequences. Physical fitness with regular exercise and healthy dietary habits can significantly decrease side effects of cancer treatments and may prolong survival. Botanical extracts and vitamin supplements may interfere with active cancer treatments, and should be discussed with the oncologist or pharmacist before use.

Keywords

acupuncture; botanical supplements; cancer; complementary therapies; leukemia; massage therapy; mind; body therapies; nutrition; physical fitness

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Complementary versus alternative therapies

Patients with leukemia often seek additional treatments not prescribed by their oncologist in an effort to improve their cancer treatment outcome or to manage symptoms. The term 'complementary and alternative medicine' has been in common use to describe therapies that are not typically part of mainstream medicine. Unfortunately, the term is misleading because it combines two very different approaches. 'Alternative treatments' are unproven or disproved remedies promoted for use instead of gold-standard cancer care, and they have no role in the treatment of cancer or other life-threatening illnesses [1]. Combining the terms 'complementary' and 'alternative' lends an unwarranted legitimacy to the alternative treatments and taints the value of adjunctive, evidence-based complementary modalities.

There are no viable 'alternatives' to mainstream cancer care. The so-called 'alternative therapies' are not effective and often delay receipt of needed treatment until the tumor has advanced to a later stage, thus impacting survival. They should be avoided. Many over-the-counter agents directly interfere with medical treatments by chemically blocking the action of the cancer treatments, as seen with the use of many botanical extracts or antioxidants concurrent with radiation or chemotherapy [2,3], or by stimulating cancer cell growth [4], as occurs with botanical extracts such as cat's claw and dragons blood, which have often been used by parents in an effort to treat their child's leukemia.

By contrast, complementary therapies are used in conjunction with mainstream medical therapies and are evidence-based. They decrease side effects associated with cancer or its treatment. These therapies do not directly treat the cancer. Rather, they decrease side effects and improve quality of life. Complementary therapies are rational, evidence-based and cost effective. They are pleasant and, importantly, provide patients with a sense of control.

Prevalence of complementary therapy use

The main complementary therapies include massage, acupuncture, mind–body interventions, including self-hypnosis, meditation, yoga and tai chi/qi gong, botanical and other supplements plus fitness (nutrition and physical activity).

There is minimal specific information regarding patients with leukemia and their utilization of complementary therapies. Approximately a third of children with cancer have leukemia; however, the studies do not separate the results into different cancer types when reporting complementary therapy use concurrent to cancer treatment. Only two reports specifically discuss complementary therapy use in patients with leukemia. Gupta documented that 56% of patients with leukemia in northern India used complementary therapies, with 33% using Ayurveda [5]. Hensel *et al.* surveyed 247 chronic lymphocytic leukemia patients in Germany, with 44% using complementary therapies [6]. Massage and mind–body therapies were not utilized in this German cohort. In total, 26% used vitamin supplementation, 18% mineral supplementation, 14% homeopathy, 9% mistletoe therapy and 7% used acupuncture. Patients largely used these treatments without physician recommendations and 32% of patients received their information through the internet. Of particular concern is the high percentage of patients who reported using vitamin supplementation, as these products are not necessarily safe when taken concurrent to cancer treatment. Mistletoe therapy is not legally available in the USA, but is commonly used in Europe.

In the UK, complementary therapy use in adults with all cancers is similar to that of the general population with approximately 33% of patients using these therapies [7]. While 33% reported that they had used complementary therapies prior to diagnosis, 29% used them after the cancer diagnosis. Of patients using the complementary therapies, 64% chose aromatherapy and

reflexology treatments, both of which were offered at their cancer center. Another 23% of patients used acupuncture, 22% herbal medications and 20% yoga.

When pediatric cancer patients are questioned regarding their use of complementary therapies, 30–80% used one or more complementary therapies in conjunction with traditional cancer care [8–10]. Children have an especially high percentage of vitamin and nutritional supplement use, with over 40% of patients consuming these products [11]. Parents most often state that they want to "do everything possible" as the reason for including these therapies with the cancer treatment [12]. The mind–body therapies were the second most commonly used complementary therapies. In adolescents with cancer, 80% report to have used complementary therapies in their lifetime, with 50% having used them in the previous month [11].

Many patients do not report their use of complementary therapies to the oncologist, with the main reason being that the oncologist did not ask [6]. Of particular concern is that herbal teas, plant extracts and therapeutic vitamins comprised the highest percentage of use in most patient surveys, as these therapies risk directly interfering with cancer treatment [13,12]. The complementary therapies of guided imagery, self-hypnosis, massage, acupuncture and physical fitness do not have the same potential for adversely affecting the cancer treatment.

