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Review

A Review on the Chemical versus Alternative Treatments of Leukemia

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Abstract

Common treatments for leukemia, such as chemotherapy, have played a key role in the treatment of this life-threatening disease. However, they are associated with many side effects such as cardiovascular diseases, ocular diseases, lung toxicity, and endocrine dysfunction. The adverse effects of the common treatments are aggressive for elderly patients and patients who are unable to tolerate the treatments, resulting in their lower survival rate. Thus, more than ever before, leukemia patients are now turning to complementary and alternative treatments. The objective of this study was to review recent literature to compare common and traditional treatments based on efficacy and associated side effects. Chemotherapy and radiation therapy are associated with many side effects, as is stem cell transplantation, which often accompanies these two treatments. Not many studies have been done on alternative, traditional treatments; however, a small number of studies showed that traditional medicine are effective in vitro. Thus, more scientific studies and clinical trials are needed to be done on alternative treatments to find the efficacy, potency and safety of their associated medicines and procedures. As medicinal concepts of the alternative, traditional treatments usually differ from the common medical treatments-although they both have the same curative goal-greater research and communication between traditional medical researchers and practitioners in alternative therapeutic traditions may lead to new and effective medicine with fewer side effects.

Keywords: Leukemia; Alternative medicine; Traditional medicine; Herbal medicine; Pharmaceutical lead compounds

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Introduction

Leukemia is a type of blood cancer which is caused by the over proliferation of white blood cells, leading to many life threatening symptoms such as the suppression of red blood cells and platelets [1].

In the late 1800s it was found that the disease is linked to bone marrow, which led to the idea of blood-letting as a treatment. Some patients seemed recovered after blood-letting, even though it is unclear how long the patients survived [1]. In the 19th century, iron supplements were used as a treatment. Later, radioactive phosphorus was found to be effective for myeloid leukemia patients while not benefiting lymphatic leukemic patients. Leukemia was known as a fatal disease in the early1900s, as the 5-year relative survival rate for childhood leukemia was 50%. It was not until the mid-1970s, when chemotherapy along with stem cell transplantation was discovered, that the 5-year relative survival rate of children diagnosed with leukemia rose to 87%. However, the survival rate was seen to decrease as the age of the patient increased, which was due to the lower efficacy of the new therapies resulting from a lack of tolerance in the older patient to the more aggressive potential curative treatments. Age was not the only factor and, in addition, the type of leukemia was also a key factor in the survival rate of leukemia patients[2].

There are many different types of leukemia, depending on the type of the malignant white blood cell and on whether it is acute or chronic. The disease is acute when symptoms appear and condition progresses rapidly, which is usually seen in children. It is chronic, when the symptoms and disease develop over a number of years, this is seen in adults and older patients [3]. Also based on the type of leukocytes involved, the disease is divided into two subdivisions: Myeloid or Lymphoid. Thus, the four major types of leukemia are: Chronic lymphoid leukemia (CLL), chronic myeloid leukemia (CML), acute lymphoid leukemia (ALL), and acute myeloid leukemia (AML) [1]. ALL and AML have bad prognosis. This is because they are caused by young immature white blood cells, lymphoblasts and myeloblasts. CLL and CML have better prognosis as they are caused by myelocytes and lymphocytes, and mature white blood cells that are capable of some function [4]. The malignant immature white blood cells are functionless and occupy bone marrow space, thus preventing normal growth of erythrocytes causing anemia; a decrease in normal leukocytes resulting in susceptibility to infections [4]. Therefore, common symptoms of this disease include swelling of the liver and spleen, bone pain, frequent nose bleeding, fatigue and weakness, petechiae, and frequent infections due to low immunity [5]. Leukemia is found to be associated with many genetic and environmental predispositions, such as viral infections, chemicals and drugs, hormonal imbalances, inappropriate diet, and ionizing radiation [6].

Today, we rely on chemotherapy, radiation therapy, targeted therapy, and stem cell transplantation to treat Leukemia. These treatments are usually associated with many potential side effects. Thus, Leukemia patients

are increasingly turning to complementary treatments, commonly known as complementary and alternative medicine (CAM), to reduce the side effects caused by the potential curative treatments and also to reduce the symptoms caused by the disease. Some patients also use CAM as a curative treatment, while influenced by the pseudoscience from different sources such as the internet, news-papers, and different lectures. A survey in Italy showed that seventy-three CLL patients (16.5%) were using CAM [7]. Also out of 247 CLL patients in Germany, 44% were using complementary therapies [8]. Moreover, out of 533 leukemia patients, 56% used complementary therapies in northern India [9].

The objective of this study was to review recent literature to compare the common and alternative treatments with each other, based on their efficacy and associated side effects.

1. Conventional treatments

1.1. Chemotherapy

Chemotherapy is the most common treatment for leukemia. In a standard treatment, patients are treated in three different phases: remission induction, consolidation and intensification, and maintenance. Remission induction is the first phase where the leukemia cells are killed in the bone marrow, leading to a reduction of their malignancy. Second, consolidation and intensification therapy is applied. This phase will kill any remainder leukemia cells, however, it may lead to retrogression of the disease. The last phase is maintenance, which prevents retrogression of the disease, and kills any cells that might grow into leukemia cells. In this phase the dose of the chemotherapy drug is lower than the first and second phases, however it is important as the disease might relapse [5]. The chemical drugs in chemotherapy result in the destruction of rapidly growing cells, in order to kill leukemia cells. Thus, the most common side effects of chemotherapy are: hair loss and gastric symptoms, such poor appetite, nausea and vomiting, ulceration of anus, diarrhea and impaired mobility. These side effects usually last for one to three weeks [10].

Tyrosine kinase inhibitors (TKI) are common chemotherapy drugs, as the over activation of tyrosine kinase leads to malignancy. Imatinib (Gleevec®), Dasatinib (Sprycel®) and Nilotinib (Tasigna®) are the most common TKI for the treatment of CML patients.

CML is mostly seen in adults, however, 2% of cases are diagnosed in children. The discovery of TKI led to an increase in the 5-year survival rate for adults with CML, from 30.6% during 1990 to 58.6% for those diagnosed in 2009 [2]. In addition, the use of tyrosine kinase inhibitors, such as Imatinib (Gleevec®) doubled the survival rate for children with CML, from 31% in the early 1990s, to 63% in 2011 [2]. However, studies show that 70% of CML patients treated with Imatinib (Gleevec®) develop ocular diseases such as optic edema [11]. In addition, TKI are highly involved in cellular homeostasis. Thus, some other potential side effects include congestive heart failure, reduced ejection fraction, acute coronary syndromes, and myocardial infarction; however, these side

effects have a very low chance of occurring (0.45%- 5%) and the exact causal relationship of TKI remained unclear [12,13].

Dasatinib (Sprycel®) induces hair and eyelash depigmentation [14], but more importantly lung toxicity and pulmonary hypertension [15]. A long term study showed that pulmonary hypertension increases over time after induced by dasatinib in 37% of CML patients [16]. Nilotinib (Tasigna®), another common chemotherapy drug which is used for CML patients caused cardiovascular complications, such as the prolongation of the QT interval in 20% CML patients [17,18]. Although chemotherapy drugs are associated with the development of many cardiac diseases, studies have shown that cardiac protective drugs such dexrazoxane will reduce the risk of cardiac diseases in leukemia patients [19].

Fludarabine, cyclophosphamide, and rituximab (FCR) are commonly used in CLL and ALL patients. CLL is the most common type of leukemia in adults, although treatment is not likely to cure CLL and it is not clear whether such treatment increases the survival rate. Thus, treatment is only given to patients who are symptomatic or have complications such as cytopenia. The 5-year relative survival rate for CLL patients is 79.2%; however, there is a large variation in survival among individual patients, ranging from a few months to a normal life expectancy [2].