Complementary therapies for leukemia symptom relief

Many of the symptoms associated with both the acute and chronic leukemias are decreased by the complementary therapies, including the symptoms of fatigue, nausea, stress, decreased appetite, bone and joint pain, fevers and sweats. In addition, symptoms associated with chemotherapy and radiation therapy to treat leukemia are very responsive to the complementary therapies of massage, acupuncture, mind–body interventions, physical fitness and good nutrition. While many of the clinical trials evaluating specific complementary therapies did not include leukemia patients, the symptoms addressed by the treatments are common to patients with leukemia, and the study results can be extrapolated into the leukemia patient population.

Massage

Massage has been demonstrated to be very beneficial for decreasing symptoms of pain, nausea, fatigue, anxiety and insomnia in clinical trials [14,15]. Massage techniques range from light touch to deeper tissue pressure and include reflexology treatments involving only foot massage. The choice of technique is dependent on the patient's clinical condition. Although there are no studies evaluating the platelet level required for deep tissue massage, thrombocytopenia is a relative contraindication to deep tissue massage and, in this setting, light-touch massage or reflexology may be a better treatment option. Those who are frailer and who are near the end of life may tolerate the reflexology treatment rather than full body massage. Symptom management is achieved equally through the reflexology and the full body massage, with an average decrease in symptom intensity by 50% for all presenting complaints, and the relief lasted at least 48 h post massage/reflexology treatment [14]. The massage treatments have a very favorable risk–benefit ratio and very low risk of adverse side effects.

Acupuncture

Acupuncture is part of the ancient Chinese traditional system of medicine and has been used for millennia. The acupuncture points used are based on the theory that energy or 'qi' is thought to flow along multiple channels or 'meridians', which approximately correspond to tissue planes. Disease occurs when these energy channels become blocked. Insertion of the thin, sterile, filiform needles superficially into these acupuncture points is thought to release the blocked energy, thereby restoring health.

There is minimal risk of injury from acupuncture treatments, with reports of less than one adverse event in over 10,000 acupuncture treatments [16]. Acupuncture needles are 38–40 gauge and filiform, as opposed to the 21–25 gauge hollow needles used for phlebotomy. The acupuncture needles are only inserted approximately a quarter inch or less depending on the exact insertion site, and, therefore, acupuncture is considered safe during acute anticoagulation with Coumadin® or heparin. Thrombocytopenia is not a contraindication unless the platelet count is below 50,000. There is one report of acupuncture ear studs causing auricular hematomas during acute dilutional thrombocytopenia [17]; however, acupuncture has also been safely administered repeatedly during acute pregnancy-induced thrombocytopenia for analgesia [18]. Electroacupuncture should be avoided during anticoagulation or acute thrombocytopenia, although there are no reports demonstrating acute toxicity.

Research has demonstrated acupuncture to be beneficial for many cancer-related symptoms [16]. Certain chemotherapy agents, such as paclitaxel, can cause neuropathy. This chemotherapy-associated peripheral neuropathy has favorably responded to acupuncture treatments [13]. Chemotherapy dose reduction is at times necessary to prevent further neuropathy progression. Decreasing the neuropathy symptoms through acupuncture can maximize the chemotherapy delivered to a patient, thereby increasing the chance for successful cancer outcome.

Nausea prevention and treatment is also very successful with weekly acupuncture [12]. Optimal timing of the acupuncture treatments is 1–2 days prior to the chemotherapy infusion, and continues weekly throughout the chemotherapy. Xerostomia, or extreme dry mouth. following head and neck radiation therapy is also very responsive to acupuncture treatments with increased salivation compared with control [19,20]. Acupuncture also decreases the vasomotor symptoms of hot flashes [21,22] and decreases pain [23].

Mind–body

The mind–body practices, such as meditation, self-hypnosis, guided imagery and music therapy, have been demonstrated to decrease cancer-related symptoms [24]. A recent trial examined a 15-min presurgical self-hypnosis session compared with empathetic listening in women who were undergoing excisional breast biopsy or lumpectomy. The self-hypnosis group experienced decreased nausea, pain, fatigue and discomfort when compared with the control group. In addition, the self-hypnosis group required less time in the operating room and the recovery room, less anesthesia and was more cost effective, saving the hospital nearly US$800 per patient through decreased resource utilization [25].