ALL is the most common type of leukemia diagnosed in children. More than 95% of children and about 80% of adults with ALL attain remission. Survival rates for patients with ALL have increased significantly amongst children due to the discovery of TKL; the 5-year relative survival rate for children increased from 57.2% in the mid-1970s to 91.7% in 2009 [2]. Survival rate declines as age increases; the 5-year survival rate is 41.8% for patients aged 20 to 39 years, 28.2% for 40 to 64 years, and 11.8% for 65 years and older [3].

One of the most serious potential long-term side effects of ALL therapy in children is the development of AML, which occurs in approximately 5% of patients who receive Cyclophosphamide [2]. Cyclophosphamide was found to develop systolic dysfunction and pericarditis in 7%–22% of the patients that is thought to be dose related [12,20]. In addition, studies show that FCR will also result in long term immunosuppression, especially for elderly and less fit patients. The combination of bendamustine and rituximb (BR) is used for older patients who cannot tolerate FCR, as BR results were associated with a lower infection rate and neutropenia [21]. Moreover, studies show that chemotherapy drugs are associated with long-term consequences on the motor performance and physical fitness of childhood leukemia survivors [22].

1.2. Targeted therapy

Unlike chemotherapy, targeted therapy allows the drugs to interact with specific molecules involved in cell proliferation. Thus it reduces the damage to healthy cells and minimizes side effects. Targeted therapy is used for CLL patients. The discovery of targeted therapy led to a significant 76% decline in the death rate in childhood leukemia from 1970 to 2012, despite

the increase in the incidence of the disease. For example, the 5-year survival rate for childhood ALL increased from 41% during the mid-1970s to 70% in 2011 [2].

Alemtuzumab (Campath®) and rituximab (Rituxan®) are two common drugs used in targeted therapy. Targeted therapy minimizes side effects significantly, however, it is associated with treatable adverse events. 10% of patients treated with rituximab were infected with hepatitis B virus and cytomegalovirus [23]. The drugs used in targeted therapy are used as single-agents or in different combinations, although it is unclear which one is more effective [24].

1.3. Radiation therapy

Radiation therapy is also used to kill malignant cells or stop the growth of cancer cells, prior to stem cell transplantation. The therapy includes two types of radiation: external radiation therapy in which the radiation is sent from a machine outside the patient's body to the leukemia cells; internal radiation therapy in which the radioactive substance is injected near or inside leukemia cells. It is sometimes used for bone damage caused by leukemia as the bones become swollen due to the over production of marrow and also used to reduce the discomfort from an enlarged spleen or liver [5].

The adverse effects of radiation therapy are lower than chemotherapy, however, studies show that the former therapy may result in coronary artery diseases, fibrotic changes to the valves pericardium and myocardium in older patients [25]. In addition, a long term study showed that 50-80% of ALL children treated with radiation therapy developed cognitive and endocrine dysfunction, such as the deficiency of the growth hormone and hypothyroidism [26].

1.4. Stem cell transplantation

Allogeneic bone marrow transplantation is recommended for those who develop recurrence after remission. It may also be used if the leukemia does not go into remission after successive courses of induction chemotherapy [2]. After a high dose of chemotherapy, stem cells of a donor are infused into the patient's bone marrow. Stem cell transplantation (or myeloablative transplantation), stimulates bone marrow growth, helping patients rebuild their immune system [5]. Stem cell transplantation resulted in a 5 year survival rate of 70% amongst CML patients [27]. Graft-versus-host disease (GVHD) is caused in allogeneic bone marrow transplantation; when the graft marrow immunologically recognizes the patient's body as foreign, and attacks it [28]. Statistics show that the leading cause of premature death in leukemia patients after stem cell transplantation was the recurrent of the disease (29%), followed by chronic GVHD (22%). The death rate among 15-years survivors was twice as high as that of the general population. In addition, nonrelapse-related death was increased in 18 years and older patients and also among those who developed GVHD [29]. The patients treated with stem cell transplantation have a 30% less life expectancy as it is seen that amongst these patients the incidence of breast cancer is 5% at 20 years; renal complications are also frequent,

23% at 2.5 years; also pulmonary and cardiac complications occur later and after 20 years of follow-up, the incidence rate was 22% [30].