Music therapy has been demonstrated to be effective in decreasing mood disturbance in patients undergoing stem cell transplantation [26], with significantly decreased anxiety and depression in those who received music therapy compared with usual care. Music therapy involves more than simply listening to music. Music therapy is delivered by professional musicians who have received advanced training in music therapy. Rather than using words as in psychotherapy, music is utilized. Music bypasses many higher cortical centers, and allows people who are frailer or who do not have access to words to derive benefit from the music therapy.

Sahler *et al.* examined music therapy in conjunction with guided imagery for persons receiving stem cell transplantation [27]. In contrast to the results seen by Cassileth *et al.* [24], the combined music therapy with guided imagery participants encountered difficulty in adhering to the imagery. The researchers concluded that the patients were often too ill to actively focus on the imagery. A more passive and receptive intervention may be more appropriate for those patients who are very ill and who are frail.

Botanical & nutritional supplements

A large percentage of cancer patients, as well as the German Chronic Lymphocytic Leukemia (CLL) patients patients, surveyed used botanical and nutritional supplements in conjunction with their cancer treatments. In contrast to the aforementioned complementary therapies, which are appropriate for all patients with leukemia, botanical and nutritional supplements may be contraindicated depending on the therapy used and the cancer treatments received.

Potential risks of using botanical supplements—The consumption of large quantities of supplements may interfere with obtaining adequate nutrition through decreased food intake, especially for children [10,28]. In addition, the metabolism of these supplements may not be similar in children compared with adults, leading to increased toxicity. The botanical extracts are a complex mixture of chemical structures, which can have unpredictable effects on the immune system. There is ongoing research through the National Institute of Health funding regarding botanical use as immunomodulators. Outside of a well-designed clinical trial, using botanical extracts in patients with leukemia for affecting the immune system is not advised [10].

Patients can interpret *in vivo* or animal studies as definitive evidence and begin using the product before any safety and efficacy data are available from human studies [29]. The aggressive marketing of botanical products and nutritional supplements to cancer patients can add to the confusion and convince patients that these products are safe to use when there may not be scientific evidence of safety. Unfortunately, some of the popular botanical therapies that parents are giving to children with leukemia can actually increase growth of the cancer cells. A study evaluating cat's claw, dragon's blood and mistletoe in childhood leukemia cells showed high resistance to these products. There was increased leukemic cell survival by 45% for mistletoe, 96% by cat's claw and 83% for dragon's blood [4].

Another risk of using botanical extracts in cancer treatment is that many of these products are advertised to "boost the immune system". While this may sound positive, boosting the immune system may be detrimental for persons who are receiving immunosuppression through corticosteroids, methotrexate or other medications [30]. Corticosteroids are commonly used with chemotherapy for leukemia. Patients taking unregulated botanicals to boost their immune system may directly interfere with their chemotherapy. There is also at least a theoretical risk for leukemia patients of inducing cancer recurrence through stimulating the immune system [10].

In addition, these agents are not regulated by the US FDA and, as such, there are issues of quality control, possible heavy metal contamination, endotoxin presence and stability issues that can make using these products problematic. The United States Pharmacopeia (USP) is an independent agency with offices in Rockville, (MD, USA), Hyderabad (India), and Shanghai (China). The USP verifies the identity, strength, purity and quality of dietary supplement finished products, dietary supplement ingredients and pharmaceutical ingredients. Products that bear the USP seal have been verified to contain what is stated on the label. This verification, however, does not address issues of safety and efficacy. A minority of manufacturers have the USP verification, as this process is not required by any federal agency.

Potential benefits of botanicals—Shanafelt *et al.* from the Mayo Clinic reported that, after their initial *in vitro* report of epigallocatechin gallate (EGCG) extract inducing apoptosis in leukemic B cells from CLL patients, a large number of their patients began using EGCG despite no evidence regarding clinical efficacy and no available data regarding possible toxicity, or optimal dosing or schedule. This increased patient use resulted in a case series using EGCG in early CLL patients [29] and a newly released dose-escalation trial examining EGCG extracts in asymptomatic stage (e.g., stage II patients with CLL) [31]. The Phase I study used

decaffeinated green tea extract administered in increasing doses up to 2000 mg twice daily. There were few dose-limiting toxicities, with two out of 33 patients experiencing a grade 3 toxicity. More than 75% of the patients who were receiving between 1200 and 2000 mg twice daily experienced at least a partial response, defined as reduction in the absolute lymphocyte count of greater than 20% from the pretreatment level for at least 2 months. Less than 20% of those receiving 400–1000 mg twice daily achieved a biologic response. The mechanism of action is unknown and there are multiple possible theories under investigation.