As stem cell transplantation was associated with many risk factors, non-myeloablative transplantation, commonly known as mini-transplantation, is considered an alternative. Mini transplantation is given after the patient undergoes a low dose of chemotherapy. Thus the patient's hematopoietic system is damaged but not destroyed. After mini transplantation, the immune cells from the graft and the host form a chimeric immune system, resulting in the recognition of the malignant cells by the "new" immune system. Mini-transplantation is usually used for older patients as it is associated with lower side effects, due to low chemotherapy doses. However, mini-transplantation is also associated with many risk factors, such as invasive aspergillosis (10%), while GVHD was significantly associated with invasive aspergillosis (27% vs 3%). Lastly, there was no significant decrease observed in the chances of developing GVHD in comparison to standard transplantation [31].

Stem cell transplantation can also be an autograft, where patient's very own stem cells are collected before chemotherapy. The amount of GVHD is significantly lower (8%) [32].

1.5. Immunotherapy: AlloStim®

Recently, researchers are trying to come up with new methods that stimulate the immune system of the patient to overcome the malignant white blood cells. This treatment is called immunotherapy. AlloStim® is an immunotherapy drug which is currently under phase 1 and 2 clinical investigation. The healthy immune cells of a patient are taken out of the body and differentiated into hyper stimulated immune cells. Unlike common treatments, the patients are not treated with chemotherapy [33]. Instead they are injected with AlloStim that secretes Th1 cytokines and "awakens" the host immune system, leading to the process of Th2 to Th1 cytokine shift [34], in which the host immune system destroys the malignant cells. Thus, it is thought to have the same anti-tumor mechanism as allogeneic stem cell transplantation as it reactivates the immune system. In addition, AlloStim can be used as an alternative to stem cell transplantation as it does not require HLA match of a donor and there is no chance of GVHD toxicity [33].

Chemo-immunotherapy is when a patient receives immunotherapy as well as chemotherapy drugs. This treatment is only suitable for patients with specific favorable features, for example patients with a low-risk for IGHV-mutated disease were benefited. Although chemo-immunotherapy is effective for some patients, many questions are yet to be answered. Some of the major questions are the effect of the length of therapy, and how to avoid or overcome resistance to drugs [24].

1.6. Chimeric antigen receptor T-cell therapy

Chimeric antigen receptor T-cell (CAR-T) therapy is also a type of immunotherapy which became popular as it saved a seven year old girl from the recurrence of ALL. In this treatment, the T-cells of the patients are extracted from

their blood, then engineered to kill tumor cells, and lastly injected into the patient's blood [35]. However, CAR-T therapy is also a harsh treatment as it is associated with many life threatening side effects such as very intense fevers, dangerously low blood pressure, cytokine release syndrome, neurotoxicity which can lead to confusion, seizures, and severe headaches. It also might result in serious infections, a weak immune system and low blood cell counts [36]. The seven year old girl treated with CAR-T therapy surprisingly survived from all the severe side effects, while the doctors had lost hope, as she had a fever of 105 °F, a swelled face, and also hardly breathing as fluid folded her lungs. She was then put on a ventilator and also coma was induced to prevent death. The result, a cancer free child. However, she still has long term side effects such as occasional sinus infections as CAR-T cell therapy destroyed her healthy B-cells along with the tumor cells. Thus, she is now dependant on B-cell replacement which is infused every other week [35].

Immunotherapy has been a recent area of research, however, there are many complicated problems such as finding a leukemia specific target antigen, and also the high expenses of this treatment. Thus, the treatment may work for some patients while not for others. However, there is hope individualized immunotherapy can be achieved for each patient based on risk factors and biomarkers. Researchers think that in a few years, immunotherapy will replace the high mortality associated treatments such as stem cell transplantation [37]

2. Traditional medicine

The conceptual understanding of physiology in traditional medicine differs from that of modern medicine. Here we will look at the three most common traditional medicines practiced in the world today.