While these EGCG extract results are encouraging for early-stage CLL patients, it is important to note that these patients were not receiving any concurrent cancer treatment aside from the EGCG extract. Another recent study demonstrated that EGCG extract completely blocks bortezomib activity, rendering the agent useless in its anti-tumor activity [32].

The medicinal mushrooms show promise from *in vitro*, *ex vivo* and animal models for increasing cancer cell death and decreasing tumor growth. The *Agaricus* mushroom has shown promising results in *in vitro* studies using human myeloid leukemia cell lines regarding decreasing leukemic cell growth [33]. Additional research evaluating various medicinal mushrooms and their immunomodulatory properties are ongoing, but until clinical trial results are available and more data is present regarding safety and potential toxicity, it is prudent for leukemia patients to avoid using these supplements.

Multivitamin use & potential risks

Currently US$20 billion are spent annually on nutritional and botanical supplements in the USA [101]. Much of this is in the hope of preventing or curing disease. The most common complementary therapy for many cancer patients is multivitamin and multimineral use. Unfortunately, clinical trials that have examined the use of high dose single vitamin and nutrient supplement for cancer prevention and cancer treatment have not shown benefit [34–36]. The Selenium and Vitamin E Cancer Prevention Trial (SELECT) was stopped early owing to adverse outcomes with increased risk of prostate cancer in the vitamin E group and increased incidence of diabetes in the selenium group [36]. The Physicians Health study examining vitamin C and E for cancer prevention also did not show any benefit [35]. A recent publication demonstrated reduced activity of bortezomib in healthy volunteers taking 1000 mg of vitamin C orally. The results were confirmed in a xenograft model of human multiple myeloma in severe combined immune-deficient (SCID) mice [37]. This suggests that oral doses of vitamin C that are routinely consumed in over-the-counter supplements clinically block the effects of boronate class proteasome inhibitors. Similar effects of ECGC blocking bortezomib activity was mentioned previously [32].

The 2008 World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) formal recommendations are to meet our nutritional needs through food products alone rather than through vitamin and mineral supplements; supplements are also not advised for cancer prevention [38]. The marketing for these nutritional supplements is very strong and the public can easily be convinced to purchase and consume these products.

Antioxidant controversy

Many of the multivitamin supplements available today through health food stores, pharmacies and nutritional supplement retailers contain doses of individual vitamins well above the current recommended daily intake or recommended daily allowance set by the Food and Nutrition Board of the National Academy of Sciences. Certain cancer treatment regimens that work through generating reactive oxygen species (ROS) can have decreased efficacy when combined with a high dose of vitamin supplementation. Specifically, the high antioxidant-containing vitamins A, C and E can interfere by blocking ROS.

A randomized clinical trial among 540 head and neck cancer patients examining the effects of α-tocopherol (400 IU/day) and β-carotene (30 mg/day) supplements concurrent to radiation therapy demonstrated decreased effectiveness of the radiation therapy and more aggressive tumors in those who were receiving the antioxidants [2]. Similar results were found from the β-carotene studies in male smokers, demonstrating an 18–28% increased incidence in lung cancers in the group who received β-carotene compared with placebo [39,40]. Additional analysis of the β-Carotene and Retinol Efficacy Trial (CARET) showed a benefit for increased fruit and vegetable intake only in the placebo arm. The placebo participants in the top quintile of fruit intake had a risk ratio of 0.63 for lung cancer and the risk ratio was 0.68 for cruciferous vegetable intake. Those who had increased intake of β-carotene through supplements did not benefit from higher fruit and cruciferous vegetable intake [41].

Concerns have been demonstrated by vitamin C adversely affecting chemotherapy agents by decreasing the production of ROS. A prominent meta-analysis of antioxidant use concurrent to chemotherapy and radiation therapy consensus is that outside of a well-designed clinical research trial, the use of antioxidants in conjunction with chemotherapy and radiation therapy is not advised [42].

Fitness: nutrition & physical activity

The importance of healthy nutrition also cannot be overemphasized. The WCRF/AICR 2008 Summary of Food, Nutrition, Physical activity and the Prevention of Cancer: a Global Perspective recommendations regarding diet and physical fitness stress the importance of increasing plant foods and decreasing animal foods in our diet [38]. According to the WCRF data, approximately a third of the cancers in Western, high-income countries are attributable to factors relating to food, nutrition and physical activity [43]. Changing the patterns of behavior through increasing education, as well as other means, will be of great benefit in cancer prevention [44]. Diets that are rich in cured meat or smoked meat and fish have been associated with an increased risk for childhood leukemia, while consumption of increased vegetables and bean-curd were associated with a decreased risk [45].