2.1. Traditional Islamic/Persian medicine

Traditional Persian medicine, which originated from ancient Iranian, Greek, Chinese, and Indian medicines, has treated diseases for more than 12 centuries. Physicians such as Avicenna have contributed valuable services to the scientific world in general and medicine in particular [38]. This ancient medicine treats patients from an individualist perspective; according to one's body temperament and humor. There are four types of body humors: Sanguinous- or blood (Arabic: *Dam*), bilious- or yellow bile (Arabic: *Safra*), phlegmatic– or phlegm (Arabic: *Balgham*), and melancholic- or black bile (Arabic: *Sauda*) [39]. The humor of a human being changes with many factors such as season, weather, age, and environmental conditions [40].

This system of medicine held that the universe is based on four elements Earth, Fire, Air, and Water, each of them having its own nature, features and potentials. The traditional Persian scholars believed that a human being is a smaller version (microcosm) of the universe (macrocosm or *cosmos*) and that his humors are guided by the nature of these elements as per the following (Table 1).

Table 1. The four temperaments of the body, their nature and major functions.

Humor	**Dam (Blood)**	**Safra (Yellow bile)**	**Balgham (Phlegm)**	**Sauda (Black bile)**
Nature	Warm and wet Like air	Warm and dry Like fire	Cold and wet Like water	Cold and dry Like soil

The conceptual framework of traditional Persian medicine is completely different from that of modern medicine. For example, traditional Persian medical practitioners believe that a proper balance between the humors is positively correlated with one's physiological health such as their efficient metabolism. In addition, the human being is safe from diseases and the building up of toxins, as all body organs perform perfectly. However, they also believe that the fifth factor is the soul. The soul can change and balance any condition [39].

Avicenna believed that leukemia is a result of the swelling of the black bile, when the yellow bile is burnt! Thus, medicine used for cancer treatment should be able to dissolve the carcinogen, and excrete the dissolved carcinogen. These drugs should not be strong or irritant because strong drugs increase the cancer's malignancy [38].

In order to discover the traditional medicines used today, I have travelled to the Islamic Republic of Iran on May 2017. By exploring the Attari (traditional medicine store) and interviewing a few students of traditional practitioners such as Dr. Ravazadeh, Dr. Ziyayi, and Shaikh Tabriziyan's students. I found out that traditional practitioners prescribe different prescriptions for leukemia patients. Some of the common compounds prescribed are Calendula flowers, *Turnips, ginger* (extract), ginger infused honey, *Senna* plant and *Convolvulus scammonia*. Some compounds such as *Myrobalan, Balila, Indian Gooseberries*, and Bdellium are prescribed for blood purifying functions. These compounds are extracted through different procedures. Some compounds are made with different ratios of different natural products. The dose prescribed also differs according to different factors, such as the patient's health history, diet, temperament, season and many more.

Figure 1. The Attari (traditional medicine store) in Qum, Iran. Various herbs are found in these stores, such as *Indian Gooseberries, Myrobalan,* and many other uncommon herbs.

To find out if these traditional medicines have any scientific evidence behind them, I have searched for peer reviewed articles to find any studies done on these medicines.

A study done in humans and mice showed that *Calendula* extract inhibits tumor cell proliferation 70-100%, by acting on the cell cycle at the G0/G1 phase [41]. Another study showed that the exposure of leukemia cells to *ginger* galanals resulted in their apoptosis, as caspase-3 was activated and induced DNA fragmentation [42]. Furthermore, *Senna* plant extract also induced leukemic cell apoptosis by activating intracellular calcium and caspase-3, decreasing mitochondrial membrane potential, and inhibiting the cell cycle in S and G2 phases [43]. *Indian Gooseberries* were also effective against leukemia cells *in vivo* [44]. Also studies show that Myrobalan does have anti-cancerous activities and purifies the blood [45].

However, there are no clinical trials done on these medicines. Also, the medicines are not scientifically approved and their pharmacodynamics and pharmacokinetics remains unknown. In addition, they might interfere with other medicines as their mechanisms are unknown.

Traditional Persian medicine does not just focus on edible treatments. Other than edible treatments, it also focuses on psychological and

spiritual treatments, which they call food for thought. In addition, they believe other than *food for thought* and edible treatments, one must have auditory foods, visual foods, olfactory foods, somatosensory foods, sexual foods, and social relationships as food. According to them this is the only way to balance one's temperament, ensuring their health and well-being. Thus other than edible treatments for leukemia, they also prescribe many spiritual, psychological and physical practices [46].

2.2. Traditional Chinese medicine

Traditional Chinese medicine is known to have treated people for over 3000 years. The common treatments they use are herbal medicine, massage therapy, dietary therapies, and acupuncture. A study done in 466 AML patients showed that they had a lower risk of mortality when treated with Chinese herbal medicine [47]. Also, a study done in 616 ALL patients showed a higher survival rate when modern treatments were integrated with traditional Chinese treatments such as acupuncture, moxibustion, Chinese orthopedics and traumatology, and Chinese herbs, as the mortality rate was less than half compared to the control group [48]. However, acupressure and acupuncture can be dangerous for pediatrics as it may lead to bleeding or infection [49].

Some common Chinese traditional herbs are *Realgar*, *Indigo, red sage root, and Hedyotis* diffusa.

Studies show that *Hedyotis diffusa* inhibits the G0/G1 phase of leukemia cells by affecting on the caspase cascade signaling and altering gene expression [50]. A herbal Chinese formulae of *Realgar, Indigo and Hedyotis* was also found to be effective, as the arsenic in Realgar directly attacked the receptor on co-protein in leukaemia cells, Indirubin in *Indigo* antagonized the toxicity of arsenic and slowed the malignant cell growth while Tanshinone in *red sage root* restored pathways that inhibited the spreading of leukemia cells [51].

Many people in China and around the globe use traditional Chinese medicine, and research has increased recently in this field. However, there is still little evidence on the effectiveness of therapies such as acupuncture. In addition, there is little to no clinical trials done.

2.3. Traditional Indian medicine

Ayurveda is a traditional Indian medicine which has been practiced for thousands of years. The therapy is based on three "Doshas" of the body, Vata, Pitta and Kapha, which represent the nervous system, the metabolic system and the nutritive system, respectfully. These three "Doshas" are known to keep the body in balance, and diseases are a result of a disturbed balance. Thus, the aim of this traditional treatment is to restore the original health and equilibrium of the body [52].

A twelve-year follow-up study showed that traditional Indian medicines, such as Ayurvedic, are effective in the treatment of AML, while not associated with any side effects. Ayurvedic therapy resulted in remission of patients who did not undergo modern treatments after their second relapse of the disease. However, the practitioners in Indian traditional medicine

stated that proper clinical trials are needed to validate their observations [53]. In addition, a 12-year old leukemia patient treated with chemotherapy for six months had a relapse in the disease. Thus, he started Ayurvedic therapy and has completed 12 years of disease free survival [54].

Recently, there have been many studies done on different Ayurvedic herbs, and it was found that many of them such as *herbomineral Navjeevan Ras, Kamdudha Ras, Keharuba Pisti, and Somal* are very effective in the treatment of leukemia [55]. However, there is still a lack of data for clinical trials and scientific based evidence.

3. Complementary and Alternative treatments

The aggressive and complex treatments of leukemia result in a need for complementary therapies. These include nutrition, nutritional supplements, exercise, cardiac rhythm, massage therapy, and acupuncture [56]. Although these treatments are commonly used as a complement, a few cases have been reported in which they have helped in treating the disease after all hope being lost from common treatments.

3.1. Natural compounds

A patient diagnosed with leukemia was treated with chemotherapy, radiation therapy, TKI and standard transplantation. After 34 months with no progress, she was treated with *Cannabis* extract on a dose dependant therapy. *Cannabis* reduced the toxic effects of chemotherapy agents and controlled the proliferation of leukemia cells. In addition, Cannabis had no side effects except for psychosomatic complications, however non-psychoactive cannabinoids such as cannabidiol can be used instead [57].