The benefits of increased adherence to a plant-based diet similar to the Mediterranean style diet have been shown in a number of studies and in one recent meta-analysis involving 1.5 million patients [46]. Those people who had increased adherence to the Mediterranean diet had a 9% reduction in overall mortality, 9% reduction in cardiovascular mortality, 6% reduction in cancer mortality and 13% decreased incidence of Parkinson’s and Alzheimer’s disease. Unfortunately, most people do not comply with the Mediterranean diet recommendations [47,48].

Children with acute lymphoblastic leukemia (ALL) are at increased risk for cardiovascular disease and obesity as complications of their cancer treatment [49]. Increased adherence to dietary recommendations regarding the Mediterranean plant-based diet may decrease the risk for these complications [46]. Unfortunately, many survivors do not follow these dietary recommendations. In a group of 72 adult survivors of childhood ALL surveyed regarding their dietary patterns, no study participant reported complete adherence to any of the guidelines set forth by the WCRF/AICR, the Dietary Approaches to Stop Hypertension (DASH) diet, or the 2005 USA Department of Agriculture food guide [49]. Approximately half of the participants reported consuming at least five servings of fruits and vegetables per day, adhering to the AICR recommendations; however, the consumption of both sugar and sodium were above the AICR guidelines and consumption of whole grains was inadequate.

An analysis of dietary adequacy was undertaken in patients who received treatment for B-cell lymphoma at the MD Anderson Cancer Center [50] and 94% of participants were found to have either excessive or inadequate intakes of nutrients, including folate, vitamin A, iron,

selenium and calcium. Of particular concern is that high dietary vitamin A intake may increase the risk of lung cancer in smokers [39,40], while selenium may increase the risk of prostate cancer in men [36].

The decreased level of activity present in children who have leukemia has been studied extensively [51–59]. Implementing physical fitness programs, both during the acute hospitalization phase [60,61] and following the cancer treatment, may be beneficial for decreasing side effects, such as osteoporosis, decreased muscle tone and slowing the weight gain often associated with postcancer treatment [43,51,53,62–65]. These programs will also assist in establishing healthy lifestyle habits for decreasing secondary cancer risks in this population.

A 3-week in-patient walking program intervention consisting of 12 min of daily walking significantly improved fatigue, and decreased symptoms of distress and depression in patients undergoing bone marrow transplantation [60]. Another study evaluating the effects of increased fitness on decreasing osteoporosis for children undergoing treatment for ALL [61] did not show any benefit; however, the exercise intervention group did regain their pretreatment weight through significantly faster weight loss compared with the control group. The authors postulated that the lack of improvement in bone mineral density was due to the low level of patient adherence to the fitness program and recommended that future studies find methods to increase patient participation.

Expert commentary

The complementary therapies are of great value for decreasing leukemia-related symptoms and these therapies are safe to use concurrent to cancer treatment. Complementary therapies have been investigated regarding symptom control; however, we do not always have optimal dosing determined for these therapies. For example, is it better to administer acupuncture on a weekly basis for chemotherapy-induced peripheral neuropathy, or will twice-weekly treatments be more effective? How many sessions are required before we determine the intervention as effective or ineffective? Is there a difference between specific meditation techniques versus self-hypnosis in pain management? Are all physical fitness interventions equal for decreasing cancer-related symptoms? How many minutes should a person exercise at one setting in order to derive the maximum benefit from the intervention? Are three 60-min sessions weekly the same regarding symptom management as six 30-min sessions? Do we need to cycle our physical exercise with small bursts of physical activity alternating with periods of rest, or can we exercise continuously and derive the same benefits from, for example, immune system enhancement and increased natural killer cell activity? These areas will be addressed in future research to further refine our recommendations to patients and the general population.

What is confused by the general public and ignored by the nutritional supplement marketers is that there is a difference between primary cancer prevention and cancer treatment. While antioxidants are beneficial for protecting cells from oxidative damage and for primary cancer prevention, this does not necessarily translate into directly benefiting all cancer patients. The antioxidant fruit juice marketing for noni, gogi, açai and mangosteen, for example, imply that the antioxidants will protect only the healthy cells and not the cancer cells, which is not necessarily what occurs. There are no adequate human studies examining these claims for the fruit juices. The studies that have examined high doses of antioxidants in conjunction with chemotherapy or radiation therapy have either not shown benefit or have shown harm. In patients who are at increased risk for cancer, high dose antioxidants have also been demonstrated benefit, such as the β-carotene lung cancer prevention studies in male smokers, where the group receiving the β-carotene had an 18% increased incidence of lung cancer compared with the placebo group.