Agaricus blazei extracts showed inhibitory activity against human leukemia as it induced apoptosis of the malignant cells in vitro and in vivo. However, polysaccharides in *Agaricus blazei* may not possess direct anti-leukemic activity in vitro [58].

Triticum aestivum, commonly known as wheat grass also has been proven to have anti-leukemic activities which might be due to flavonoids and polyphenolics. The study was done in vivo on Wister rats and also tested for the effective dose, which was found to be 2000mg per 1kg of body weight [59].

There are many natural compounds that are associated with the inhibition of the malignant cell's life cycle and apoptosis. However, the exact bioactive substance and mechanism of action are unknown. Thus, further studies should be done to improve the significance of the previous findings [59]. In addition, more clinical trials should be done to improve the significance of the therapy.

3.2. Mind-body therapies

A study done on 40 leukemia patients showed that there was a significant positive correlation between spiritual well-being and a fighting spirit with the patient's quality of life. In contrast, it was negatively correlated with hopelessness [60]. In addition, a study showed that out of 85 patients, 29% patients with a higher spiritual absence passed away 1-year after receiving stem cell transplantation [61]. Thus, the functional psychological adjustments (psychosomatic)

also plays a key role in complementing the treatments.

Discussion and Conclusion

The treatment of leukemia has changed and improved greatly over time. We can now cure many types of leukemia in the younger populations. Common therapies such as chemotherapy, radiation therapy, and stem cell transplantation have played a key role in the treatment of leukemia, increasing the survival rate in many different types of leukemia. However, these treatments accompany with many aggressive adverse events, making it intolerable for older/weaker patients. In addition, the long term side effects in children are also considered a disadvantage. Other treatments such as immunotherapy are not systematically effective, as they do not work for all leukemia patients, and are still under study.

There is none to very few clinical trials done for traditional treatments. A study showed that about 60% of leukemia patients in northern India use complementary or alternative treatments, while only 3% inform their doctor about it [3]. This can be dangerous as the drugs might interfere with each other and cause more harm than good. For example, the increasing popularity of alternative medicine in the Western world led to a CLL patient using the treatment, who later developed severe hyponatremia. The case illustrates a need for better education and control of alternative medicines [62].

Traditional practitioners claim that they are able to treat leukemia with herbal treatment along with many other psychological and physical treatments, with less or no side effects while only boosting one's immune system and overcoming the deficiencies of the patient's body. Although some of the herbs used in the alternative treatments have been tested and proven to be effective in vitro, many more studies should be done to find the pharmacodynamics and pharmacokinetics of the drug, such as its potency, efficacy, associated side effects, and potential interference with other drugs. Assuring the safety and potential associated risks of alternative medicine may lead to new medicines with less side effects, especially for the elderly population and patients who cannot tolerate the common treatments.

Complementary interventions to the conventional treatments such as herbal therapies, enhancement of diet, and physical treatments such as yoga and massage therapy, have proven to play a critical role in one's survival. However, most of the data collected for these treatments are from clinical trials and more research should be done in order to investigate molecular evidence. In addition, some complementary interventions such as patient care, are not physical but rather psychological, and spiritual in focus. Thus the physician in charge of giving the treatment to the patient should be aware of the other care options and not just focus on solely the physical treatment.

While the conceptual framework of traditional medicine is different from that of modern medicine, they both have the same curative goals [63]. One difference is that traditional medicine looks at the patient from a holistic point of view, while in modern medicine the treatment

is determined by giving attention to physical particularities such as the type of leukemia and to chemical therapies such as chemotherapy and targeted therapy. In contrast, alternative treatments are not based on the recognition of the different types of leukemia.

With more research and communication between traditional medical researchers and practitioners in alternative therapeutic traditions, we will hopefully one day arrive at better treatments, or even a cure for leukemia.

Conflict of interest

None.

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