Regarding botanical supplements and cancer prevention and/or treatment, additional research is urgently needed to determine the efficacy and toxicity of these agents. The purity and consistency of these products is not guaranteed, unless the botanical source is grown and harvested through controlled conditions, which is not always the case. All research should incorporate stability testing and exert quality control to ensure that the product used has batch-to-batch standardization in order to replicate the research results in a clinical setting. Plant source verification is also important. The issue of bioavailability is a key component for all botanical research. Simply following serum levels of a botanical compound may also not be indicative of the mechanism of action or of the botanical's bioavailability, as the pharmacodynamics may depend on a mechanism other than serum transport.

The medicinal mushrooms hold great promise for immune modulation; however, their use must be closely monitored. It may not always be in a patients' best interest to broadly stimulate the immune system, especially for patients with leukemia. Altering one aspect of the immune system has a cascade effect, which can produce unexpected results. A botanical supplement may have very different immunomodulatory effects with different doses and serum concentrations, and the maximum tolerated dose may not necessarily provide the optimal desired effect [66].

Translating *in vitro* experimental results into animal models and human clinical results requires careful interpretation of the experimental data. Unlike pharmaceutical drugs, which consist of one chemical structure, the botanical extracts can contain hundreds if not thousands of chemical constituents. The botanical agents may have unpredictable clinical results based on factors not necessarily related to their proposed mechanism of action or chemical constituents. One such example is the EGCG and vitamin C inactivation of bortezomib; although the mechanism of action of bortezomib does not use an antioxidant mechanism, these two supplements do block bortezomib activity.

Five-year view

Over the next 5 years, research will continue regarding the importance of nutrition not only not only in cancer treatment, but also in primary and secondary cancer prevention. Public health safety issues, such as establishing adequate and optimal serum levels of various nutritional compounds, will be increasingly addressed. While ensuring nutritional adequacy is important, avoiding toxicity is also of paramount interest, especially with widespread food fortification. Folate supplementation is one such example, while supplementation has decreased neural tube defects, excessive inadvertent consumption of folate is possible through overeating fortified products. Avoiding the potential for overdose and subsequent adverse health outcomes is of vital importance.

Increased regulation of the marketing and advertising of nutritional supplements will also be important issues. Simply because a product is available over the counter without a prescription, does not ensure its safety for use in all persons. The adverse effects of high-dose multivitamin supplementation will probably be increasingly encountered, as the prevalence of multivitamin and multimineral use is very high. It is possible that an increase in the adverse effects of the antioxidant supplements will result in increased cancers and other chronic diseases.

The potential role of folate, calcium, vitamin D and other nutritional ingredients in cancer prevention and altering modifiable risk factors for decreasing cancer recurrence are gaining increasing attention from the scientific community, as well as the general public. The importance of lifestyle modification for increasing physical fitness and mind–body therapies for stress reduction will also be more widely emphasized in the next few years. As we have additional scientific data regarding the cost–effectiveness of regular physical fitness, mind–body, acupuncture and massage therapies, the healthcare system will probably expand

insurance coverage for these therapies. Self-hypnosis is increasingly covered through health insurance, as this intervention has been shown to be cost effective, as well as effective for decreasing patient symptoms. The opportunity for reimbursement for these services will increase patient access and improve care for patients with leukemia.

Key issues

- Complementary therapies provide symptom relief during the active leukemia treatment and improve quality of life for cancer patients.
- The so called ‘alternative’ therapies are not effective and have great potential to interfere with traditional cancer treatments.
- Achieving adequate nutritional intake through foods and not through the use of supplements is very important for decreasing side effects of treatment and improving overall survival for cancer patients.
- Routine physical fitness plays an important role in maintaining physical strength and decreasing side effects from the leukemia treatments.
- Maintaining healthy lifestyle habits through good nutrition and regular physical fitness can reverse many of the leukemia treatment-related side effects and can decrease the risk of cardiovascular complications from the leukemia treatments.
- Mind–body practices, acupuncture and massage are very beneficial for decreasing side effects of cancer treatments.
- Botanical and nutritional supplements have the potential to interfere with cancer treatments and are to be used only with the supervision of the oncologist.

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